

Effects of Caffeine and Coffee on Women's Health: **Fertility, Menopause, Breast and Uterine Health**

Reviewed by Meri Rafetto, RD, Theresa Grumet, RD, and Gerri French, RD, MS, CDE.
© 2004 Teecino Caffé, Inc.

Women share unique physiological processes and lifecycle transitions related to their hormonal systems and physical bodies. Women suffer from many of the same diseases as men, and some conditions, like cardiovascular disease, affect women at high rates with devastating consequences. But many health challenges are faced only by women. Some of these have to do with sexual organs and hormonal systems, others center on the processes of mothering, menstruation and menopause. In regards to caffeine and coffee drinking, caffeine affects women differently.¹ Women not only have a greater sensitivity to caffeine than men, but they also may take much longer to detoxify caffeine and recover from its stimulating effects.² It is suggested that caffeine's influence on a variety of conditions in a women's body may be due to its demonstrated effect on the body's sex hormones. One of the actions of caffeine is that it causes increases in estrones, or female hormones, while it decreases available testosterone.³

Menstruation and Premenstrual Syndrome:

Throughout a woman's monthly cycle, hormone levels naturally fluctuate. Up to 40% of women of childbearing age experience some degree of premenstrual syndrome, and up to 10% suffer from severe symptoms.⁴ PMS (premenstrual syndrome) is a complex array of symptoms occurring between ovulation and menstruation that include: breast swelling and tenderness, weight gain, headache, abdominal cramping and bloating, nausea, joint pain, acne, pain, irritability, lethargy, fatigue, depression, anxiety and even hostility and aggression. PMS is not adequately explained by vitamin deficiency or hormone imbalance and most treatments including oral contraceptive, vitamins, diuretics or hormones are ineffective against all symptoms. Lifestyle changes including exercise, stress reduction and sodium and caffeine restriction can have a positive impact on PMS symptoms,^{5,6,7} and elimination of coffee drinking can reduce breast tenderness, nervousness and irritability.⁸

Fibrocystic Breasts:

Fibrocystic breasts are a common condition in which there is an increase in the fibrous and glandular tissue in the breasts. This results in noticeable tenderness, lumpiness that is non-cancerous and small nodular cysts. There is no specific treatment for fibrocystic breasts, but many women have found relief and pain reduction with caffeine elimination.⁹ Although the effect of caffeine on the development or reduction of fibrocystic changes in the human breast has shown inconsistent results, animal models demonstrate fibrocystic changes in the presence of caffeine intake.¹⁰ The disagreement in results of human studies may be explained by the difference between positive results from studies that include only women who are already prone to fibrocystic breasts and negative results from those studies that look at the entire population of women. On a clinical basis, caffeine reduction for those women who suffer from fibrocystic breasts continues to be an important recommendation for treating breast pain and fibrocystic lumps.¹¹

Fertility:

With the vast array of contraceptive choices available, women have greater control over their pregnancies, but for women and couples who are having difficulty conceiving, infertility can be a heartbreaking experience. According to statistics compiled by the Centers for Disease Control, 6.1 million women in the U.S. between the ages of 15 and 44 have an impaired ability to have children. An amazing 9.3 million women are using infertility services in order to become pregnant. Lifestyle choices, including cigarette smoking, alcohol consumption, being under or overweight and caffeine intake negatively affect a woman's fertility.¹²

Pregnancy:

When women become pregnant, there are a number of factors that influence the health of the developing fetus. The effect of caffeine is not completely understood, yet it does cross the placental barrier and women who consume caffeine during pregnancy have infants with statistically significantly lower birth weights.¹³ The stimulant effect of caffeine also has an effect on infants, and blood levels of caffeine are significantly increased during pregnancy as the time it takes for caffeine to be detoxified increases during pregnancy.⁴² Babies born to women who had high caffeine intake during their pregnancy exhibit signs of caffeine withdrawal after birth.

