Copper Toxicity Syndrome

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It was noted in a general practice that when Hair Mineral analysis was performed a significant number showed increased copper levels. Very little reference to this problem could be gleaned from the medical literature. In time it was noted that similar symptoms were described in a number of individuals with raised hair copper. These were symptoms of the affective disorders — with individuals showing degrees of anxiety, depression and sleep disorders as well as other problems. Serum and urine assessment for raised copper rarely showed abnormal levels. Chelation therapy using D-Penicillamine would on occasion elicit a prompt reduction of symptoms. Twenty four hour urine output of copper during chelation therapy was generally proportional to the level of copper in hair analysis. Since significantly raised hair copper levels are rare in most other geographical areas, it is postulated that there are high levels of copper in domestic water supplies of the area (Vancouver, B.C.).

In recent years many of the public and some medical practitioners have become very aware of the influence of dietary constituents on health. Studies on the constituents of the diet and their effect on human metabobolism have accelerated beyond the knowledge of the average practitioner. The environmental influences on health change rapidly. With the advent of highly accurate spectrographic analysis equipment, assessment of the mineral content of human tissues has in the last few years become a useful diagnostic parameter. Hair analysis has not yet been accepted as an accurate diagnostic tool by the medical establishment but is being widely used by many nutrition and prevention oriented health practitioners in North America, and will inevitably become part of the average medical assessment when nutrition is accepted as a significant part of medicine (Laker, 1982; Katz, 1980; Marlowe, 1983; Bland, 1980).

Mineral analysis through hair sampling is generally accepted as being a useful tool to screen for heavy metal poisoning for such minerals as aluminum, arsenic, cadmium, lead, mercury and perhaps nickel. It is also considered a useful method for assessment of tissue zinc levels. Copper levels have not been considered much in the medical literature (Passwater, 1983). There has been some concern regarding deficient levels of

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copper in the diet (Klevay, 1979). It is considered generally harmless in the environment. Toxicology texts do not mention copper toxicity except in respect of obvious acute industrial poisoning.

There is a literature on the serum levels of copper. Orthomolecular physicians will be very aware that serum copper levels can be raised in specific types of schizophrenia, especially histapenic schizophrenia, but there is little mention of hair or tissue levels in these cases (Pfeiffer, 1975). Serum copper is closely tied to the protein "ceruloplasmin", and factors governing ceruloplasmin levels will generally affect serum copper levels proportionately. Ceruloplasmin can be significantly raised due to accelerated synthesis in pregnancy or in those taking contraceptive pills or estrogens (Pfeiffer, 1975; Vir, 1981) and in some cases of carcinoma or lymphoma (Capel, 1982; Schwartz, 1975).

Little mention has been made of the effect copper may have on the general population. In areas where copper levels in the water are high, a significant percentage of the population may be suffering due to the interference of a heavy tissue load of copper in their metabolism, without however, showing symptoms of psychosis (Pfeiffer, 1977).

Using hair mineral analysis as a screening tool, it has been noted in our practice that a large proportion (over 50 percent) of those screened had varying degrees of significantly increased copper levels, above 40 mcg/g or 40 ppm *(Eatough, 1973). It was determined from contacting various analytical laboratories undertaking hair assays that this was not usually a significant problem in their geographical areas.

This immediate concern of the trained medical professional when confronted by evidence of raised tissue copper levels is to attempt to make a diagnosis of Wilson's Disease. This disease, otherwise known as hepato lenticular degeneration is a well recognized clinical entity with a familial tendency, characterized by incoordination, ataxia, progressive mental deterioration and post necrotic hepatic cirrhosis. Wilson's disease shows decreased serum copper and ceruloplasmin (below 20mg/100ml) and increased urinary excretion of copper (in excess of 100 mcg/24 hr). There may be evidence of liver damage, haemolysis and anaemia. Often corneal deposits of copper known as Kayser Fleischer rings are noted (Scheinberg, 1981; Burch, 1975).

In the cases in our practice, mentioned above with high hair/tissue copper, none were found to have any of the features indicating the rare presence of Wilson's disease.

It was noted that those individuals with high copper levels did suffer a symptom complex. This may be extremely disabling for some, or less severe for others. There is some suggestion of more severe symptoms if the hair copper level is higher, but not necessarily so. Some individuals with high hair copper have insignificant symptoms or claim excellent health. Others may feel in good health until it seems that a threshold of a particularly high level of copper is reached at which point they start having symptoms.

A survey of the symptoms was performed and it was found that similar features were often present. Serum and urine tests performed for levels of copper were found to be inconclusive, and generally within normal limits. However, using a D Penicillamine (trade names — Depen; Cuprimine; Dista-mine; Pendramine) challenge test, it was noted that an increased 24 hour urinary output of copper was elicited for individuals with higher hair copper levels whether they were symptomatic or not (table II). This did tend to indicate that at higher levels of hair (tissue) copper there was a correlation with urinary excretion, following oral chelation with D Penicillamine.

