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COPPER AND HUMAN HEALTH AND SAFETY

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INTRODUCTION

If a pharmaceutical manufacturer were to advertise a new product by saying: "Absolutely essential, you cannot live without it!" it would create quite a sensation. If he were to add: "You won't have energy, your skin and hair will turn white and your joints will come apart, unless you take it regularly", most readers would be incredulous. Yet, science has determined that the above accurately describes copper and its action in human health. Copper is one of a relatively small group of essential metallic elements. Also, like essential amino acids, essential fatty acids and vitamins, these metals are required for normal metabolic processes. However, the body cannot synthesize them so that regular dietary intake and absorbtion are required.

It has been established that copper combines with certain proteins to produce enzymes that act as catalysts to facilitate required bodily functions. In these catalysts the chemical nature of the copper is so affected by the molecular environment of the attached protein that it has a uniquely specific action. Cytochrome oxidase is the copper compound needed to drive energy requiring biochemical reactions. Tyrosinase is the enzyme required for synthesis of dopa and its subsequent transformations to melanin, required for pigmentation. Lysyl oxidase is required for cross-linking of collagen and elastin in maintenance and repair of all connective tissues. In relation to heart disease, to be discussed later, it is important to note that collagen is the fibrous component that binds heart muscle cells together and that elastin is the component that makes heart and artery walls elastic.

COPPER IN THE DIET

From the above, it is obvious that it is important to have adequate copper in one's diet. Formerly, it was generally believed that most people consumed adequate quantities of copper. Modern research, however, has shown that this is not true. In the U.K. and in the U.S., for example, many typical meals have been analyzed for their metals content. According to recent surveys, only 25% of the U.S. population consumes the two milligrams of copper a day estimated to be adequate by the

U.S. Food and Nutrition Board of the National Academy of Sciences. Typical diets in the United States provide only about half that amount and some diets there and in other industrialized countries contain only about 0.8 milligrams of copper a day.

There are some foods which are especially rich in copper. These include oysters, liver, most nuts (especially brazils and cashews), seeds (especially poppy and sunflower) and chickpeas.

The adult body contains between 1.4 and 2.1 mg. of copper per kg. of body weight. The infant body contains three times this amount, consistent with the fact that metabolic needs are much greater than for adults.

The amount of copper in each tissue correlates with the number and kind of metabolic processes requiring copper in that tissue. For this reason it is especially interesting to note that the brain and heart contain more copper than all other tissues except the liver (which is the major copper storage organ).

Ionic copper has a particularly high affinity for other molecules capable of bonding with it. In biologic systems, these ligands or chelating agents combine so readily with the ionic copper that, as a result, the amount of ionic copper left in these systems is too small to be measured using the most sensitive instrumentation available.

In addition to the relatively low quantities of copper in many diets, there are other factors which can cause copper deficiency. A high intake of zinc or other substances may interfere with the body's use of copper - preliminary findings point to vitamin C as one of these materials. While normal levels of zinc will not upset the copper to zinc balance, excessive or unnecessary zinc supplements can cause a problem. Fructose and other sugars that contain fructose - such as sucrose (table sugar) also increase the risk of copper deficency. Unfortunately, in many countries the amount of fructose has been greatly increased since the introduction of high-fructose corn sweeteners used in many prepared foods and soft drinks. Foods high in fat generally have high ratios of zinc to copper. For this reason, diets designed to lower serum cholesterol are favorable. They decrease fat and cholesterol and increase polyunsaturated fat which tends to have lower ratios of zinc to copper. In addition, polyunsaturated fat seems to decrease retention of dietary zinc without affecting the retention of copper.

COPPER IN MEDICINE

Copper has been used in medicine literally for thousands of

years. One of the earliest references was written between 2600 and 2200 B.C. and describes the use of copper to treat infected chest wounds and to purify drinking water. A number of other uses and a range of various copper medicines have been recorded over the years.

In very recent times, a number of exciting research developments have taken place. Dr. J.R.J. Sorenson and co-workers at the University of Arkansas in the U.S., for example, have studied the effect of copper and copper complexes as agents against the inflammatory component of a number of important diseases. Results of these studies have been reviewed recently and confirm as well as extend original observations that copper complexes of inactive ligands and of active antiinflammatory drugs are more active that the parent ligand or inorganic copper. This increased effectiveness of the copper complexes is consistent with the finding that the body, when affected by an inflammatory disease, mobilizes copper to fight the inflammation.