Breastfeeding:

As women are encouraged to breastfeed their infants, it is important for them to consider not only nutrition, but the effects of what they are consuming on their developing infant. What a woman eats and drinks while breastfeeding influences her child's health as substances pass from her bloodstream into breast milk. Caffeine becomes a component of breast milk, and it has been detected in breast milk even days after a woman has ingested it.¹⁴ Breastfeeding mothers are encouraged to limit their consumption of caffeine.¹⁵

Menopause:

Menopause is a natural transition experienced by all women in their life, but some women suffer from more pronounced symptoms than others. Many of the symptoms and conditions associated with menopause including hot flashes, difficulty sleeping, vaginal dryness, osteoporosis and increased risk of heart attack are exacerbated by coffee drinking and caffeine consumption. Coffee seems to have multifaceted effects on this life transition. The age at which a woman reaches menopause varies; height, socioeconomic status, moderate alcohol consumption and giving birth before age 25 delay the age of natural menopause, while a diet high in fat, cholesterol and coffee consumption accelerate the age at which menopause begins.^{16,17}

Mineral Absorption, Bone Density and Osteoporosis:

Caffeine interferes with the absorption of minerals including calcium, magnesium, potassium, and iron that are essential for good health. Menstruating women often lose more iron through blood loss than they are able to recover through diet alone and caffeine further compounds this problem by reducing iron availability up to 50%. The high acidity of both regular and decaf coffee increases the body's need for calcium to rebalance the body's natural alkalinity. There are several lifestyle factors

that influence bone density, and increase a woman's chance of developing osteoporosis, including: smoking, alcohol use, hormone replacement therapy, exercise, diet and coffee consumption.¹⁸

Heart Disease:

Heart disease has become the number one killer of women in the U.S. and much of the western world. Caffeine intake has been linked to many risk factors in heart disease, including high blood pressure, high cholesterol and high homocysteine levels. Women can exert some control over many of the lifestyle factors linked to cardiovascular disease by making modifications in diet, exercise, smoking, stress and caffeine consumption.

Of all the dietary habits that people find difficult to change, coffee drinking is one of the most challenging because it is so entrenched in cultural habits and caffeine addiction.¹⁹ Withdrawal symptoms can involve painful headaches, nausea, vomiting, and loose stools, as well as depression, fatigue and anxiety.^{20,21} People whose health problems would be ameliorated if they gave up coffee can improve their chance for successfully quitting coffee if they have both a satisfying alternative and a method to slowly decrease their caffeine intake to reduce withdrawal symptoms.

The following characteristics of coffee have an adverse effect on women's health:

- **Caffeine Increases Symptoms of Premenstrual Syndrome**
 - Drinking caffeine-containing beverages, including coffee, is associated with higher prevalence of premenstrual symptoms. This effect is dose-dependent; women who consumer larger quantities of caffeine experience more symptoms.²² Caffeine aggravates premenstrual syndrome,²³ including associated anxiety and depression.²⁴ In a treatment plan that is often self-defeating, women often self-medicate with caffeine while experiencing symptoms of PMS in an attempt to alleviate them. Unfortunately, this only exacerbates their negative symptoms.²⁵
- **Caffeine Combined with Pharmaceuticals Slow Detoxification**
 - Caffeine is metabolized by the liver, specifically the cytochrome P450 pathways. When caffeine is consumed with other drugs metabolized through this pathway, the rate of clearance of both caffeine and the drugs from the body are significantly reduced.^{26,27,28,29} Caffeine therefore remains in the body for much longer periods of time, increasing the effect of the morning cup of coffee. Most pharmaceutical drugs utilize this metabolic pathway, including oral contraceptives and antidepressants.
- **Caffeine Increases Breast Pain and Fibrocystic Breasts in Susceptible Women**
 - Caffeine consumption is associated with breast pain.³⁰ Women with breast pain who were counseled to eliminate caffeine found that abstaining from caffeine decreased or abolished their breast pain. This pain relief continued after one year of eliminating caffeine.³¹ Epidemiological studies link caffeine consumption with increased risk of developing fibrocystic breasts.³²

