



These results showed evidence of an association between elevated ferritin level and risk of developing GDM among women without evidence of inflammation. Transferrin receptor levels were not associated with the development of GDM. Future studies are needed to confirm these results, to determine if there is utility in the routine measurement of ferritin, and to identify other markers of iron and inflammation.

Antihypertensive and Vascular Benefits of Blueberries in Postmenopausal Women

Written by Brian Hoyle

Daily consumption of about 1 cup of fresh blueberries may help reduce arterial stiffness and decrease blood pressure (BP) by improving vasodilation due to the increased production or bioavailability of nitric oxide (NO), said Sarah A. Johnson, PhD, RD, CSO, Florida State University, Tallahassee, Florida, USA.

Hypertension (HTN) is a modifiable risk factor for cardiovascular disease (CVD) [Go AS et al. *Circulation* 2013; Rosamond W et al. *Circulation* 2008]. HTN currently affects >77 million Americans [Go AS et al. *Circulation* 2013]. Postmenopausal women seem to be affected disproportionately. [Barton M, Meyer MR. *Hypertension* 2009; Rosenthal T, Oparil S. *J Hum Hypertens* 2000]. The causes of HTN are multifactorial but are partly due to endothelial

dysfunction, which results in decreased vasodilation and increased vasoconstriction. Endothelial dysfunction also increases stiffness of arteries, which is involved in the development and progression of both HTN and CVD [Wallace SML et al. *Hypertension* 2007; Bonetti PO et al. *Arterioscler Thromb Vasc Biol* 2003; Taddei S et al. *Curr Pharm Dis* 2003; Widlansky ME et al. *J Am Coll Cardiol* 2003; Koh KK et al. *J Am Coll Cardiol* 2001].

The treatment of BP in prehypertensive individuals and those with stage 1 HTN focuses on lifestyle modifications (eg, diet) [Chobanian AV. *Hypertension* 2003]. The polyphenol constituents of berries, including blueberries, appear to be beneficial in reducing cardiovascular risk, as judged from their effects on BP, endothelial function, and arterial stiffness [Rodriguez-Mateos A et al. *J Agric Food Chem* 2013; Basu A et al. *Nutr Rev* 2010]. However, the influence of blueberries on arterial stiffness measured by pulsed wave velocity (PWV) had not previously been studied.

Dr. Johnson and colleagues hypothesized that eating 22 g of freeze-dried blueberry powder daily for 8 weeks would reduce arterial stiffening and improve endothelial function, in turn reducing BP. The double-blind placebo-controlled trial comprised 48 postmenopausal women with pre-HTN or stage 1 HTN. They were randomly assigned to receive the daily blueberry powder (n=20) or the same daily quantity of placebo powder (n=20). Brachial BP and brachial-ankle and carotid-femoral pulsed wave velocity were measured at baseline, 4 weeks, and 8 weeks. Plasma levels of NO were measured at the same times.

Table 1. Effects of Blueberries on Blood Pressure

	Systolic Blood Pressure (mm Hg)		Diastolic Blood Pressure (mm Hg)	
	Blueberry	Control	Blueberry	Control
Baseline	138	138	80	78
4 week	136	136	77	78
8 week	131 ^a	139	75 ^b	80

^aSignificant difference (p < .05) compared with baseline. ^bSignificant difference (p < .01) compared with baseline.

Table 2. Effects of Blueberries on Arterial Stiffness

	Brachial-Ankle Pulse Wave Velocity (cm/s)	
	Blueberry	Control
Baseline	1498	1470
4 week	1464	1466
8 week	1401 ^a	1477

^aSignificant difference (p < .05) compared with baseline.

Table 3. Effects of Blueberries on Nitric Oxide Levels

	Nitric Oxide (μM)	
	Blueberry	Control
Baseline	9.11	9.81
4 week	13.86	9.20
8 week	15.35 ^a	10.73

^aSignificant difference ($p < .05$) compared with baseline.