It has recently been found, as a result of this work, that copper complexes have antiulcer, anticonvulsant, antidiabetic, anticancer, antimutagenic and radioprotectant activities in animal models of these disease states. Copper complexes are known to have an anti-inflammatory effect in man as a result of their effectiveness in the treatment of arthritic diseases.

As a demonstration of efficacy as a radioprotectant, groups of mice were pretreated with the copper complex. Thirty-three percent and fifty-eight percent of the mice pretreated with the complex 3 or 24 hours, respectively, before irradiation, survived the duration of the experiment, 30 days after irradiation, while all nontreated control animals died by day 18 after irradiation.

Similar demonstrations have been made with the animal models of the other diseases listed.

Patents were issued several years ago on antiulcer and antiinflammatory copper complex medicinals. A patent on the use of copper as a radioprotectant was issued in April 1987, and one on methods for treating convulsions and epilepsy with organic copper compounds was issued in June 1987. Two additional patents on the latter subject were issued in July 1988. Additional copper medicinal patents are pending.

COPPER IN HEART DISEASE

Many people are concerned about coronary heart disease - a leading killer in a number of countries. Hundreds of different factors associated with this disease have been studied for many years. However, Dr. Leslie M. Klevay, research leader at the Grand Forks Human Nutrition Research Center, part of the U.S. Agriculture Research Service believes that copper deficiency

could be the single most important factor among dietary causes. While it is only one of a number of factors that may contribute to coronary heart disease it appears to be one that definitely warrants additional study.

Dr. Klevay has analyzed and studied the effects of copper deficiency on mice, rats, rabbits, pigs and three species of monkeys. When these animals were severely deprived of copper they developed abnormal electrocardiograms, had elevated blood cholesterol and impaired ability to metabolize glucose. Also, they developed high levels of triglycerides and uric acid, widely believed to increase the risk of heart attack.

Relatively few human studies on copper deficiencies have been done. In one study at Grand Forks, a healthy 29 year old man received a diet containing 0.8 milligrams of copper a day in a 6 month study. His blood cholesterol increased steadily from 202 to 234 mg/dl. When adequate copper was added to his diet, his blood cholesterol steadily dropped to 198 mg/dl. High cholesterol levels are often associated with heart disease.

Another study by Dr. Sheldon Reiser and coworkers at the Beltsville Human Nutritions Center in Maryland, U.S.A., reported in the American Journal of Clinical Nutrition, had more disturbing results. Four male subjects, aged 20 to 57, out of a total of 23, exhibited "Heart Related Abnormalities" when being fed diets comparatively low in copper (1.03 mg/day). The subjects consumed a typical American diet in which either fructose or starch provided 20% of the carbohydrates. Because of the abnormalities experienced, the researchers terminated the experiment. While they were unable to prove that there was a direct relationship between the experimental conditions in their study and the occurence of the heart problems, they calculated that the probability of the heart problems being due to chance were less than 5 in 10,000.

SUDDEN INFANT DEATH SYNDROME

Research reports published in 1987 by Dr. G.M. Reid relate to the effect of congenital copper deficiency on Sudden Infant Death Syndrome. It was concluded that copper deficiency may be involved in the pathogenesis of this syndrome and defective elastin formation was specifically mentioned.

MENKES' KINKY HAIR SYNDROME AND WILSONS DISEASE

Both of these rather rare diseases are inherited afflictions. In Menkes' disease, there is a lack of copper transport resulting in a copper deficiency that is always fatal by three to five years of age. In this X-linked disorder the afflicted boys are mentally retarded and have hair of an unusual kinky or steely nature. Although various methods of supplementing copper have been attempted, none has significantly prolonged life. In Wilsons disease, an opposite action occurs, there is

a defect in the hepatic excretion of copper and toxic levels of copper accumulate. When detected, this disease is treated with chelating agents like D-penicillamine which remove the excess copper. With this treatment, many patients appear to have as long lives as individuals without the disease.