- **Caffeine Decreases a Woman's Fertility**
 - Consumption of caffeine can negatively affect a woman's fertility and her ability to achieve pregnancy; this is particularly the case with heavy caffeine intake.^{33,34,35} Caffeine has been shown to interfere with the egg's ability to implant in the uterus.³⁶

- **Coffee Drinking Is Associated with Presence of Heart Rhythm Irregularities in Pregnancy**
 - Pregnancy can often precipitate the occurrence of cardiac arrhythmias not previously present in women. Coffee drinking is shown to be a predictor for the incidence of heart palpitations.^{37,38} It is also implicated in the potential to produce cardiac arrhythmias.³⁹ Women who develop arrhythmias in pregnancy should eliminate coffee and caffeine.⁴⁰

- **Caffeine Affects Fetal Development**
 - Caffeine consumed during pregnancy affects the developing fetus as it crosses the placental barrier. One effect is lower infant birth weight.⁴¹ Infants born to women who consumed caffeine while pregnant have also been shown to sleep less and exhibit irritability, jitteriness and vomiting, due to their experience of caffeine withdrawal after birth.^{42,43}
 - Caffeine has a negative effect on pancreatic cells and fetal development. Continued research is being conducted to explore a link between coffee consumption and childhood diabetes.⁴⁴
 - Coffee drinking during pregnancy increases fetal breathing rates; this effect is seen even with consumption of decaffeinated coffee.^{45,46}
 - Blood levels of caffeine are significantly higher in pregnant women. The half-life of caffeine, or the amount of time it circulates in the bloodstream before being detoxified, is tripled in the last two trimesters of pregnancy, which further intensifies the experience of infants' caffeine withdrawal after birth.⁴⁷
 - The caffeine a woman drinks becomes rapidly incorporated into her breast milk.⁴⁸ Caffeine has been detected in breast milk even days after a woman has ingested it.⁴⁹ This affects newborns, particularly since caffeine has a prolonged half-life in infants.⁵⁰ Breastfeeding mothers are encouraged to limit their consumption of caffeine.⁵¹

- **Coffee Drinking Interferes with Mineral Absorption**
 - Caffeine affects absorption and excretion of a number of minerals crucial for women's health. Caffeine reduces the reabsorption of calcium and magnesium in the kidney, causing minerals to be excreted in the urine.^{52,53} Calcium is necessary for the prevention of osteoporosis along with healthy heart and nervous system function. It is difficult for older women to compensate for the calcium loss due to caffeine.⁵⁴
 - Caffeine negatively affects magnesium absorption, and magnesium deficiency is implicated in many women's health conditions including PMS.⁵⁵ Magnesium is an essential mineral utilized in more than 300 enzymatic reactions and physiological processes including energy metabolism, effective utilization of glucose, hormonal balance and proper heart function.⁵⁶
 - Coffee drinking reduces iron absorption.^{57,58} Iron is an essential component of red blood cells and iron deficiency contributes to menstruating women developing anemia. Caffeine is not the only ingredient thought to interfere with iron absorption;

cholorgenic acid, also present in decaffeinated coffee, reduces iron absorption from food sources.⁵⁹

- **Coffee Consumption is Related to Lower Bone Density**
 - High coffee intake is associated with an increased risk of lower bone density in older women.^{60,61,62} Some studies that do not observe this result hypothesize that it may be due to low levels of caffeine consumed in women studied.⁶³ Variations in the correlation between bone density and caffeine intake are associated with the amount of consumption. Women with high caffeine intakes experience higher rates of bone loss than those with low intakes.⁶⁴ Bone loss associated with caffeine consumption is especially pronounced in women who do not consume adequate calcium.⁶⁵
 - Coffee drinking significantly increases serum levels of the amino acid homocysteine, even more so than caffeine alone. The negative effect of coffee occurs with caffeinated and decaffeinated coffee, and with filtered and unfiltered coffee. It is noted within hours of coffee consumption.^{66,67, 68} High homocysteine levels are a significant risk factor for developing osteoporotic fractures.^{69,70}

