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Women in Balance
In this issue, Dr. Bland discusses the ever evolving field of hormone metabolism and the challenges of modulating the neuroendocrine system with therapy.

Risk of Thromboembolism in Postmenopausal Women
The *British Medical Journal* recently published a systematic review and meta-analysis that aimed to assess the risk of venous thromboembolism in women using hormone replacement therapy. The researchers analyzed eight observational studies and nine randomized controlled trials. The meta-analysis of observational studies showed that oral estrogen, but not transdermal estrogen, increased the risk of venous thromboembolism. Results from the nine randomized controlled trials confirmed the increased risk of venous thromboembolism among women using oral estrogen. Although the authors of this meta-analysis state that more data are required to investigate differences in risk across the wide variety of hormone regimens, they did conclude that oral estrogen increases the risk of venous thromboembolism, especially during the first year of treatment. Transdermal estrogen may be safer with respect to thrombotic risk. REF #1

Signaling Mechanisms of Foods and Phytochemicals
Dr. Mark Mattson and colleagues from the National Institute on Aging recently published an article in *Neuromolecular Medicine* that Dr. Bland discusses. While there has been compelling evidence form epidemiological studies suggesting beneficial roles of dietary phytochemicals in protecting against chronic disorders, emerging findings suggest that several dietary phytochemicals also benefit the nervous system. These researchers suggest that using neurohormetic phytochemicals as base compounds for medicinal chemistry will likely result in the development of a range of drugs that enhance neuroplasticity and protect against synaptic dysfunction and neurodegeneration. REF #2

Dr. Bland also discusses an article in *Public Health Nutrition* by Dr. RM Ortega, as well as an interesting study that was a joint effort between Italian and Greek researchers that was published under the title "Local Food and Cardioprotection: The Role of Phytochemicals." This study was prompted by an interest in endothelial dysfunction and its implications in aging and was carried out by studying the effects of food plants collected in southern Italy on vascular function. Dr. Bland, himself, has recently authored an article on phytochemicals that may be beneficial in treating the metabolic syndrome. REF #3-5

Phytohormones as Agents for Preventing Osteoporosis
It has been suggested that phytoestrogens might be a safe alternative to hormone replacement therapy. A group of German researchers has recently published the results of a study on the osteoprotective effects of genistein, resveratrol, and 8-prenylnaringenin. This was an animal study using female rats that had undergone ovariectomy. The rats

received soy-free food, and according to their grouping, were fed estradiol, genistein, resveratrol, or 8-prenylnaringenin for 12 weeks. Bone biomechanical properties and bone mineral density were evaluated on the upper tibial metaphysic. The findings of the study indicated that treatment with 8-prenylnaringenin resulted in very good biomechanical properties and showed an increase in bone mineral density. Genistein had a smaller effect on bone biomechanical strength, while resveratrol did not have an effect on bone biomechanical strength or bone mineral density. This study was published in a 2008 issue of *Planta Medica*. REF #6

Dietary Proteins and Atherosclerosis Prevention

Recently, a review focused on the impact of dietary proteins from vegetable and animal sources, both on metabolic variables and on hypertension, was published in the journal *Atherosclerosis*. This article was a collaboration between researchers at the University of Milano (Italy) and the University of Kentucky. A major interest for atherosclerosis prevention has been addressed to vegetable proteins, particularly soy proteins. A full understanding of the mechanism of action of soy protein has become vital for the selection of the most appropriate forms of soy for treating hypercholesterolemia. In the last few years, other legumes have attracted the attention of research. The general impression is that their consumption may have a very favorable role in the prevention of dislipidemia, but the clinical data on legumes are still very scarce. In the case of biologically active peptides, there has been major progress in the area of blood pressure reduction by the use of ACE inhibitory peptides. REF #7

Because it remains unclear which components of soy protein are responsible for beneficial lipid changes, much research has focused on efforts to identify these. Clinical investigators have used a variety of isolated soy proteins; differing concentrations of isoflavones, trial lengths, and criteria for selecting subjects; and a variety of protocols. In a meta-analysis published in the *American Journal of Clinical Nutrition* in 2005, researchers attempted to combine the results of multiple studies with small or moderate sample sizes to increase their statistical power and enhance precision of the estimates of the effects of soy protein containing isoflavones or isoflavone extracts on changes in lipid concentrations. The conclusions of this analysis of 23 randomized controlled trials, which included pre-specified subgroup analyses, were that soy protein containing isoflavones significantly reduced serum total cholesterol, LDL cholesterol, and triacylglycerol and significantly increased HDL cholesterol, but the changes were related to the level and duration of intake and the sex and initial serum lipid concentrations of the subjects. REF #8

In a more recent meta-analysis—this one published in Atherosclerosis in 2008—British researchers aimed to determine the effect of a daily intake of 25 g of soy protein on blood lipids in adults with normal or mildly elevated cholesterolemia. After analyzing 30 studies containg 42 treatment arms, these researchers concluded that modest amounts of soy protein in the diet resulted in small, highly significant reductions in total and LDL cholesterol, which, when combined with other dietary measures, can make a useful contribution to blood cholesterol management. REF #9

Recent Study on Effects of Xuezhikang

The American Journal of Cardiology recently published the results of a multicenter study that was conducted to determine the effects of Xuezhikang (XZK), a partially purified extract of red yeast rice, on lipoprotein and cardiovascular (CV) endpoints in Chinese patients who experienced a previous myocardial infarction. Nearly 5000 patients participated in the study and were followed for an average of 4.5 years. Treatment with XZK significantly decreased CV and total mortality, decreased the need for coronary revascularization, and lowered total and low-density lipoprotein cholesterol and triglycerides, but raised high-density lipoprotein cholesterol levels. These researchers concluded that log-term therapy with XZK significantly decreased the recurrence of coronary events and the occurrence of new CV events and deaths, improved lipoprotein regulation, and was safe and well tolerated. REF #10

Clinician/Researcher of the Month

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Dr. Jane Murray earned her undergraduate and medical degrees from the University of California at Los Angeles. She completed her residency in family medicine at Santa Monica Hospital in Southern California and has taught and practiced medicine for over twenty years. Dr. Murray served as Director of Education for the American Academy of Family Physicians from 1986 to 1991 and as Chair of the Department of Family Medicine at the University of Kansas Medical Center from 1991 to 1998. Dr. Murray then co-founded the Sastun Center of Integrative Health Care. In addition to her practice, Dr. Murray continues to teach, conduct research, and speak widely to national audiences about the need to integrate conventional Western medicine with non-conventional approaches to health and illness.

Dr. Murray is Board Chair of Women in Balance, a national non-profit association of women, doctors, health professionals, and national organizations dedicated to helping women achieve optimal health, wellness, and hormone balance. Dr. Bland and Dr. Murray discuss a recent scientific publication about hormone therapy the group has authored; more information about this paper can be found at www.womeninbalance.org. In addition, Dr. Bland and Dr. Murray discuss the current state of research on hormone replacement therapy, including the results of some very large published studies by French researchers. REF #11-12

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