Daily consumption of blueberry powder for 8 weeks significantly reduced systolic and diastolic BP (Table 1) and brachial-ankle PWV (Table 2). Also, NO production was significantly elevated at 8 weeks in those whose daily diet included the blueberry powder (Table 3).

While noting that these results need to be confirmed in a larger study, the researchers concluded that blueberry ingestion may result in increased NO production by endothelial cells, which may directly result in vasodilation and reductions in BP. Moving forward, further study is needed to assess the influence of dose on BP response and the effects of blueberry powder over more prolonged periods and in other populations.

Study Results Suggest That Flavones and Flavan-3-ols Protect Against Breast Cancer

Written by Toni Rizzo

Consumption of fruits, vegetables, and carotenoids has been shown to reduce the risk of breast cancer, in particular estrogen-negative (ER-) breast cancer [Jung S et al. *J Natl Cancer Inst* 2013; Aune D et al. *Breast Cancer Res Treat* 2012; Eliassen AH et al. *J Natl Cancer Inst* 2012; Zhang X et al. *Am J Clin Nutr* 2012]. Fruits and vegetables are rich in flavonoids, which are potential anticancer agents. Flavonoids have antioxidant, anti-inflammatory, anti-proliferative, and pro-apoptotic effects. A recent meta-analysis reported that flavonols and flavones, but not other flavonoid subclasses, were associated with a decreased risk of breast cancer, especially in postmenopausal women [Chang H et al. *PLoS ONE* 2013].

Most previous studies have focused on the association between 1 or 2 subclasses of flavonoids, and no studies have investigated proanthocyanidins. Furthermore, only 3 studies have stratified subjects by the ER status of the breast cancer. The objective of the Cancer Prevention Study II [CPS-II] Nutrition Cohort, presented by Ying Wang, PhD, Epidemiology Research Program, American

Cancer Society, Atlanta, Georgia, USA, was to evaluate the association of several flavonoids on the risk of invasive breast cancer in women stratified by ER status.

The study population included 73,640 women who returned a modified Willett food frequency questionnaire. A total of 56,630 postmenopausal women were included in the analysis after 1752 were lost to follow-up. Women previously diagnosed with cancer and those women who reported energy intake that was outside the acceptable range were excluded from the analysis. The women were followed until they developed breast cancer, they died, the last survey was returned, or June 30, 2009.

At a mean follow-up of 8.5 years, 2116 cases of invasive breast cancer, including 1498 ER+ and 218 ER- cancers, were diagnosed. Flavonoid exposure was assessed with the food frequency questionnaire; information from the USDA flavonoid, proanthocyanidin, and isoflavone databases; and scientific publications. The flavonoids assessed included flavones, flavonols, flavanones, anthocyanidins, flavan3ols, isoflavones, and proanthocyanidins. The women were categorized into quintiles of flavonoid intake. The median intake and range (mg/day) of total flavonoids for each quintile (Q) were Q1=9.5 (≤ 118.7); Q2=143.7 (> 118.7 to 171.0); Q3=201.4 (> 171.0 to 239.2); Q4=288.6 (> 239.2 to 363.8); and Q5=522.9 (> 363.8 to 2062.8). The mean age ranged from 68.4 to 68.9 years in each quintile, and ~98% of the women in each quintile were white.

The intake of flavones, but not other flavonoids, was inversely associated with total invasive breast cancer risk when evaluated by quintiles (p value for trend = .04) and continuous exposure (RR, 0.96; 95% CI, 0.92 to 1.00). When evaluated by quintiles, intake of no flavonoids was associated with ER+ or ER- breast cancer risk. When evaluated by continuous exposure, flavones intake was inversely associated with ER+ breast cancer risk (RR, 0.96; 95% CI, 0.91 to 1.00), and flavan-3-ol intake was inversely associated with ER- breast cancer risk (RR, 0.81; 95% CI, 0.67 to 0.97; Figure 1).

Dr. Wang concluded that these findings are consistent with the results of other research. The results suggest that