The symptoms relating to copper toxicity syndrome can often be described as an affective disorder of neurotic rather than psychotic nature. They can be the "bread and butter" of general practice, treated often with anxiolytics, anti-depressants, lithium or psychological counselling. The symptoms are related to the biochemical syndrome of histapenic schizophrenia, which is characterized by high serum and tissue copper levels and low serum histamine levels. The

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clinical features include rapid thought patterns, insomnia, depression, memory loss, but also psychotic symptoms of hallucinations, paranoia, and to a lesser extent, obsession - compulsion (Table 1).

However it should be pointed out that many patients with high tissue copper may have simple "neurotic" features rather than any full blown "psychotic" illness. Therefore even the physician with an interest in orthomolecular medicine may not consider it worth investigating for mineral imbalance. And indeed if serum analysis for copper is performed, it is likely to be normal. The symptoms may be continuous or intermittent. Often if intermittent they are related to the pre-menstrual period (at which time hormonal changes may alter the tissue balance of minerals). Historically the symptoms start at a certain point in time and persist steadily after this, gradually getting worse over the months. In a significant number of women, the symptoms initially occurred a few months after childbirth. It is well established that serum copper is greatly increased in the third trimester of pregnancy (Vir, 1981).

Management and treatment of those individuals found to have high hair (tissue) copper is considered as follows.

Many people will present with a multi-symptom complex often involving many of the features described above. They will probably have had most of the routine medical tests performed and will have been told that nothing physically is wrong, or they may be under various treatments for anxiety, depression, allergies, hormonal problems, hypoglycemia, but still have not had a particular reduction in symptoms.

Even though a seemingly thorough workup has previously been performed, a complete review of the history and test should be performed. Often evidence of vitamin or hormonal deficiencies may have been overlooked. Many women may have an associated premenstrual syndrome which may be treated with progesterone or estrogens (Dalton). Another problem which is commonly overlooked is Intestinal Candidiasis which can produce a chronic symptom complex — but can be easily reversed in some instances by treatment with Mycostatin or Ketoconazole (Nizoral) and acidophilus orally (Truss, 1978). We see many individuals who have masked food or environmental allergies. The bowel pathologies induced by the above problems may wreak havoc on the normal absorption of minerals.

When a hair analysis is returned showing a high copper level, levels of other essential metals such as zinc, calcium, magnesium, manganese, chromium, selenium, iron should be noted. (High levels of calcium or magnesium usually indicate **actual** low tissue levels). High copper levels can be associated with other raised toxics such as aluminum, cadmium, lead, and mercury, and are often

TABLE 1

Some significant clinical features of Copper Toxicity and an indication of degree of likelihood of occurrence in the average affected individual.

Fatigue - profound Mental.	++++	Headaches - severe.	+++
Physical.	++++	Cold extremities.	++++
Poor Memory.	+++	Hot flushes.	++
Lack of concentration.	+++	Dizzy Spells.	++
Inability to get to sleep.	+++	Muscle tremors.	+
Wakefulness, inability to stay asleep.	+++	Aching Joints.	+
Depression - severe.	++++	Heart palpitations.	++
- suicidal.	++	Ringing in ears.	+
Apprehension.	+++	Metallic taste in mouth.	+
Sensitive temperament with extreme over-reaction to events	+++	Excessive perspiration.	++

associated with low levels of essential minerals due to poor diet and malabsorption. It is possible that the presence of significantly high toxic metals in the hair may mask the true level of other heavy metals (such as copper) (Table II).

When copper toxicity (or tissue overload) is suspected in symptomatic individuals the level of body copper load can be estimated by measuring the amount of copper removed from the body through the urine in a 24 hour period, utilizing the oral chelation agent D Penicillamine (D-pen). This is given at a dose of 250 mg q6h (on an empty stomach). The 24 hour urine test should be taken on the third day of treatment (Walshe, 1981). From Table II it can be seen that copper hair / 24 hour urine, should correlate on the graph vector. This also clearly validates "hair mineral analysis" as an accurate monitor of the total body copper load.

Often a short course of D-pen will bring about a dramatic cessation of all symptoms in some very sick individuals. It may be necessary to continue treatment for some months. In other cases, short courses of D-pen given intermittently when symptoms start again may be all that is necessary to produce a complete remission of ill health. In other individuals there may be no reduction in symptoms unless the D-pen is given on a longer term basis, of up to three or four weeks. For those on long term therapy with D-pen, daily supplements of zinc gluconate 50mg, manganese 30mg, pyridoxine (B6) 200mg, vit. E 200 IU, vit. C l-2g and any other trace minerals which might be deficient should be given in divided doses 3-4 times a day. It is known that zinc especially is chelated out of the body by D-pen and therefore should not be taken within an hour or two of that drug. Pyridoxine requirement is also increased when D-pen is administered.

Those with mild elevation of tissue copper, and few symptoms, might be treated with supplements alone since treatment involving D-pen might involve unnecessary side effects and expense. Such supplements might include calcium 500mg, magnesium 250mg, zinc 50-100mg, manganese 30mg, vit. C 1-2 g and digestive enzymes if necessary. It has been suggested that bioflavinoids, one gram 3-4 times daily may be a powerful copper antagonist.

There are side effects which may arise from the use of penicillamine. Early side effects are less common and include nausea, anorexia, vomiting and rashes (Huskinson, 1981). Loss of taste is cited but this is undoubtedly due to loss of zinc through chelation.

