Centre For Natural Healing

Nutritional protocol for PATRICK SCRANTON
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Type of protocol: Nutritional/immune support, anti-cancer (desmoplastic small round cell) including antiangiogenic and marrow support.

Description	**Amount**
NUTRITIONAL SMOOTHIE)	
Protein Powder eg Paleomeal or equivalent	1 scoop
Beyond Whey (Natura)	1/2 scoops
Buffered C Powder – one teaspoon delivering 2500 mg C	1 teaspoon
Beyond Essential Fats (Natura)	2 teaspoon
Betaplex 5 drops (sticky! drop in on slow mix) 25,000IU equ	5 drops
Selenium – 10 drops ~ 500mcg †	10 drops
Glutamine powder – up to 10 gms	6 gms/2 tsp
Mycelized A liquid	3 drops
Mycelized E` liquid	6 drops
Molybdenum	10 drops
Add Probiotic of choice (eg Saccharomyces) HMF	1/4 teaspoon
1/2 cup raspberries or strawberries OG fresh or frozen	
1/2 cup blueberries – OG fresh or frozen organic if possible	
Liquid Of Choice – 1 to 2 cups to desired consistency (OG goat milk, goat yogurt, coconut milk, raw milk, unsweetened soy or nut milk)	

The smoothie should be made and taken in the morning as your breakfast. It is designed to provide an optimized foundation for your nutrition for the day, and to minimize insulin as well being a handy delivery system for several essential supplements. Place the ingredients in a blender, except for the Beyond whey which is fragile and should be added right at the end of the mixing at a low speed. Add a liquid of your choice, such as organic nut milk, or raw goat yogurt, unsweetened soy. Dark red/purple/blue berries should also be added. (Sweet fruit such as banana should be avoided). For those having difficulty with taking other supplements, capsules can be emptied in, tablets can be gently ground, gelcaps can be punctured and squeezed in. Probiotics are an essential addition. Do not leave these in a premixed smoothie – it will ferment. Glutamine is best purchased in bulk and used up to 15 gms a day during chemo. Green foods can be added., chlorella is good. The smoothie can be omitted on the day of chemo if necessary.

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Description	**DOSE**	**PER DAY**
HERBAL FORMULAE		
Immucare 1 Powdered Formula Take 1.5 teaspoon daily with meals.(white cell restorative)	1.5 teaspoons	3x daily until WBC restored
Botanical Treasures Powdered Formula Take 1 teaspoon 3 x daily with meals (antiangiogenic.antiinflammatory)	1 teaspoon	3 x day
Powders can be taken together in a little apple sauce, yogurt, or in a		

strongly flavored fruit juice or other beverage to help with the taste.		
Individual Herbal Formula	1 teaspoon	3 x day
Vital Adapt (natura)	1 teaspoon	3 x daily
SUPPLEMENTS		
Zinc	2 cap	nightly
Cal-Mag Pioneer	1 tab	nightly
Tocotrienols (mixed)	1cap	1 x day
Alpha Lipoic Acid 300mg	1cap	1x day
CoQ 10 –1 gelcap 1 x day 200 mgm	1 cap	1 x day
Cytoredoxin (Tyler)	1caps	3 x day
Coenzyme B complex (Cardiovascular Research)	1 cap	1x day
Immune Builder Mushroom Complex between meals	3 caps	3 x day
Melatonin		At night
Wobenzyme* before meals at least 1 hour optional	5 tabs	3 x day
Nutrient 950 * without copper without Iron (Pure Encap) *	optional	
ART (follow separate instructions)		
Artemisinin (See ART protocol Instructions)	400mg/500 mg	3 x day
A Annua (See ART protocol Instructions)	2 droppers	3 x day
Vitamin C /K3 (follow separate instructions)		
Menadione	20 mg	At night
Vitamin C (use powder)	2000mg	At night

Patrick Scranton – Individual Herbal Formula: 240 ml/ 8 ounces.

Baical skullcap 40
Trifolium flos 40
Milk thistle 40
St. John's Wort 40
Arctium seed 40
Licorice root 20
Poke root 20

Sig 1 teaspoon 3 x day in water at meal time

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ARTEMISININ - PATIENT PROTOCOL UPDATE – June 2004
Jonathan Treasure, MNIMH, (RH) AHG

1. Product
All patients should now be using the ARG (Allergy Research Group) product. The exception to this is a few patients with brain involvement who may be using, in addition, the WellCare artemether gelcaps.