- **Coffee Drinking Is Associated with Increased Incidence of Hot Flashes**
 - Women who drink less coffee report lower rates of experiencing hot flashes.⁷¹ Coffee drinking also interrupts sleep and increases the intensity of hot flashes.⁷² Generally, it is recommended that women who experience hot flashes reduce coffee consumption.⁷³

- **Caffeine Negatively Interacts with Hormones and Oral Contraceptives**
 - Postmenopausal women who take hormones and also drink coffee have an increased risk of developing Parkinson's Disease.⁷⁴

- **Coffee Increases Serum Cholesterol Levels**
 - Coffee drinking is linked to higher levels of serum cholesterol, with particularly high levels noted in people who drink boiled coffee or coffee processed at high temperatures (which includes espresso and espresso drinks).^{75, 76} Other forms of coffee have also been shown to increase serum cholesterol levels including decaf coffee.^{77,78}

- **Coffee Drinking is Associated with Increased Heart Attack Risk**
 - Cardiovascular disease is the foremost killer of women in the U.S. Independent of any other risk factors for heart disease, heavy coffee consumption has been shown to increase the short-term risk of heart attack, coronary death, or acute myocardial infarction.⁷⁹
 - Coffee drinking increases plasma homocysteine within hours of coffee consumption and high levels of homocysteine increases a person's risk of suffering from a heart attack.⁶⁶

- **Coffee Elevates Stress Hormones**
 - Caffeine in coffee elevates the stress hormones cortisol, epinephrine (also known as adrenaline) and norepinephrine.^{80,81,82,83} These hormones are responsible for increased heart rate and blood pressure, and a sense of "emergency alert". Circulation of

oxygen to the brain and extremities is decreased and the immune system is suppressed.

- o The purpose of this “fight or flight” response is to provide the body with a temporary energy boost for intense physical activity. With today’s sedentary lifestyle, the continual state of increased stress resulting from caffeine consumption can negatively affect all aspects of women’s health.
- o Stress levels account for a significant amount of variation in the symptoms felt throughout a women’s menstrual cycle.⁸⁴

▪ **Caffeine Interferes with GABA Metabolism**

- o GABA (Gamma-aminobutyric acid) is a neurotransmitter naturally produced in the brain and nervous system as well as the heart. It plays an important role in mood and stress management and influences heart rate and function.
- o Caffeine has been found to interfere with binding of GABA to GABA receptors, preventing it from performing its calming function.⁸⁵ GABA’s role in stress management is compromised in the presence of caffeine. Stress is a complicating factor in many women’s health concerns, including PMS, fertility, and menopausal symptoms.

Recommendation:

Caffeine affects almost every aspect of a woman’s life and health and women who are susceptible to any of the above conditions would do well to avoid coffee. Dietary changes that include weaning off of coffee and all other sources of caffeine can help relieve symptoms of these disorders as coffee decreases mineral absorption, exacerbates symptoms of PMS, increases the reactivity of the body to the stress of everyday life, magnifies heart attack risk, increases bone loss, and affects fertility and pregnancy. Nutrition professionals can support gastrointestinal patients by guiding them through the process of substituting a non-caffeinated, alkaline herbal coffee that brews and tastes just like coffee.

Kicking the Caffeine Habit:

The social prevalence of coffee drinking and the addictive side effects of caffeine can cause problems with patient compliance. Caffeine-free herbal coffee marketed under the brand name of Teccino[®] helps coffee drinkers replace their regular or decaf coffee with a satisfying alternative. Coffee drinkers need a dark, full-bodied, robust brew to help satisfy their coffee craving. Teccino satisfies the 4 needs coffee drinkers require in a coffee alternative:

- 1) Teccino brews just like coffee, allowing coffee drinkers to keep their same brewing ritual.
- 2) It has a delicious, deep roasted flavor that is very coffee-like.
- 3) It wafts an enticing aroma.
- 4) People experience a natural energy boost from nutritious Teccino.