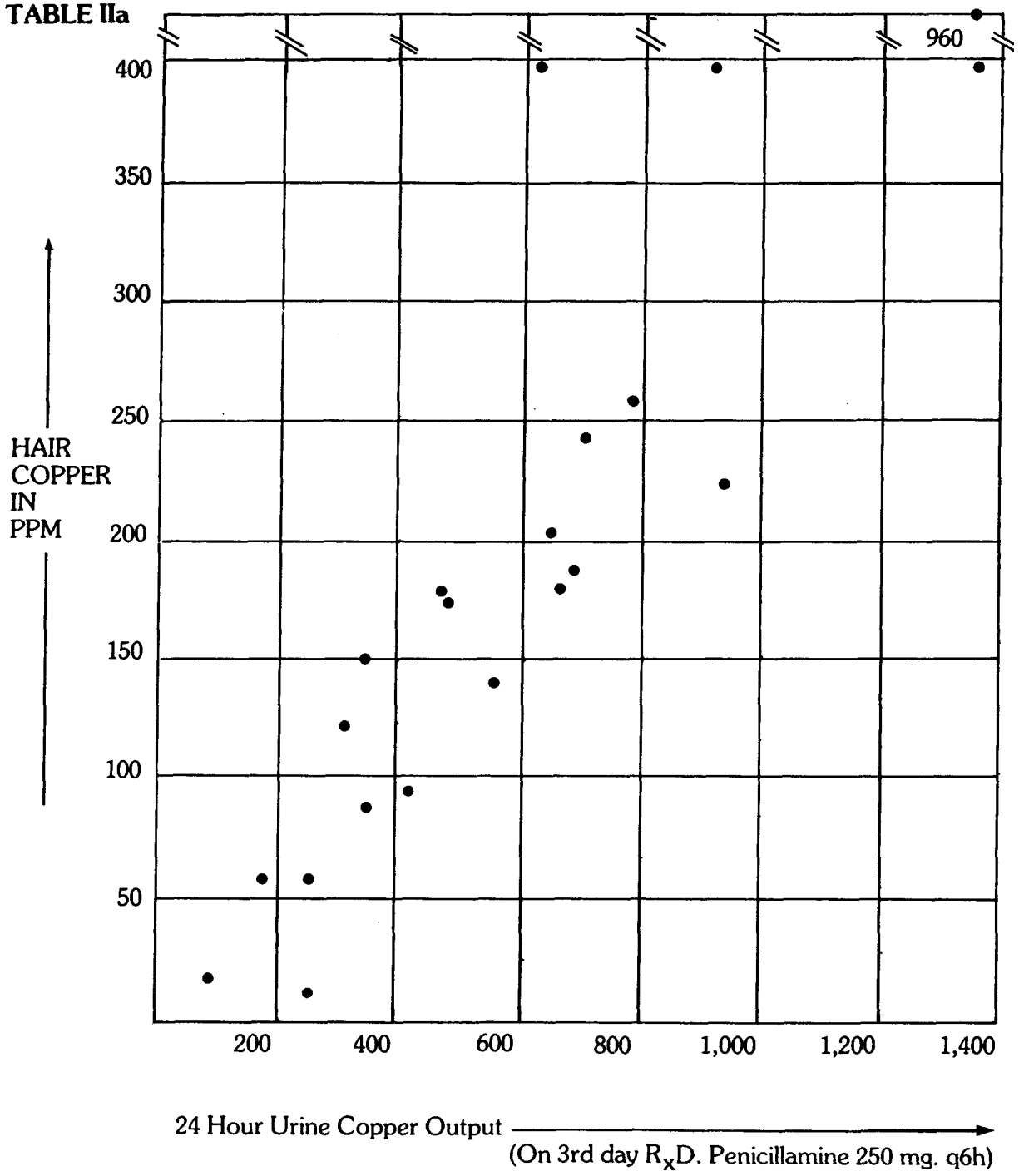
Other problems to be monitored include blood changes, especially thrombocytopenia, which is reversible. Leukopenia and aplastic anaemia are rare but more serious (Camp 1981). They have been mainly documented for rheumatoid arthritis patients and may therefore not occur in populations not affected by this condition (arthritis).

Various types of skin rash can occur after longer term therapy in arthritics, and one has been ascribed to zinc deficiency (Sternlieb et al., 1981).

Proteinuria has been described in up to 20 percent of arthritics on D-pen therapy (Crawhall, 1981). This is usually reversible on discontinuing the drug. Rare complications include acute nephritis, myasthenia gravis and systemic lupus. It should be pointed out that the side effects are documented in the main for treatment of rheumatoid arthritis. Side effects are far less when diseases such as Wilson's and cystinuria are being treated (Camp, 1981). It is possible that in rheumatoid arthritis excessive copper is being removed from the tissues, creating a mineral and possible vitamin imbalance which give rise to the side effects. It has been documented that D-pen induces autoimmune disease (Dawkins et al., 1981). Mechanisms may include destabilising the delicate balance between cellular immunity, humoral immunity and lymphocytes. This might be due to copper deficiency. It has been suggested by one authority that copper supplements should be given in concert with oral penicillamine so that the metabolic damage caused by the leaching of the tissue minerals would be reduced (Osterberg, 1980).