2. Starting ART. A) find your dose level.
Using the 100mg ARG capsules, maximum doses should be a total of between 900 and 1200mg daily, taken as three divided doses with meals. Some patients experience moderate toxicities at these levels and for them the individualized maximum would be lower. One or two patients have shown intolerance for artemisinin at low levels, around 100-300mg daily. Therefore we start at a low level and ramp the dose upward toward the maximum as follows:

Start Day 1: 1 cap 3 x daily
Day 2 ditto
Day 3 2 caps 3x daily
Day 4 ditto
Day 5 3 caps 3 x daily
Day 6 ditto
Day 7 4 caps 3 x daily

If you can tolerate 4 caps 3 x daily, that is your dose. Most people settle between 900-1200mg, however some people feel fine with 1600 mg daily. If at any time you notice symptoms that seem to be associated with your ART, then do not increase the dose further and call inform your practitioner.

2. Starting ART. B) pulsing
Studies show that our bodies adapt to artemisinin by increasing the enzymes that eliminate it. After ten days, the plasma levels are only 25 % of the steady state established by day 2. Women seem to eliminate artemisinin better than men. For this reason we "pulse" dose the ART after you have established your maximum dose as above. The basic pulse is 5 days on, 5 days off. The dose taken is always your maximum dose.

2 Starting ART. C) Add Sweet Annie
Studies suggest that components found in the whole herb synergize with the effects of isolated artemisnin. For this reason, we take a small dose of tincture (alcoholic extract) of whole herb with each dose of artemsinin. The dose of tincture is is about 1/2 teaspoon 3 x a daily, to be taken with the artemsinin. This is also pulsed (ie take only when taking the artemisinin)

3 Supplement questions Iron - It is not necessary to take iron with artemisinin under normal circumstances. We only use iron supplementation where the soluble transferrin receptor (STR) test indicates a need for iron supplementation (i.e. a level >28). STR is a special test that may not be done by your regular

laboratory and may have to be sent out for processing. STR is the most accurate test for iron deficiency. Once the STR is normal, no more iron is needed.

Antioxidants - The full complement of antioxidant supplementation can and should be maintained throughout artemisinin therapy. They do not "inactivate" artemisinin.

3. Artemisinin Toxicity
Although artemisinin is cytotoxic (kills cancer cells), as a botanical agent it is much milder than most regular cancer chemotherapy drugs. For this reason, it can be taken continuously over a six-month period. The following is based on our own patients' experiences.

Symptoms: Symptoms of mild artemisinin toxicity can include cold extremities, numbness, ringing in the ears (tinnitis), or headache. In addition, there may be some gastric discomfort, anorexia and occasional diarrhea. At times, the diarrhea may be moderate to severe. In this case, do not stop the artemisinin, but see if the situation persists. If the diarrhea lasts

more than a few days, and involves more than moderate fluid loss, contact the PFH office for instructions. All of these mild toxicities are a sign that the artemisinin is acting effectively and they usually disappear once the body is accustomed to the dosage.

Signs - Slight elevations of liver enzymes (AST and ALT) may be expected. These rises should level off, possibly to a marginally supra-normal baseline during ART. Persistent and increasing elevations have not been associated with artemisinin and should be investigated if present. Bilirubin levels should not be affected. If abnormal reticulocyte counts appear in association with higher doses, this is likely an artemisinin effect. The office will automatically contact individuals whose labs show abnormalities that may be related to ART. *(You are responsible for assuring that lab work is faxed to us in a timely manner).*

4. Radiation contraindication.
Although the available evidence is sparse, we currently consider that artemisinin is contraindicated during radiation, particularly generalized head and neck radiation. This does not necessarily apply to certain forms of radiation such as gamma-knife. Existing artemisinin patients considering radiation should stop ART two weeks prior to radiation and discontinue it for the duration of radiation treatment and for a short period thereafter as determined by consultation with PFH staff. New patients should not commence ART if radiation has already been started, or is about to be administered.

