

## June 1997 Issue | Clinical Nutritionist and Compounding Pharmacist

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Welcome to *Functional Medicine Update* for June 1997. This month we will focus on Food, Nutrients, and Pharmacology in Functional Medicine and explore the clinical applications of specific biomimetic or nutritional substances in modulating physiological function and improving health in individuals with certain types of diseases.

In men, one possible side effect of anti-hypertensive drugs is impotence, a situation that reduces compliance or quality of life. As a consequence, the search continues for managing the hypertensive individual who has no obvious organicity that contributes to the elevated blood pressure. Instead, it is a functional change in the vascular tone that relates to what we call essential hypertension. The term "essential" is rather humorous, suggesting that hypertension is a requirement for every middle-aged, success-oriented individual in our society.

Elevated blood pressure is associated with increased risk of stroke and heart disease and would be considered a morbid covariable with a number of other risk factors that could decrease life expectancy and health span.

A recent issue of *New England Journal of Medicine* (1997;336:1117) reported on a clinical trial studying the effects of dietary patterns on blood pressure. The results of this study showed a reduction of blood pressure, on average, of 11.4 mm Hg systolic and 5.5 mm Hg diastolic by dietary intervention in individuals with essential hypertension. These were individuals who had systolic pressures above 140 mm Hg and diastolic pressures above 90 mm Hg at rest, who would typically be candidates for traditional anti-hypertensive therapy. The results of this study, which were brought about by nutritional intervention alone, are comparable to those achieved with many anti-hypertensive drug therapies.

What was the nutritional intervention? We all know that obesity, sodium intake, saturated fat intake, and alcohol consumption have an adverse influence on blood pressure. It would be no surprise, therefore, if this was a sodium-, saturated fat-, or alcohol-restricted diet. But those substances were not the principal focus of this clinical trial, which was conducted at the Welch Center for Prevention, Epidemiology, and Clinical Research at the Johns Hopkins University in Baltimore, Maryland. This study used a diet enriched in fruits and vegetables, as contrasted to a placebo-controlled diet, which was a lower total fat diet with reduced saturated fat and sodium.

The concept of food as an alternative to pharmacological intervention applies as well to other diseases,

such as breast cancer. In a recent paper in the *Journal of the National Cancer Institute* (1997;89:466), Boyd et al. discussed reductions of mammographically dense tissue among women undertaking a low-fat, high complex carbohydrate diet in a randomized diet trial. The women, aged 30 to 65 years, had baseline mammographic images showing radiological densities in at least 50 percent of the breast area. This is known to be an early-warning risk factor for breast cancer. The women assigned to dietary intervention were taught to make a major isocaloric dietary change, with a goal of approximately 15 to 20 percent of total calories as fat. Among the 817 women (403 in the intervention group and 414 in the control group), there was marked reduction in radiographically dense tissue in the women on the lower-fat, higher complex carbohydrate dietary intake.

A higher complex carbohydrate diet contains more unrefined foods and less processed foods. Not only do you increase unrefined starch and fiber and reduce total fats with such a diet, but you also increase the intake of literally thousands of phytonutrient compounds contained in unrefined foods. These phytonutrients have profound biological response-modifying function in the body. It is this rich array of substances -- vitamins, minerals, essential amino acids, essential fatty acids, accessory nutrients, and the phytonutrients -- that is opening the door for nutrient pharmacology as a primary tool in functional health and functional medicine.

To further extend the discussion of the endocrine effects of dietary intake, let us look at soy protein isolate. We have, in *FMU*, previously discussed the influence of genistein and daidzein, two isoflavones found as phytonutrients in soy, on estrogen reception, estrogen binding, and estrogen metabolism in women and men. Dr. Herman Adlercreutz and Dr. Kenneth Setchell have studied soy isoflavones and hormone balance for 25 years and published hundreds of papers in this area. As a principal presenter at the Third International Symposium on Functional Medicine in Vancouver, British Columbia, in 1996, Dr. Adlercreutz gave some powerful admonitions about the need for increasing our dietary intake of soy products, as well as flax, barley, and rye. These foods contain lignans that work along with the soy isoflavones genistein and daidzein to improve digestive flora, hormone metabolism, and hormone signal messaging systems.

A recent paper in *Cancer Epidemiology, Biomarkers & Prevention* (1996;5:785) discusses the stimulatory influence of soy protein isolate on breast secretion in pre- and postmenopausal women. It shows once again that soy products contain bioactive substances that modulate and influence the function of the endocrine system. Soy foods have previously been reported to have protective effects against premenopausal breast cancer in Asian women. This study, however, followed up on the potential physiological effect of dietary soy on the function of the breast gland function itself. Investigators evaluated the influence of the long-term ingestion of commercial soy protein isolate on breast secretory activity.