General monitoring of blood count, liver function, and renal function should be performed at monthly intervals to eliminate the possibility of serious side effects. The possibility of Wilson's disease will have been excluded initially by assessment of cerulo-plasmin level of more than 20mg/dl and a 24-hour urine copper output of less than

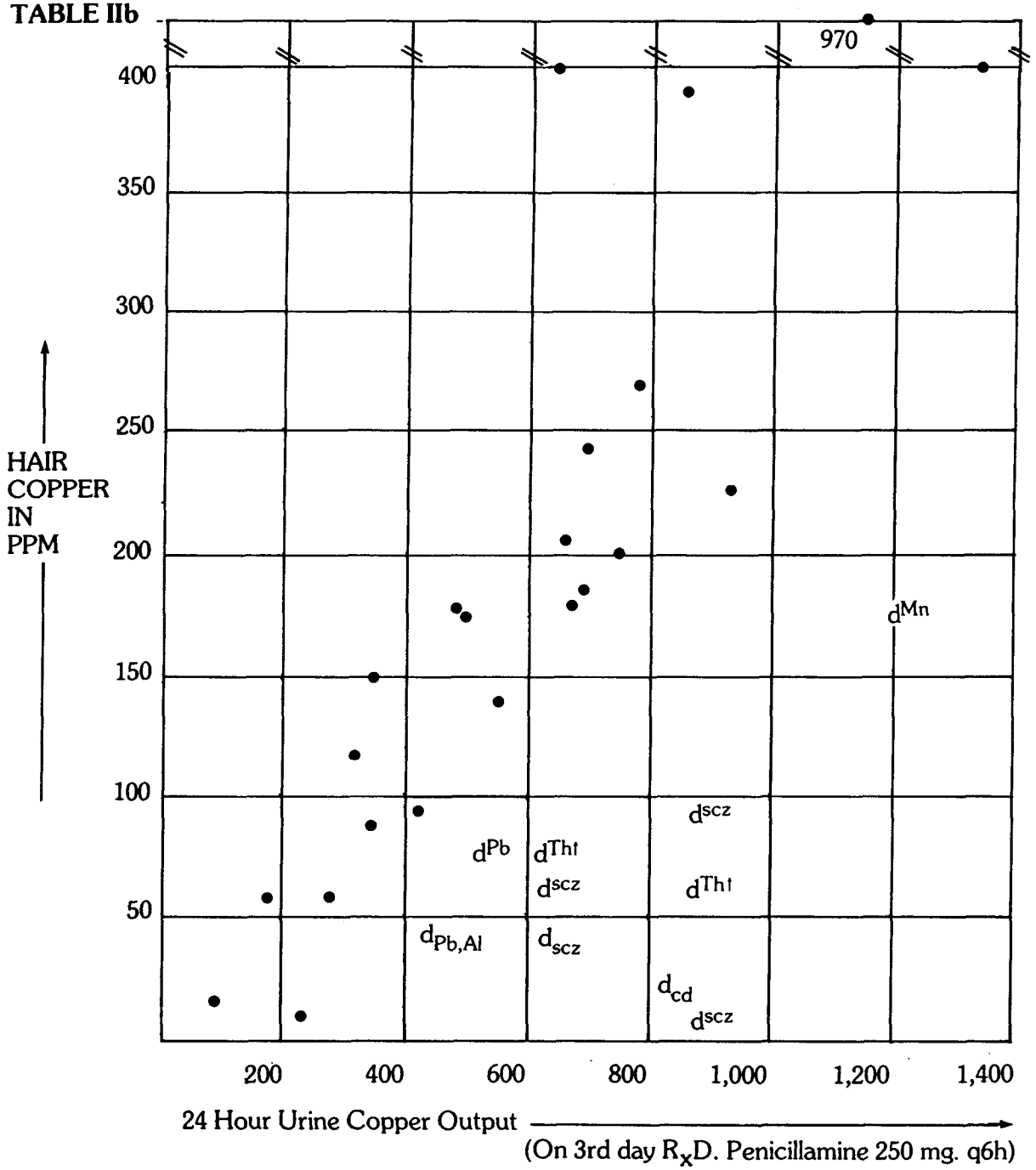
TABLE IIa



See Table IIb for additional amended levels

100mcg/24 hour. There will also be normal liver function and absence of the Kayser Fleischer ring in the cornea. Copper levels in the hair are not expected to be raised in Wilson's disease. Response to treatment may be assessed 1-3 monthly by monitoring the symptoms and repeating the hair mineral analysis and 24-hour urine copper output. Treatment intensity and dosage may be varied depending on the results of these tests.

TABLE IIb



Amended Levels:
SCZ - Schizophrenia
THt - Hyperthyroid
Pb
Al
Cd
Mn
} Toxic Levels in Hair

*Plotted from Table III Criteria

****d's (and Amendments) rather than full dots on the chart indicate individuals with additional diagnosed syndromes or toxic levels on hair analysis. It is assumed that metabolic disorders or additional toxic metals in the hair will reduce the level of copper in the hair tissue in proportion to the body tissue levels.**

Some Case Histories

Case 1. N.A., aged 40 with two children.