5. Chemotherapy
There is no evidence to suggest that ART cannot be combined with mainstream chemotherapies. In fact, the available science at this time suggests that there is most likely a beneficial interaction between ART and many chemotherapeutic agents that will enhance the effectiveness of the chemo.

6. New Patients, Baseline Labs, Progress Monitoring
Baseline laboratory tests should be performed, if possible, before ART is commenced. The tests required are CBC with reticulocyte count, STR (soluble transferrin receptor) and liver function panel. ART may be started, however, before results are reported.

Close monitoring of ART with lab data is not required, because most patients will be obtaining CBC's and LFT's (liver function tests) on a regular basis. However, if adverse effects do appear, more frequent testing may be needed to monitor the situation, especially if concurrent therapies such as TM copper chelation, or chemo are being administered.

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Ascorbate-Menadione (vitamins C and K3) as non toxic adjuncts to cancer treatment

Vitamins C and K-3 have been evaluated as antitumor agents. Several in vitro studies demonstrated that vitamin C (VC) exhibits selective toxicity toward malignant melanoma cells, human leukemia cells, neuroblastoma cells, tumor ascitis cells as well as acute lymphoblastic leukemia, epidermoid carcinoma and fibrosarcoma, with VC acting as a pro-oxidant. (DeLaurenzi et al., 1995) In the form of ascorbate, VC can be oxidized either by a single or two-electron transfer and can be converted back to ascorbate by NADH-dependent semidehydroascorbate by NADH-dependent dehydroascorbate reductase or glutathione-dependent dehydroascorbate reductase (DeLaurenzi et al. 1995). This cycling process generates H_2O_2 and other reactive oxygen species (ROS) that deplete cellular thiol levels, initiate membrane lipid peroxidaton and result in tumor cell death.

Vitamin K-3 (menadione, 2-methyl-1, 4-napthoquinone) is a synthetic derivative of vitamin K-1, which exhibits antitumor activity against liver, cervix, nasopharynx, colon, lung, stomach, breast, leukemia and lymphoma cell lines (Nutter et al. 1991, Wu et al. 1993a and 1993b). Vitamin K-3 is reduced intracellularly via one- or two-electron transfer. The two-electron reduction of quinone to hydroquinone can form non-toxic conjugates or slowly auto-oxidize

to reform quinone. As a result, redox cycling can ensue and produce large amounts of superoxide, which can dismutate to form H2O2 and O2 or take part in metal-catalyzed reactions to form more toxic species of active oxygen. Therefore, if the single-electron reduction pathway predominates and the rate of redox cycling of VK-3 exceeds the capacity of the detoxifying enzymes, oxidative stress occurs (Stubberfield and Cohe, 1989). This oxidative stress causes a variety of effects on cells, including reduction of NADP and ATP pools, depletion of glutathione, induction of single stranded DNA breaks and oxidation of sulfhydryl group I cytoskeletal proteins (Gant et al. 1988, Mirabelli et al. 1989).

The Combination Of Vitamins C And K-3 As Antitumor Agent

Redox cycling oxidants such as VK-3 may trigger apoptosis or cause cell necrosis, depending on the dose and duration of exposure and the subsequent amount of oxidative stress (Juan and Wu 1993, McConkey et al. 1988, Wu et al. 1993a). When VC and VK3 are combined, their interaction fosters the reduction of VK-3 via one-electron reduction and increases the rate of redox cycling of the quinone (Jarabak and Jarabak 1995, Pething et al. 1983). These results suggest that coadministration of VC can increase the potential toxicity of VK-3. In fact, when Taper and co-workers (Noto et al. 1989) combined VC and VK3 in a ratio (VC/VK3) of 100:1, the combination exhibited tumor specific antitumor activity against human breast, oral epidermoid and endometrial tumor cell lines at doses that were 10-50 times lower than when either vitamin was administered alone. Additional studies using a murine ascites transplantable liver tumor model showed that the VC/VK3 combination is an effective chemosensitizer and radiosensitizer that induces little systemic or major organ pathology (Taper et al. 1987 and 1996, Taper and Roberfroid 1992). A single intraperitoneal injection of the VC-VK3 combination into immunocompromised mice increased life span by 46%. Furthermore, administration of VC-VK3 combination 3 h before administration of a variety of chemotherapeutic agents increased life expectancy up to 143%. Although the mechanism of action of these vitamins has not elucidated, their antitumor activity has been attributed to redox cycling of the vitamins and the possible generation of peroxides and other ROS followed by membrane lipid alteration, Dnase activation and DNA destruction by the VC-VK-3 combination in the catalase-deficient cancer cells (Noto et al. 1989, Taper et al. 1987 and 1992).