COPPER IN PUBLIC BUILDINGS

Dr. Phyllis Kuhn at the Hamot Medical Center in Erie Pennsylvania recently made a study of possible causes of cross-infection within her hospital.

She made cultures from the surfaces of doorknobs made from various metals. In a controlled test she found that bacteria proliferated on the surface of stainless steel doorknobs. On the brass doorknob (67% copper), there were very few bacteria. That the metal itself was responsible was demonstrated by testing a varnished brass doorknob - which supported bacterial growth.

She also made a number of other tests using strips of stainless steel, brass, aluminum and copper inoculated with E. coli, Staphylococcus aureus, Streptococcus group D and Pseudomonas species. The strips were air-dried for 24 hours at room temperature, inoculated onto blood agar plates and incubated. The copper and brass showed little or no growth while the aluminum and stainless steel produced a heavy growth of all microbes.

Finally, she took some scanning electron micrographs of various surfaces. Figure 1 shows colonies of Straphlococcus living in the grooves of a brushed stainless steel doorknob.

As a result of the work she recommended that in any renovation of the hospital the brass hardware should be retained - even if the stainless steel did look reassuringly clean.

Dr. Kuhn next plans to extend this line of investigation to various copper containing paints formulated especially for hospitals and public buildings to determine if some of them have bactericidal properties like the metal itself.

BACTERIA IN SWIMMING POOLS

Dr. Charles P. Gerba, a microbiologist at the University of Arizona, has recently reported (August 1988) that copper and silver ions can control bacteria and viruses in home swimming pools. In commercial pools the contamination level is higher and some chlorine is also needed to speed up the killing action.

If a pool is not properly maintained, swimmers may suffer from respiratory diseases and ear infections. Other problems like

entero virus, viral eye infections and swimmer's itch may arise.

The combined treatment is better than chlorine alone since eye irritation is reduced and overall costs, including corrosion and maintenance, are reduced. When combined with silver and copper, 0.2 to 0.4 mg. of chlorine/liter kill bacteria more effectively than the 1 to 2-3/4% free chlorine normally used in commercial pools. In addition, there is always a residual amount of copper and silver, they are not used up as fast as chlorine - especially in the presence of sunlight.

The exact reason for the faster kill rate of the combination compared to heavy chlorination alone is not known. However, Gerba surmises that the chlorine may injure the organisms and allow the copper and silver to enter and disturb food transport enzymes.

Gerba also notes that copper water tubing may be better for home use than plastic because it has an anti-bacterial effect. (See also below)

COPPER IN POTABLE WATER SYSTEMS

Authorities in charge of supplying potable water are concerned not only with the purity and taste of the water in their supply reservoirs, they also want to be sure that the whole distribution system will safeguard their product until it reaches the tap in the customer's home.

In their reservoirs they often add copper sulfate which has been shown to be effective in controlling many different algae which give water a bad taste. As shown in Figure 2 and Figure 3, objectionable algae were killed in a pond a few weeks after an application of copper sulfate. The World Health Organization and other agencies such as the U.S. Environmental Protection Agency (E.P.A.) have set standards which allow up to one part per million of copper in drinking water.

Chlorine or other disinfectants are often added to potable water to protect it during the time it is in transit through the distribution system to the ultimate consumer. However, organic matter in the water often uses up the chlorine before it reaches the customer. Use of chlorine must be limited since it converts certain organics into trihalo- amines which are carcinogenic.

Since many different disease outbreaks have been traced to drinking water, the microbial content is closely monitored. It has been found that a certain species of bacteria, E. coli, is present whenever there is fecal contamination of water supplies. Special tests have been devised to detect and count this so called "marker" microbe.

It has been known for a long time that copper has a bactericidal action in water but the effect had never been quantified. For this reason, research, still underway, was established at Midwest Research Institute in the U.S. Recently, the work has been extended to the Thames Water Authority and the Public Health Laboratory Service in the U.K.

Midwest started with the marker microbe. Water containing E. coli was circulated through identical separate lengths of copper, glass and plastic tubing of the same diameter-as shown in Fig. 4.