Past history — nil of note. Father manic depressive.

Complaints: One year of severe suicidal depression with continuous fatigue and insomnia. She had lost her powers of concentration, was frequently argumentative, had a poor appetite, had slightly cold extremities, aching muscles, palpitations on occasion and continuous headaches at the front of the head.

Investigations: Hair copper 240ppm (normal < 40ppm) repeated 189, serum copper 78, regular 24-hour urine copper 88, 24-hour copper after chelation 704, ceruloplasmin 20, LFT and CBC normal.

Treatment: Vitamin therapy had not shown efficacy. Family counselling produced some slight improvement in relationships, but in retrospect the patient said it had not been that helpful. On treatment with penicillamine 250mg q6h on an empty stomach the patient noted an improvement within the first day. She felt less tired, less nauseated and slept fully for the first time and felt like eating. She could get through her working day without fatigue. She said that previously she had literally felt like dying each day.

After one month of therapy she continued to take D pen bid, and if she did not do so, she felt sick, depressed, could not sleep well and wept. After six months she continues to feel well, is functioning much better. She takes D pen bid. However her copper body load remains the same at 690 meg/ 24 hour urine.

Case 2. P.L., Female, aged 38 with two children.

In the past she had been diagnosed as a psychotic with a number of short stay admissions to psychiatric wards for being out of touch with reality.

Family. One child abnormally hyperactive on occasion.

History. One year feeling intermittently profoundly depressed and lacking energy. On occasion especially pre menstrually she would develop a tingling or tight feeling in the head associated with a metallic taste and queasy stomach. She would soon after become very emotionally charged to the extent of mania. She would also suffer insomnia at these times.

Investigations: Hair copper 59, serum 94 and 120, 24-hour urine copper after chelation 413, CBC LFT normal.

Treatment: Megavitamins, niacin, pyri-doxine, zinc and manganese reduced the symptoms slightly. Intravenous pyridoxine 200-400mg would reduce the symptoms dramatically. Oral B6 in high doses would reduce symptoms significantly for a few hours. It would seem that she must suffer from Pyrrolurea. D penicillamine therapy caused complete cessation of all her symptoms within one day. She now finds that if she takes 2-3 D pen caps once a month when the prodromal symptoms of her problem arise, she never develops any disability and has been virtually symptom free ever since.

It is of interest that her daughter, age 8, becomes extremely overactive at times. Her mother states that when she gives her daughter 1-2 caps of D-pen on these occasions, immediately normal behavior will be resumed.

Case 3. H.E., female, aged 29, no children.

Past History: Petit Mal since youth. Mother has asthma and arthritis.

Symptoms: For as long as she could remember she had been very fatigued physically and mentally. She had petit mal blanks briefly 2-3 times a day. She suffered cold extremities, aching hands and knees, insomnia, frequent periods of apprehension and premenstrual tension with severe menstrual cramps. She was allergic to coffee.

Investigations: Hair copper 265, serum copper 116, 24-hour urine copper after D-pen 790, LFT and CBC were normal. Treatment with D-pen produced a reduction in her symptoms within a week. She was less tired, depressed, irritable or cold. She continues however to suffer petit mal to the same extent and has the same painful menstrual cramps, but she states she feels much better and in control.

Case 4. W.C., aged 36, single female. No children. She had a healthy past history. Her brother is schizophrenic and her mother suffered chronic depression, insomnia and anxiety.

She was well until 18 months previously except for some problem with insomnia. She

then developed a persistent pain in the left shoulder and upper arm. After six months the pain had spread to both shoulders. This was preventing her performing her work duties efficiently but specialists were unable to come up with any specific diagnosis. Anti inflammatories were not very helpful. At that time she was slightly concussed in a motor vehicle accident. She then discovered she suffered what was diagnosed as petit mal when she had 3-4 blank spells for a few seconds each day. For six months since that time she became progressively more anxious, depressed, apathetic, unable to sleep, agitated, having constant headaches, was considering suicide, developed continuous ache in her lower back and knees as well as the shoulders.

She was having these problems when first seen by me. She was taking Dilantin, and various anti-inflammatories with physiotherapy to little effect. The relevant tests showed a hair copper 148, (with low calcium, manganese, and magnesium). Serum copper 138 ceruloplasmin 40 LFT and CBC were normal. 24-hour urine output after chelation was 350 (and 515 at a later date).

After a two day treatment with D penicillamine she felt happier and more energetic. After one month her shoulder, back and knee pains were much improved and for the first time in months she was able to do some exercises and typing. At this time six months later she continues to feel in excellent health; however she has some residual aching in the left biceps and continues to have petit mal blackouts for brief seconds each day. She continues to take D pen and if she does discontinue for more than 2-3 days all her symptoms start recurring.

Case 5. S.L., aged 33 with a young son.

Past history of prolonged toxaemia of pregnancy. Family history of nil significance.