Nipple aspirate fluid of non-Asian women was examined to see if it was altered before and after the consumption of soy products. At monthly intervals for one year, 24 normal pre- and postmenopausal white women, ages 30 to 58, underwent nipple aspiration of breast fluid and gave blood and 24-hour urine samples for biochemical studies. No soy was administered in months 1-3 and 10-12. Between months 4 and 9, however, the women daily ingested approximately 38 grams of soy protein isolate, which contained 38 mg of genistein. (In previous editions of *FMU* we discussed evidence that modulation of hormones can be clinically demonstrated with genistein intake between 20 and 40 mg a day.) Nipple aspirate fluid volume, gross cystic disease fluid production concentration, and fluid aspirate cytology

were biomarkers of possible effects of soy protein isolate on the breast. Plasma concentrations of estradiol, progesterone, sex hormone binding globulin, prolactin, cholesterol, HDL-cholesterol, and triglycerides were also measured. Compliance, which was assessed by measuring genistein and daidzein and their metabolites in a 24-hour urine sample, was excellent in this study. Compared with nipple aspirate fluid volumes obtained in months 1-3, volume increased two- to sixfold during months 4-9. This was the soy-supplemented period in all premenopausal women. Minimal or no response was found in postmenopausal women. No changes were found in plasma prolactin, sex-binding hormone globulin, cholesterol, HDL-cholesterol, or triglyceride concentrations.

Compared with concentrations found in months 1-3, when there was no soy, plasma estradiol concentrations were elevated throughout a composite menstrual cycle during the months of soy consumption. No significant changes were seen in plasma progesterone concentrations. The authors concluded that the findings do not support an *a priori* hypothesis that soy is necessarily bad or good for premenopausal women. It does indicate that prolonged consumption of soy protein isolate has a stimulatory effect on breast tissue in some women, characterized by increased secretion of breast fluid, appearance of hyperplastic epithelial cells, and elevated levels of plasma estradiol. These findings suggest an estrogenic-like stimulus in these women from the isoflavones genistein and daidzein and indicate once again that soy contains bioactive ingredients that can modulate function. In women who consume large amounts of soy, the metabolism and excretion of these estrogen-like compounds and estradiol would depend, therefore, on proper liver detoxification, gut function, and enterohepatic recirculation and excretion of the metabolized steroids. It is a complex process, and we cannot assume soy would have the same effect in every woman. It is necessary to match diet to specific physiologies and look at responses to these isoflavones in the endocrine systems of premenopausal women

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## INTERVIEW TRANSCRIPT

Clinical Nutritionist and

Compounding Pharmacist

**JB:** Gary, you come from a rich tradition. It is wonderful to have you on *Functional Medicine Update*. Why would a pharmacist with the traditional training of pharmacy become a clinical nutritionist and a compounding pharmacist?

**GO:** Approximately 15 years ago, when I was working with a well-known environmental physician in Dallas, I saw a unique niche where medical patients had very special needs and nothing was available. I had been taught to specialize in any profession, so I joined this organization and started sourcing out raw materials, developing formulas and delivery techniques for hard-to-find hypoallergenic nutritional supplements such as preservative-free sterile injections. I felt like Klinger in the old "Mash" show: I could find anything. It was exciting and mentally challenging. I found that I had to figure out how the body functioned. I was fortunate enough to work with bright M.D.s and registered dietitians. After I had done this for six or eight months, people were coming to me to ask me for my expertise. I think that's when I was bitten with the desire to do custom compounding. That is how I got into custom compounding.

**JB:** With your company, ApothèCure, you serve the needs of practitioners around the country. I am sure you get many requests for unusual new compounds. What is the legal status right now for compounding pharmacists?

**GO:** As one of my attorneys told me this morning, law is an art and not a science. Compounding pharmacy is growing by leaps and bounds, and as long as we stay within the boundary of what we call the triad -- the physician, the patient, and the pharmacist involved -- there are no problems involved. If we knew what the FDA was going to be thinking tomorrow, however, we would be geniuses.

Compounding pharmacy is growing as pharmacists get shoved out of the corner drugstore. They get burned out by the managed healthcare system and are looking for specialties. This seems to be one of the biggest specialties they're going into. Pharmacists call me and ask what I think about their getting into compounding pharmacy. I tell them that if we had 10 times the number of compounding pharmacists there would still be plenty of business to go around. People now desire therapies and medications other than the off-the-shelf variety. We know that is happening from the reports of pollsters. The demand is increasing for compounding pharmacists to make the things desired by alternative and progressive physicians, chiropractors, dentists, doctors of veterinary medicine, and naturopathic physicians.

**JB:** For those who may not be familiar with how compounding pharmacy is actually related to the law and the pharmacist's field of expertise, tell us a bit about how this tradition grew up and why it lay dormant for so long and seems to be now having a resurgence.

**GO:** In compounding pharmacy we are basically taking an old art and bringing it forward with added new technology and new availability of raw materials. Before 1920 or so, all prescriptions were compounded by the pharmacist. Then, with the evolution of pharmaceutical companies, Lilly, Upjohn, and other companies started making these things. Medications were then made for average patients, so the physician had to match the patient to the drug instead of, as in custom compounding, matching the drug to the patient.