In previous experiments conducted in their laboratory, the VC-VK-3 combination exhibited synergistic antitumor activity against two androgen-independent human prostate cancer cell lines (DU145 and PC3) and a battery of seven other urologic tumor cell lines. Although the individual vitamins exhibited antitumor activity at high concentrations, coadministration of the vitamin in a VC-VK3 ratio of 100:1 potentiated antitumor activity 4-to 61-fold even when exposure times were as short as 1 h. Exogenous catalase destroyed this antitumor activity and implicated H2O2 and other ROS in the mechanisms of these vitamins (Venugopal et al. 1996a and 1996b). Electron microscopy revealed vitamin induced perturbation of nucleolar, mitochondrial and lysosomal structures (Gilloteau et al. 1995, Jamison et al. 1996). Despite the mitochondrial damage, tumor cells did not die from ATP depletion. However, vitamin treatment decreased DNA synthesis, slightly increased protein synthesis, induced a G1 phase block in the cell cycle, triggered the degradation of DNA and decreased cellular thiol levels (Jamison et al. 1996, Venugopal et al. 1996a and 1996b). These results suggest that redox cycling of the vitamin combination increased oxidative stress until it surpassed the reducing ability of the cellular thiols and cellular or genetic damage ensued.

In-Vivo Antitumor Activity Of The Vitamin C-Vitamin K-3 Combination

In recent in vivo studies designed to determine the effect of vitamin administration on the life span of nude mice, DU145 cells were given by i.p. injection; the vitamin combination was administered orally for 1 week before tumor implantation in a single i.p. injection 48 h after tumor implantation or both orally and by i.p. injection. Sham-treated mice lived on average of 60 +- 4.7 d. Mice receiving i.p. vitamin and mice receiving oral vitamin survived 66 +- 12 and 71 +- 15 d, respectively. Mice receiving both oral and i.p. vitamin lived an average of 69 +- 4.6 d. The difference in mean survival time of the control mice and the mice receiving oral and i.p. vitamin is significant ($P << 0.01$). In addition, 25% of the mice receiving oral vitamins were long-term survivors. One month after the death of the last mouse, surviving mice were killed and autopsied. These mice showed little if any tumor burden.

The results of additional in vivo studies, designed to determine the effect of vitamin administration on the growth of solid tumors in nude mice, demonstrated that administration of clinically attainable doses of oral vitamins given free access in drinking water could significantly reduce the growth of solid tumors in nude mice ($P < 0.05$). These result suggested that the continuous presence or periodic reintroduction of vitamins into the host to maintain elevated circulating levels of vitamins may be required to obtain the optimum antitumor activity and probably mirrors the lability of the vitamins.

Analysis of sections of tumors taken from mice used in solid-tumor growth experiments indicate that the vitamin combination induced a novel type of cell death called autoschizis (Gilloteaux et al. 1998), with degradation of tumor cell DNA (RNA) induced by alkaline and acid Dnase (and possibly Rnase) as one of the principal effectors of tumor cell death (Taper et al. 2000). Furthermore, nude mice receiving the vitamin combination by oral gavage for 4 weeks did not exhibit any significant bone marrow toxicity, changes in organ weight or pathologic changes in these organs. Because the vitamin combination is a chemosensitizer (Taper et al. 1987) and a radiosensitizer (Taper et al 1996), combined VC and VK-3 administration may be considered a new nontoxic adjuvant cancer therapy than can easily be introduced into the classical protocols of clinical therapy without any supplementary risk for patients (Taper et al. 2000).