Symptoms: She had been exhausted since the birth of her son on an intermittent basis both physically and mentally. This had been diagnosed as possible hypoglycemia and she had responded moderately well to a well balanced refined carbohydrate free diet. She continued however to be fatigued and was temperamental and irritable.

Investigations: Hair copper 400 (1978); 230 (1980). Serum copper 145, 24-hour urine copper after chelation 1350mcg. LFT and CBC were normal.

Treatment: After taking D pen for 2-3 days she felt less irritable and had more energy.

Of interest is the fact that her ten year old son has been investigated for behavioral problems, and was diagnosed by a psychiatrist as having low stress tolerance. His hair copper level was 91 (with low levels of trace minerals). It is possible that high tissue copper levels in the mother may be passed on to the children during gestation. Further follow up was not done on this child.

Case 6. H.C., aged 26.

This woman had a ten year history of anxiety, depression and more recently paranoid schizophrenia. She denied any family history of significant illness. She was recently given the orthomolecular diagnosis of pyrol-luric schizophrenia and responded reasonably well to zinc and pyridoxine therapy.

Of interest is her biological response to becoming pregnant. She became quite a normal stable person and said she had never felt better.

Investigations showed pre pregnant low normal histamine but a raised urinary pyrrole 35. A pregnant hair copper was 10 (low for childbearing age). Immediate post partum serum copper 190 (high), ceruloplasmin 42 (high), a 24-hour urine copper output after chelation 900. Two months later found the following; serum copper 130, ceruloplasmin 25, and a 24hour urine copper (without chelation) 72. It is interesting to observe the loss of serum capacity for copper at this time, and to wonder where the copper load was released. It can be seen from the moderately low urinary output that it cannot have been by that route. Copper must have been released into the tissues. It was about this time that clinically the patient became paranoid and psychotic and very agitated for the first time since she had become pregnant. Treatment with penicillamine produced a good reduction of her symptoms which prevented the need to institutionalize her. The 24hour output of urinary copper during treatment was 660. After two months of therapy she had reverted to a more normal state of mind. During the treatment phase she had not needed to take antipsychotic

drugs.

When eventual normalization of tissue copper is achieved, preventive measures should be taken to reduce further build up in the future. It is assumed that more normal tissue levels will have been assessed by the usual urine and hair tests. Most important is advice regarding drinking water. The level of toxic substances including copper in the domestic water supply can be assayed; usually the local water or health authority will oblige for a small fee. If there is a higher than 1 ppm level of copper in the water, an alternative source might have to be considered. Often flushing water through the drinking faucet for a few minutes will provide a much purer supply. It might be helpful to obtain a water purification device, such as one utilizing reverse osmosis. Copper cooking utensils should not be used. It is also inadvisable to utilize aluminum pots and pans since this can cause a different problem (Sohler, 1981).

Some foods have a high copper level. This is found more particularly in animal liver and shellfish. Some animals are given excessive copper in their feed which may create unnaturally high levels in the livers which are then sold for human consumption (Pfeiffer, 1977).

It is in vogue these days for many people to take vitamin supplements. These supplements often contain zinc and copper in more than a few milligram strength. It is quite possible that the absorption of copper through the intestinal wall is enhanced by its association with zinc. It has been shown in animal experiments that active transportation of zinc and copper (and cadmium) is facilitated in the intestinal wall by the protein "Metallothionein" (Bremner, 1980). Zinc and possibly copper supplements may stimulate a greater uptake of copper into the bowel mucosa, where large amounts may be stored. It might be safer if multiple minerals including copper were not in such widespread use, especially in endemic areas, where the water copper is high. It would seem that man has evolved with a very sensitive homeostatic mechanism to control copper uptake, when historically the element has been present only in minute quantities in the environment.

A clinical syndrome has been postulated, and therefore the question must be asked: Why has this phenomenon not been documented in the medical literature previously? It has been documented with respect to high levels of serum copper, as noted previously, but not in respect of high tissue loads of copper. The following points may be made. Hair Mineral analysis has only been available in the last few years as an accurate method to assist physicians in clinical diagnosis. Normal standards and tables of relevant normal ranges in human hair have only recently been compiled from sufficiently large population bases. Most practicing physicians are unaware of hair analysis and if they are aware they would consider it as an "untried method of analysis". Indeed only physicians with an interest in nutrition would be likely to show an interest in the method. Hair analysis testing is not usually eligible for medical insurance refunding and is therefore less likely to be utilized. In Canada until recently there was no experienced hair mineral analysis facility. All these factors point to the difficulty of detecting the presence of any generalized problems of mineral metabolism in the general population. Surveys have been undertaken in the United States by various analytical laboratories, of diverse populations, but no reports of persistently high copper in any given area has emerged.

Since hair mineral results in this area (Vancouver, B.C.) show about 50 percent of individuals investigated with copper levels over 40mcg/g, which is considered unusually elevated in most laboratories, it might be considered that we have a localized problem. It is known that our city water supply is extremely soft and while passing through the domestic pipes is assimilating significant loads of copper. The local university is actively studying the problem since some copper pipes have been eroded through in less than ten years. The safe level of drinking water by WHO standards is less than 1ppm. Domestic water supplies are generally analyzed by taking samples from the city mains. The water will not have traversed the domestic piping. Random sampling of standing home faucet water showed a significant number over the l ppm limit for our city. It is hoped that a larger survey will be undertaken. (It is of interest that in fisheries research, the toxic level of copper in the water supply

which will adversely affect the survival of juvenile brook trout or yearly cohoe salmon is in the range of .005 to .03ppm).