Compounding then became dormant, and pharmacists basically became dispensing pharmacists. They would go to the shelf, pull a bottle off, count it out, and give advice to the patient. This happened until about 15 or 17 years ago, when more and more physicians began to demand pharmaceutical products -- over-the-counter products and nutritional products -- that were not standard products off the shelf. They were realizing that every individual had a unique biochemistry, and they wanted to design the treatment to the patient instead of the patient to the treatment. So compounding pharmacy began to take some courageous steps forward. A company in Houston made formulations, raw ingredients, and delivery techniques available to more and more pharmacists, and it grew rapidly. There are big compounding pharmacists and the corner pharmacists who make five or 10 compounds a day. I would say there are somewhere between 3,000 and 5,000 highly qualified compounding pharmacists in the country today.

**B:** At ApothèCure specifically, what kinds of compounds do your doctors seem to be most interested in? What's hot in the news right now, from your perspective, as both a pharmacist and a certified clinical nutritionist?

**GO:** Many years ago I decided I wanted to work with the really progressive alternative physicians in our organization, because this is the most challenging. You have to know how the body functions in order to

understand how the body doesn't function. The physicians I work with fall into that category. Some of the really hot things that are going on in the country today are demands for such things as natural hormone replacement therapy. This is where you have to have a compounding pharmacy to blend hormones and nutrients together according to very tight regulations. The physician probably follows up the female hormone replacement patient more closely than he or she does with a typical patient. Normally a doctor may write a prescription and not see the patient for another year.

Replacement therapy with natural hormones involves the custom formulation of hormones that occur naturally in a healthy, pre-menopausal female. They are put together in that same ratio in varying total strengths, such as the triestrogen (which is estriol), estradiol, and estrone in an 8:1:1 ratio. Also, progesterone in various delivery techniques is being prescribed for every hormone replacement therapy patient today.

The newest thing in hormone replacement therapy, in both men and women, is the administration of testosterone. Microcrystalline testosterone works best. So, hormone replacement therapy is hot today.

Custom nutritional blends are also hot today. Instead of buying a multivitamin at the drugstore, which may not contain what you really need, a lot of physicians are using laboratory techniques to determine what a patient needs. Again, the custom compounding pharmacist is involved, particularly if he or she is nutritionally aware. At ApothèCure we can put together a custom-blended nutritional supplement that exactly fills an individual's biochemistry deficiencies.

Anti-aging is coming on the scene very rapidly, and medical professionals who are operating in the anti-aging field are in need of growth hormone-releasing nutrients and human growth hormone. Again, enter the compounding pharmacist.

Through compounding pharmacies, several new things are developed, such as liposomal delivery. We do that at ApotheCure, as well as a lot of other compounding pharmacies. We can deliver several products through the skin, such as anti-inflammatories or nonsteroidal anti-inflammatories, hormones, muscle relaxants, and even nutrients. That's one of the new things. Glandular therapy is getting very big. In the anti-aging field, dermatological antioxidants for the skin are being addressed. Weight loss is getting very exotic now. Instead of just giving somebody a central nervous system stimulant, we have a lot of physicians who are actually trying to go in and duplicate brain neurotransmitters.

One of the other areas that is extremely interesting today is the treatment of parasites. Anybody who travels anywhere faces the possibility of having various parasites, and through appropriate lab work, we can determine what parasites are in the gut or in the body and then custom design a product. It could be a blend of herbs and pharmaceuticals to treat a particular patient.

Body building and antioxidants in ophthalmics are popular. Products are being researched right now to reverse cataracts and macular degeneration. A lot of physicians are using topical eyedrops. They're using IV therapy with ingredients such as taurine.

Another area that a lot of compounding pharmacists, particularly ApotheCure, are into is neurotherapy and prolotherapy where such things as procaines and irritants are injected into the body to reverse various conditions.

Alternative sleep aids are really big. We were doing a lot of custom amino acid blends for a lab up in Chicago when tryptophan was taken off the market and we could no longer get it. The lab considered taking its blend off the market. They determined that more than 70 percent of the patients whose urine they analyzed were deficient in tryptophan, and we couldn't get it. We were considering importing the bark of some West African tree that was high in tryptophan, when the Ph.D. I was working with said it was too bad I couldn't get the first metabolite, which is 5-hydroxytryptophan. Part of compounding pharmacy is the ability to source out raw ingredients, and we found 5-hydroxytryptophan and introduced that in the market nearly four years ago. Now it is being sold in health food stores over the counter. Nearly a year and a half ago, we were the first compounding pharmacy to reintroduce tryptophan onto the market by prescription. Gaba, GHB, melatonin, and pineal extract are all possibilities for custom-blended products coming out of a compounding pharmacy

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