Safety Of Vitamin C And Vitamin CK-3 In Humans

Vitamin C usage in humans is well documented and it is well tolerated in animals. Mice given daily vitamin C doses of 6.5 g/Kg body weight for 6 weeks and 2g/Kg for 2 years showed no abnormal weight changes, mortality rates, hematochemistry, hematology, histology, or pathology which differed from controls (Handbook of Vitamins, Chapt 5, Marcel Dekker, 1984). F. R. Klenner, M.D., (Physician's Handbook of Orthomolecular Medicine, 3rd Addition, Pages 51-59 supplies a treatment table of therapeutic doses ranging from 35,000 mg per day for a 220 pound man to 1,200 mg per day in infants.) He likewise uses 60 mg/kg/day or 2180 mg per day and 75 mg per day as maintenance doses for these respective groups. The only systemic toxicity noted at these doses has been diarrhea and gastrointestinal upset. If that occurs, the doses are given by injection that bypasses these complications.

Recent unsupported reports have appeared in the literature suggesting very large doses of vitamin C may have adverse effects because of the large antioxidant effect on the system. There is no animal or human data to confirm this risk. Long-term animal data does not bear this out, and no human trials are underway. To date this concern remains theoretical. In this study, the 2000 mg. per day of Vitamin C exceeds recommended daily doses, but appears by all scientific data to date to be safe and well tolerated.

Vitamin K, due to its fat solubility is sequestered in the liver, and has also been reported to disrupt the clotting mechanism, producing clots and the possibility of thrombotic phenomenon. Vitamin K_3, a synthetic VK derivative also known as menadione, is water soluble in the bisulfite form and does not appear to accumulate in appreciable amounts in the liver. We studied the livers of nude mice given appreciably larger doses of K_3 and found no toxicity. The same was true for bone marrow or clotting disturbances. A current life-span toxicity study in CH3 inbred rats is underway with the vitamin combination, with no appreciable toxicities seen to date.

The LD_{50} of VK_3 in mice is 500 mg/Kg (PSEBM 43: 125-128, 1940). No mortality was observed in mice for oral doses of 200 mg/Kg (PSEBM 43: 125-128, 1940). In the same study, chronic toxicity studies were performed in which oral doses of VK_3 (250 mg/Kg, 350 mg/Kg or 500 mg/Kg) were administered daily for 30 days. The 500 mg/Kg dose was toxic while the 350 mg/Kg dose produced a marked drop in erythrocyte count and hemoglobin. The 250 mg/Kg dose did not affect either of these two parameters or the growth curve of the animals. Furthermore, in phase I clinical trials in humans, vitamin K_3 has been administered at doses of 400-500 mg/day over 3-5 consecutive days without any appreciable toxicity (Proc ASCO 3:93, 1984). During a telephone communication with Steve Akman (one of the investigators in this study), he told us that VK_3 did not produce toxicity in humans even with protracted administration at these doses. Phase I and Phase II clinical trials have been performed using VK_3 in conjunction with

mitomycin C (a drug which is far more toxic than VC) for lung and gastrointestinal cancers have documented the chemodulatory effect of the vitamin in humans (Invest. New Drugs 13: 157-162, 1995; Cancer Chemother Pharmacol 36: 293-298, 1995; J Cancer Res Clin Oncol 121: 103-106, 1995). In these studies, VK_3 was well tolerated even though it was administered i.v. when it is more toxic than oral administration. Dr. James Doroshow, one of the investigators in these studies, has stated that they stopped their clinical trials with VK_3 because of the lack of availability of the vitamin.

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TETRATHIOMOLYBDATE ("TM")

Information and Informed Consent For Its Use

INTRODUCTION:

An experimental drug called tetrathiomolybdate (referred to from here on as "TM") is currently undergoing clinical trials at the University of Michigan. TM is known to decrease copper levels in the body by a process called "chelation". In simple language, TM binds copper to a protein, forming a complex which can then be excreted from the body. Copper is used by many organs in the body, but the use which is of interest here is that it is essential to the growth of new blood vessels, a process called "angiogenesis". ("Angio" means blood vessel and "genesis" means new formation.) Whenever tumor cells "set up housekeeping" in the body, blood vessels are necessary to provide nourishment for their growth. Once a tumor reaches the size of two millimeters it needs a blood supply to maintain itself. Without an adequate level of copper in the blood, this new blood supply cannot form and thus the tumor cannot enlarge.