Teecino offers the following health benefits for women:

<u>Beneficial Features of Teecino</u>	<u>Teecino Ingredients:</u> <small>56,87,88,89,90,91,92,93,94,95,96</small>
<ul style="list-style-type: none"> ▪ Inulin fiber from chicory <ul style="list-style-type: none"> • Unlike coffee, Teecino has nutritional value, including soluble inulin fiber, a pre-biotic that helps support a healthy population of beneficial microflora. • Inulin improves mineral absorption. ▪ 65 mg of Potassium <ul style="list-style-type: none"> • Teecino is a source of potassium. In liquid form, potassium is easily absorbed to help relieve muscle fatigue and maintain normal heart rhythm. ▪ Alkaline – helps reduce acidity <ul style="list-style-type: none"> • As opposed to acidic coffee, Teecino is alkaline, which reduces stomach acidity. ▪ Gluten Free <ul style="list-style-type: none"> • Gluten does not extract into boiling water. Tests show Teecino is gluten free although it contains barley. ▪ Naturally Caffeine-free <ul style="list-style-type: none"> • No chemical processing like decaffeinated coffee. 	<ul style="list-style-type: none"> ▪ Carob <ul style="list-style-type: none"> • Consumption of water-soluble fiber from carob lowers elevated blood cholesterol levels. ▪ Barley <ul style="list-style-type: none"> • Contains niacin, a B vitamin important for pregnancy and relieving menopausal symptoms. • Shown to have a beneficial effect on lipid metabolism. ▪ Almond <ul style="list-style-type: none"> • Lowers serum lipid levels. ▪ Figs <ul style="list-style-type: none"> • Contain antioxidants. • A good source of potassium. ▪ Dates <ul style="list-style-type: none"> • Contains potassium and magnesium. Magnesium is depleted by both coffee drinking and menstruation and magnesium deficiency is associated with PMS symptoms. ▪ Chicory root <ul style="list-style-type: none"> • Improves mineral absorption, including magnesium.

The Pain-free Way to Wean off of Coffee:

Start by mixing normal coffee 3/4 to 1/4 Teecino Herbal Coffee. Gradually reduce the percentage of coffee over a two to three week period until only 100% Teecino Herbal Coffee is brewed. Gradual reduction of caffeine is recommended.⁸⁶ Side effects such as headaches, fatigue, and brain foginess can be avoided as the body gradually adjusts to less reliance on stimulants.

Example: Use the following proportions if you make a 10-cup pot of coffee daily:

DAY	Regular Coffee	Teecino
Day 1-3:	4 tablespoons	1 tablespoon
Day 4-6:	3 tablespoons	2 tablespoons
Day 7-9:	2 tablespoons	3 tablespoons
Day 10:	1 1/2 tablespoons	3 1/2 tablespoons
Day 11:	1 tablespoon	4 tablespoons
Day 12-13:	1/2 tablespoon	4 1/2 tablespoons
Day 14:	0	5 tablespoons