Bacteria in water are counted by putting a measured quantity of the water on a nutrient agar in a shallow Petri dish which is placed in an incubator so that each individual bacterium will reproduce and grow into a visible colony which can be counted. At the start of the test the numbers, of course, are the same. At the end of 24 hours, all of the E. coli in the copper tubing were killed, glass and various types of plastic tubing had no effect, see Fig. 5.

Next, it was decided that some other types of bacteria should be tested. In the U.S., the E.P.A. expressed concern about a group of five bacteria that they called "opportunistic pathogens" which might be present in potable water. These bacteria might attack people whose natural defenses were reduced because they had, or were recovering from, an illness of some sort. In tests like those conducted on E. coli, it was found that four out of the five types were killed by exposure to water conveyed in copper tubing, but not in glass or plastic.

Another dangerous water bourne bacterium is the one shown in Fig. 6 which causes Legionnaires' Disease (named for the fact that it caused the deaths of many people attending an American Legion Veterans Convention in Philadelphia several years ago). It has been the focus of much attention since various surveys have shown that it is widely distributed in water supplies including hospitals, hotels, homes and public buildings. Infection may occur when small water droplets from showers or cooling towers are inhaled. Since it grows best in the presence of slimes produced by other bacteria, it is often studied by using a continuous culture system including other species of bacteria. Because of the dangerous nature of Legionella, all of the research on it must be conducted inside protective equipment.

Although the work is not completed, in a number of trials the Legionnaires' bacillus was killed by exposure to copper tubing but not by exposure to plastics.

Water bourne viruses are another important source of dangerous diseases - hepatitus and polio for example. The U.S. E.P.A. is now setting standards which will require a 99.9% reduction in

the number of viruses permitted in drinking water. At the University of Arizona in the U.S., research is underway to see if copper tubing may also be effective against viruses.

COPPER IN FIRE SAFETY

A noted U.S. worker in the field of fire safety has stated that the fire scenario that causes the most fire deaths in that country is one in which a cigarette is inadvertently dropped on a piece of upholstered furniture which smolders for an undetermined time before bursting into flames. The vast majority of upholstered furniture today contains flexible polyurethane foam (FPU). Great Britain has recently issued regulations effective next year requiring that such foams pass certain performance tests before being marketed. According to the London Times, these regulations were issued because of the easy ignition and production of "lethal carbon monoxide and hydrogen cyanide (HCN) fumes" from these foams. In the U.S., 80% of fire fatalities are attributed to the inhalation of toxic gases and not to burns; therefore, the concern about the production of toxic gases in fires, and specifically from FPU, is understandable.

Researchers at Clarkson University in the U.S.A. in their studies on the oxidative degradation of FPU, found that the presence of various metals would inhibit the evolution of HCN. The most efficient metal was copper or its oxide. Since reducing the amount of HCN produced from the thermal decomposition of FPU should decrease the toxicity of the combustion products, research was undertaken at the Center for Fire Research, National Bureau of Standards, Gaithersburg, Maryland, U.S.A., to determine (1) if the addition of copper or copper compounds would reduce the atmospheric concentrations of HCN when larger amounts of FPU were decomposed under conditions that simulated a realistic fire scenario, and (2) if the acute inhalation toxicity produced from the exposure to the combustion products from FPU treated with a copper compound would be less than that from non-copper-treated FPU.
At the end of the first year of work the following conclusions were reached:

1. HCN concentrations in the thermal decomposition products from a flexible polyurethane foam were significantly reduced when the foam was treated with copper or copper compounds.

2. Significant reduction of HCN concentrations occured at the lowest tested concentration of copper oxide (much less than 1% by weight).

3. Blood cyanide levels in animals exposed to combustion products from the copper oxide-treated foams were at least 4 times lower

than the levels measured in the animals exposed to the combustion products from foam without copper oxide.

4. The within-exposure deaths in concert with the HCN yields were reduced by the addition of copper oxide.

This encouraging important work is continuing.

SUMMARY

Modern scientific research is finding new ways for copper to enhance human health and safety.

Required for life itself, adequate bodily intake is needed to help fight heart disease and other ailments. As a vital component of new medicines, it will help to combat ulcers, epilepsy, arthritis, diabetis, cancer and the harmful effects of radiation.

In hardware in public buildings it can help prevent the spread of disease. Incorporated into upholstery foam it may help prevent toxic fumes.