TM has previously been used safely and successfully at the University of Michigan for children and adults with Wilson's Disease, a condition in which copper accumulates in high levels in the tissues. A Phase I clinical research study (testing safety and dosage) has just been finished at the same institution in which TM was used in patients with a large variety of Stage IV cancers. (See attached abstract.) Phase II studies on 100 patients (specifically testing efficacy) are currently underway. Five of six patients in the Phase I study who were able to achieve a target range of copper and maintain it there for 90-120 days achieved stable disease and remain stable a year later.

COMMONLY ASKED QUESTIONS:

How does TM work?

TM is a complex molecule of sulfur and molybdenum that forms a stable three-part complex with copper and protein. (Chelation). Taken with food, it binds to the copper in the food and keeps it from being absorbed. It also binds copper in the saliva and gastric juices and allows it to be excreted rather than absorbed. When TM is given on an empty stomach (2 hours away from any food), it is absorbed into the blood stream where it forms complexes with copper and serum albumin (a protein in your blood). This copper complex cannot be taken into the cells and is gradually excreted through the bile and the urine.

Does TM work for all types of cancers?

At present we cannot give a definitive answer because it has not been tried on all types, although a wide variety of cancers were used in the Michigan study. As a general rule, if the cancer depends on angiogenesis for growth, then TM should work. In addition to solid tumors, multiple myeloma, lymphoma, and leukemia are angiogenesis dependent.

Where is TM available?

TM is produced and distributed by several compounding pharmacies in this country. A physician's prescription is required to obtain it. The price is about the same everywhere and I would be very suspicious of a pharmacy that claimed to give you a cut rate. It is very sensitive material that needs to

be kept in an oxygen-free environment prior to compounding, and the compounding process is arduous. It is good to have an experienced pharmacist who does this on a regular basis and can answer all your questions accurately. We use the Prescription Center in Wisconsin. The pharmacist, Wayne Loveland, can be reached at (800) 203-9066. The cost is approximately $2.25 a capsule and you will use 180 to 300 capsules a month for about the first three months, depending on whether you are on the "fast track" or not. (See below). After that, if you have reached target, the cost decreases depending on how much it takes to keep you at your target level.

How do I get started?

First, you have to find a physician who is willing to write the prescription and follow you carefully while you are attaining target, as well as on an on-going basis. Since TM is not yet formally approved by the FDA for this indication, most oncologists will not write a prescription. We do know oncologists who are willing to order blood work and follow a patient's course if we write the prescription. (A prominent oncologist from a medical center contacted me recently to write a prescription for one of his patients.) In other cases, family doctors are willing to do the same thing once they understand the rationale and their responsibilities. If you want Partners for Health to write your prescription, you will need to make an initial visit on site.

Second, you have to get baseline blood tests for serum copper, zinc, and ceruloplasmin (the protein that carries copper in the blood.) It is also necessary to get a CBC (complete blood count) because low copper levels can sometimes depress the bone marrow and this has to be watched closely. After this is done, you can start without waiting for the results to be reported. Only a few labs in the country do copper and zinc and so your lab will have to send them out. The process takes about a week. Many labs also send out the blood for ceruloplasmin, but the turn-around time for this should not be longer than 48 hours. If it is longer, you need to find a lab that will give you a faster turn-around time because ceruloplasmin levels are the ones we follow during the lowering of copper and results are often needed on a very timely basis.

At first you will get a ceruloplasmin level and CBC one month after starting TM and then every two weeks until the ceruloplasmin is down in the low teens, at which time you will have to have the blood test once a week until you are stable. The goal is to lower the ceruloplasmin to 20% of baseline. For example, if your initial ceruloplasmin is 40, your goal will be 8. This is the level at which stable scans were achieved in the University of Michigan Study. It takes a mean of 50-60 days to get to target. Once you have been at target for three months you can expect to see "stable scans" i.e. no further tumor growth.

Why does it take three months after reaching target to see stable scans?

The target level of ceruloplasmin reflects what is happening in the blood. Once the level of copper is low in the blood, we speculate that it then comes out of the tumor. Since tumors tend to collect a lot of copper, it may take time to make the tumor itself copper-deficient. When copper starts coming out of the tumor, the copper and ceruloplasmin levels in the blood may actually appear to increase. This is actually a good sign and the level will decrease over time. Once copper is chelated out of the tumor, which takes about three months, it is postulated that the tumor is no longer able to make new blood vessels to keep it going. The recommended procedure is to have scans three months after the target is reached and then repeat the scans at the six month mark. If the TM has been successful, the repeat scans should be stable, i.e. no evidence of tumor growth. (*Note: Tumors can continue to grow to some extent during the three months after achievement of the target.)