It is common knowledge that in the Northern Hemisphere the acidity of the water supplies is increasing rapidly in many areas due to "acid rain". The ph of the rainfall may be less than 3 in some areas in the Eastern States and provinces. This extremely acid rain water may dissolve excessive amounts of minerals from the ground and pipes — which may be toxic unless buffered by sufficiently hard or alkaline soil. It had been thought that on the West coast of Canada the fresh rains from the Pacific Ocean would be reasonably neutral in ph. However it is now known that acid rain is a problem on this coast — the ph having dropped from 6.5 to 4.5 over the last ten years (Feller, 1983). This coupled with an extremely soft (mineral free) source of drinking water has been causing erosion of copper piping and at the same time creating an increasing health hazard to those drinking the water. At the same time as the copper load of drinking water has been increasing many people have discovered the fitness fetish. It has been reported in the media that at least 50 percent of the population take some form of vitamin supplementation. Many of these pills may contain significant amounts of copper.

It is possible that the condition is associated with other health problems. We know of the relationship between copper and schizophrenia, (but these patients constitute a minimal part of our practice). We do, however, see a high proportion of allergic individuals. Could high copper levels be a factor (together with others) which initiates an allergic state? Conversely, could the allergic state induce a higher than normal copper retention? Individuals with multiple allergies — including foods — often have a malabsorption syndrome. In these people there is often a deficiency of trace minerals especially calcium, magnesium, zinc, and manganese. This often occurs in individuals who are not necessarily allergic. They may be deficient in essential minerals for a number of reasons: poor dietary choices, poor digestion, inappropriate lifestyle with excessive stress and a hurried bowel. Excessive use of drugs such as antacids and laxatives may unbalance the digestive system. When the levels of essential minerals are low, copper and other toxic minerals are likely to be taken up into their binding sites and create metabolic dysfunction.

Some of the possible effects of high serum or tissue copper may be postulated by references in the literature. In reference to mental functioning, Pfeiffer (1975) has documented high levels of serum copper in some schizophrenics. Krischner (1978) has described a series of hyperactive children with significantly high serum copper levels. Patients with cerebral infarctions have been noted by Bogden et al. (1977) to have abnormally high copper concentrations in plasma and cerebrospinal fluid. In contrast, low levels have been described in anorexia nervosa- (Casper, 1978). Treatment with copper sulphate produced beneficial results (Hoes, 1980). Dietary copper deficient animals show a reduction in noradrenaline and dopamine concentrations (Hunt, 1980). Cer-uloplasmin catalyses the oxidation of the biogenic amines noradrenaline and serotonin (Frieden, 1980). Reduction of ceruloplasmin utilizing D-pen will tend to convert adreno-chrome (a hallucinogen) into Leucoadreno-chrome in the brain which will tend to reduce brain dysfunction (Hoffer, 1981).

In certain types of cancer, the copper levels are increased in the serum. The question can be asked: is there a predisposition to high copper levels in these cancer patients which might help induce the neoplastic state or does the high copper level come about as a result of the neoplasia? If the former were true, a useful predictor of cancer would be available and preventative measures could be undertaken. This has already been suggested by various therapists (Nieper, 1979; Braverman and Pfeiffer, 1982). Indeed it is standard procedure in some cancer clinics to monitor serum copper levels in patients suffering certain types of cancer, so as to get some idea of spread and prognosis.

Higher than usual levels of copper in the water supply may induce a higher rate of mortality due to ischaemic heart disease and other cardiovascular diseases. Masironi (1969) has written that soft drinking water was associated with higher cardiovascular mortality rates and it was also determined that the copper levels in the water supply and