What is my dose of TM and how is this managed?
There are two "tracks" for starting on TM:

1) If you have normal copper levels and stable or slowly progressing disease, you will be on the "usual track". You will take one 20 mg TM capsule with each meal to prevent copper absorption and three capsules on an empty stomach at least two hours away from ood. We have found that the best way to take the empty stomach dose is in the middle of the night if you get up to use the bathroom—just have the bottle of pills and a glass of water on a stand next to the toilet and make it a habit.

2) If you have high copper levels and progressive disease, you will be on the "fast track". You will take two 20 mg TM with each meal and four in the middle of the night, or on an empty stomach.

As your ceruloplasmin level decreases and you get close to target, the physician supervising you will adjust the dose accordingly. This can be a very delicate procedure and requires complete cooperation on your part, i.e. being compliant with exact doses and getting your blood work done in a timely fashion and reported to the physician. This process is called "titrating" your dose and means making fine adjustments up and down to find just the right amount that will keep you at target. This can vary widely with different people. We will give you a graph for keeping track of your progress at home. You are definitely a partner in this venture.

How should I store my TM?
Originally we were told to store it in the freezer, but now know that this is not necessary. Actually, if you do not have a frost-free freezer it may cause the TM to collect moisture. The most important thing is that the TM not be exposed to air or moisture insofar as this is possible. Always keep it in the container in a cool, dry place. Don't take capsules out far ahead of when you will use them. We have asked the pharmacist to stuff the bottle with cotton to keep down the air space as you use the capsules. The TM is stored under a special gas until it is put into capsules. When you receive your capsules, they have a 90% shelf-life of 8 weeks. This means that in two months they will not have degraded more than 10%. To be on the safe side, we ask you to order only one month's supply at a time.

What side effects might I expect from the TM?
Although the Michigan study reported no side effects, we have seen a few. None are especially serious unless you are on chemotherapy at the same time. (To be discussed later.)

–Gastrointestinal symptoms seem to be the most common, i.e. sulfur "burps" within 30' of taking the TM; slight nausea; gastric reflux; constipation at the onset of treatment and/or diarrhea later on. (All of these symptoms can be treated with Pekana remedies.)
–Some people experience leg cramps at night that can be very painful. Usually increasing your intake of magnesium will take care of this.
–When first taking TM some people experience increased fatigue. This usually resolves with time or may come and go.

–Other reported symptoms have also been transitory and consist of migratory joint pain, metallic taste in the mouth, "stomach ache", headache, and aggravation of pre-existing neuropathy.

–Bone marrow suppression can occur in some circumstances. The University of Michigan study reported no significant bone marrow suppression until the ceruloplasmin was at or below target level. We have seen some lowering of the WBC (white blood count) and Hb (hemoglobin) at higher than target levels, even in those not currently on chemotherapy. If the depression is mild, it is of no particular concern and seems to resolve with time. **If you are on regular or anti-angiogenic chemotherapy, in addition to TM, careful attention must be paid to the blood counts on a weekly basis.

Please keep track of all possible side effects on your flow sheet and report them to us.

Can I take TM if I am on chemotherapy?

Yes, however, this has to be carefully coordinated with your oncologist because the combination of chemotherapy and TM is more likely to produce bone marrow depression. You will need to have weekly CBC's and may need to take leukine (GMCFS) to increase your white blood cell count and/or procrit or epogen to increase your red blood cell count. Be sure that you take leukine rather than neupogen for the white cells because neupogen is an angiogenic agent whereas leukine is mostly anti-angiogenic. Let us know if you need literature references regarding this.

What if I have to have surgery while I am taking TM?

There is no hard evidence that low copper interferes with wound healing, but theoretically it could. When TM is discontinued, copper levels rebound quickly. Notify your physician, who will cut your dose of TM to bring you to a low normal level for approximately six weeks postoperative.

How does TM affect radiation therapy?

Actually, conventional radiation therapy is more effective when the copper level is low.