TABLE III

Patients With Significant Raised Hair Copper, Associated Investigations

Identity	Age	Female unless marked "M"	Hair Copper PPM N 40	Serum Copper Mcg/D1 Norm; 70-130	Cerulo-plasmin Norm; 20-40	24 Hour Urine Copper; Preload; Mcg/24 hr. Norm 100	24 Hour Urine Copper; After Cuprimine 250 mg. q6h - 3rd day	Symptoms to a scale of 4	Response to treatment
N.A.[1] 1st	40		240	78	20	88	704	++++	++++
2nd			189				692		
P.L.[2]	38		60	94		145	263	++++	++++
H.E.[3]	29		265	116			790	+++	+
W.C.[4]	36		148	138	40		350	+++	+
S.L.[5]	33		400	145			1350	+++	+++
H.C.[6]	26		10	190		400	900	+++ Pregnant & Schizophrenic	+++
S.B.	29		60	98	25		186	+++	o
H.S.	60		180	127	28	39	480	+	
K.C. 1st	34		180	125	44	190	669	+++ Elevated Aluminium	
2nd			95				416		
E.M.	54		225	130	29	44	930	+	
C.P. 1st	36	M	59			59	614	++++ Elevated Pb,Al	
2nd			198				740		
I.K.	58		49	176	37	98	624	+ Chronic Schizo.	
E.S.	43	M	57	118	26		890	+++ Hyperthyroid	
C.V.	70		90	117		129	356	+++	o
F.C.	62		48				445	++ Elevated Pb,Al	
J.M.	33		18	110			876	+++ Elevated Toxic Cadmium	
S.C.	40		178				485	+++	
D.B.	42		140	136			553		
J.C.	46		119		29		325	++	++
J.P.	47		91	133	30		865	+ Schizophrenic	++
R.T.	31	M	71	101		68	576	++ Hyperthyroid	o
M.S.	46		20	111	22		84	++++	
C.V.	60	M	12				235		
K.C.	32	M	72				560	+ Elevated Pb	
C.T.	41		179		31		1200	++ Elevated Manganese	
W.T.	40		413				630	++	+
C.W.	37		206	105	26		656	++	
C.A.	45		384	104			860	++	
D.M.	35		960				1370	++	
J.S.	35	M	75				428	+ Elevated lead	

1 — 6 Indicate Case Histories Reported.

TRACE ELEMENT ANALYSIS REPORT

To: MacDonald Medical Centre
205 - 2736 West 16th Avenue
Vancouver, B.C. V6K 3C4

Attention: Dr. K.R. Nolan

Sample Data

Identification: Hair Specimen, collected 20-Jan-83
Description: H.E., Age 28
Lab Ref No.: 83 Date Out: 02 Feb 83
Preparation: Acetone-water wash, N03+C104 decomposition
Analysis: Inductively Coupled Argon Plasma Atomic Emission Spectroscopy

Analysis of Human Hair — ug/g dry wt. (ppm)

ELEMENT		UNDER	NORM	OVER+	RANGE*	RATIOS		MEAN
Calcium	Ca		325.		200-600	Ca:Mg	16.2	10
Magnesium	Mg		20.1		20-100	Ca:P	2.6	2.5
Sodium	Na	17.0			100-350	Ca:Pb	34.9	20
Potassium	K	10.6			50-200	Na:K	1.6	1.8
Iron	Fe		17.0		10-30	Cu:Fe	15.6	1.3
Zinc	Zn		175.		150-250	Zn:Fe	10.3	10
Copper	Cu			265.	10-40	Zn:Cu	0.7	8
Manganese	Mn		1.36		1-5	Zn:Mn	129.	67
Chromium	Cr	0.37			0.5-1.5	Zn:Se	175.	67
Selenium	Se		1.0		1-5	Zn:Cd	2500.	>200
						Zn:Pb	18.8	> 10
Barium	Ba		0.73		0.1-3	Se:Hg	> 1.	> 1.5
Cobalt	Co	< 0.1			0.2-1.5	P :Al	11.5	≥ 8
Lithium	Li		< 2.		0.1-0.3			
Molybdenum	Mo	< 0.1			0.1-1			
Phosphorus	P		124.		120-200			
Strontium	Sr		1.1		0.5-5			
Titanium	Ti			2.3	0.1-0.2			
Vanadium	V	0.04			0.1-0.6			
Aluminum	Al		10.8		< 20			
Arsenic	As		< 2.		< 3			
Beryllium	Be		< 0.02		< 0.1			
Cadmium	Cd		0.07		< 1			
Lead	Pb		9.3		< 20			
Mercury	Hg		< 1.		< 2			
Nickel	Ni		0.37		< 2			

NOTE: This report is not intended as a diagnosis or treatment of any specific disease or condition.
Data should be interpreted by a qualified medical practitioner.
*Normal ranges were obtained from literature and statistical data and are subject to change.
+According to the literature, high values may in fact indicate a deficiency rather than an excess.

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in the serum of patients was significantly raised. It is known that copper is important for the proper growth of connective tissue especially in artery and arteriolar walls. Inadequate levels of tissue copper will give rise to growth of defective connective tissue (Harris, 1980) and may very likely give rise to premature aging.

Increased copper intake is reported to cause a loss of iron from the tissues therefore causing inefficient tissue metabolism. It does this by increasing the level of ceruloplasmin in the tissues (M. Seelig, 1972). Pierard (1979) has described a study in which higher than normal levels of copper in drinking water and in the blood and urine (of people imbibing that water) was associated with abnormal hair growth and alopecia.

In Conclusion.

It should be stated that the cases included in this survey are a small number of the eighty or so cases seen with significantly high copper levels in the hair over the past twelve months. It is known that other practitioners utilizing this test in this area are similarly finding frequently abnormally raised hair copper. The cases included in my survey are

those who have had a reasonable laboratory workup and who have been seen sufficiently frequently to become aware of the consistency of clinical features. There are others who are in various states of investigation who most probably suffer the syndrome. Others have not wished to pursue the investigations, have been transient visitors, or have become involved with other physicians' therapies.

A syndrome has been described; and a probable correlation between high hair copper level, urinary output after oral chelation, and clinical symptoms has been documented. It is hoped that agencies with the time, expertise and facilities may be able to analyse more accurately the extent of this problem.

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