What if I neglect to take my TM or decide to stop it once my copper level is lowered?

In the Michigan study they found that when TM is discontinued, the copper level reverts to normal in a few days and tumor growth seems to spurt. DO NOT UNDER ANY CIRCUMSTANCES STOP TM ONCE YOU ARE CLOSE TO TARGET WITHOUT CHECKING WITH YOUR PHYSICIAN.

What is the role of zinc in my TM treatment?

Studies at the University of Michigan showed that maintaining zinc at 140-150 micrograms in the blood helped to decrease copper. The ideal copper to zinc ratio is 1:3, i.e. your zinc level should be three times your copper level. A direct correlation between cancer and zinc deficiency has been shown. On the other hand, too much or too little zinc can be immunosuppressive. We usually recommend that you take 60 mg of zinc specifically in the form of zinc citrate at night before you go to bed on an empty stomach. Since zinc can sometimes cause gastric irritation, you may take it with a couple of rice crackers if that is the case. NOTE THAT RAISING ZINC LEVELS MAY SOMETIMES GIVE A FALSE HIGH PSA (prostate specific antigen) READING.

What if I am totally compliant with taking my TM and my ceruloplasmin will not go down?

We postulate that when the liver is not functioning properly it has a need for extra sulfur. In this situation it uses sulfur from the TM, leaving TM unavailable to chelate copper. In that case we give extra supplements such as MSM, etc to supply sulfur to the liver and allow TM to do its job. Your physician will discuss this with you.

Do I need to stay on a low copper diet while I am taking TM?

Patients in the Michigan study were not put on low copper diets. We have found that it is best (and faster) if you stay

away from high copper foods. Two foods that you should definitely not have are organ meats and shellfish which are very high in copper (except for scallops). So far we have not found a very reliable table of copper content of foods since a lot of the content depends on the area of the country in which the food is grown. Generally, whole grains, especially buckwheat and wheat, nuts, chocolate, molasses, dried beans, tofu, black pepper, yeast, and dark leafy greens are known to be high in copper. Be sure if you do eat these foods you are taking your TM with the meal so the ingested copper can be chelated out. Generally, the TM taken at the conclusion of a meal will chelate copper out of the food ingested.

Do I need to fast before getting my blood tests?–the lab says that I should.
The tests done in the Michigan study were not done fasting. It is probably a good idea not to take zinc for 24 hours before you do a zinc test. (You will only need to do copper and zinc levels once a month. The rest of the time we will be following only the ceruloplasmin.)

What supplements do I need to take to support the copper-lowering process?
This varies somewhat from individual to individual. Basic recommendations are for zinc, taurine, alpha-lipoic acid, N-acetyl-cysteine, as well as an all-around good supplement program for your particular challenge. Quality supplements are essential -- many on the market have been shown to be ineffective at best. We can help you devise such a program if you so desire. Most of our patients are also taking either Vioxx or Celebrex, pharmaceutical COX-2 inhibitors which have an additional anti-angiogenic action, as well as various herbal formulas that have been shown to be anti-angiogenic. Green tea has such an action, and it is good to drink a moderate amount each day. (We have a separate paper on COX-2 inhibitors.)

How does low-dose chemotherapy fit into this picture?
Fairly new on the oncology scene is the concept of low-dose anti-angiogenic chemotherapy. Used in small weekly doses, many chemo agents act to inhibit growth of blood vessels to tumors rather than killing the tumor directly. A number of our patients with Stage IV disease have responded well to a combination of TM and low-dose chemotherapy. Everything is anecdotal at this point so most oncologists are not participating. Some are, however. We are writing a separate information sheet on low-dose chemo so if you are interested, just request it.

What about copper in my drinking water?
This can be a significant source of copper ingestion, especially if you have copper pipes. The best thing to do is to get your water tested (look under Water Systems in your yellow pages for a lab near you.) Your water should have less than .1 mg of copper. DO NOT UNDER ANY CIRCUMSTANCES USE DISTILLED WATER - it is energetically “dead” and can leach minerals out of your body. The best filter to install in your home is a reverse osmosis filter. Some patients have found that the Multi-Pure filter removes an adequate amount of copper. It is best not to get most of your drinking water from plastic bottles, since carcinogens are leached from many types of plastic.