References

- ¹ Mathias, S., Garland, C., Barrett-Connor, E. and Wingard, D.L. 1985. Coffee, plasma cholesterol, and lipoproteins. A population study in an adult community. American Journal of Epidemiology. 121(6):896-905.
- ² Cherniske, S. Caffeine Blues. Copyright 1998.
- ³ Ferrini, R.L. and Barrett-Connor, E. 1996. Caffeine intake and endogenous sex steroid levels in postmenopausal women. The Rancho Bernardo Study. American Journal of Epidemiology. 144(7):642-4.
- ⁴ Ugarriza, D.N., Klingner, S. and O'Brien, S. 1998. Premenstrual Syndrome: Diagnosis and Intervention. Nurse Practitioner. 23(9):40,45,49-52.
- ⁵ Dickerson, L.M., Mazyck, P.J. and Hunter, M.H. 2003. Premenstrual Syndrome. American Family Physician. 67(8):1743-52.
- ⁶ Barnhart, K.T., Freeman, E.W. and Sondheimer, S.J. 1995. A clinician's guide to the premenstrual syndrome. Medical Clinics of North America. 79(6):1457-72.
- ⁷ Massil, H.Y. and O'Brien, P.M. 1987. Approach to the management of premenstrual syndrome. Clinical Obstetrics and Gynecology. 30(2):443-52.
- ⁸ Budoff, P.W. 1983. The use of prostaglandin inhibitors for the premenstrual syndrome. Journal of Reproductive Medicine. 28(7):469-78.
- ⁹ Russell, L.C. 1989. Caffeine restriction as initial treatment for breast pain. Nurse Practitioner. 14(2):36-7,40.
- ¹⁰ Wolfrom, D. and Welsch, C.W. 1990. Caffeine and the development of normal, benign and carcinomatous human breast tissues: a relationship? Journal of Medicine. 21(5):225-50.
- ¹¹ Norlock, F.E. 2002. Benign breast pain in women: a practical approach to evaluation and treatment. Journal of the American Medical Women's Association. 57(2):85-90.
- ¹² Barbieri, R.L. 2001. The initial fertility consultation: recommendations concerning cigarette smoking, body mass index, and alcohol and caffeine consumption. American Journal of Obstetrics and Gynecology. 185(5):1168-73.
- ¹³ Balat, O., Balat, A., Ugur, M.G. and Pence, S. 2003. The effect of smoking and caffeine on the fetus and placenta in pregnancy. Clinical and experimental obstetrics & gynecology. 30(1):57-9.
- ¹⁴ Ryu, J.E. 1985. Caffeine in human milk and in serum of breast-fed infants. Developmental pharmacology and therapeutics. 8(6):329-37.
- ¹⁵ Liston, J. 1988. Breastfeeding and the use of recreational drugs--alcohol, caffeine, nicotine and marijuana. Breastfeeding review. 6(2):27-30.
- ¹⁶ Biela, U. 2002. Determinants of the age at Natural Menopause. Przegląd Lekarski 59(3):165-9.
- ¹⁷ Nagata, C., Takatsuka, N., Inaba, S., Kawakami, N. and Shimizu, H. 1998. Association of diet and other lifestyle with onset of menopause in Japanese women. Maturitas. 29(2):105-13.

-
- ¹⁸ Forsmo S, Schei B, Langhammer A, Forsen L. 2001. How do reproductive and lifestyle factors influence bone density in distal and ultradistal radius of early postmenopausal women? The Nord-Trondelag Health Survey, Norway. Osteoporosis International. 12(3):222-9.
- ¹⁹ Braun, S. Buzz: The Science and Lore of Alcohol and Caffeine. Copyright 1996.
- ²⁰ Strain, E.C., G.K. Mumford, K. Silverman, and R.R. Griffiths. 1994. Caffeine dependence syndrome. Journal of the American Medical Association, 272:1043-1048.
- ²¹ Silverman, K., Evans, S.M., Strain, E.C. and Griffiths, R.R. 1992 Withdrawal Syndrome after the Double-Blind Cessation of Caffeine Consumption. The New England Journal of Medicine. 16(327): 1109-14.
- ²² Rossignol, A.M. and Bonnländer, H. 1990. Caffeine-containing beverages, total fluid consumption, and premenstrual syndrome. American Journal of Public Health. 80(9):1106-10.
- ²³ Rossignol, A.M. 1985. Caffeine-containing beverages and premenstrual syndrome in young women. American Journal of Public Health. 75(11):1335-7.
- ²⁴ Clementz, G.L. and Dailey, J.W. 1988. Psychotropic effects of caffeine. American Family Physician. 37(5):167-72.
- ²⁵ Rossignol, A.M., Bonnländer, H., Song, L. and Phillis, J.W. 1991. Do women with premenstrual symptoms self-medicate with caffeine? Epidemiology. 2(6):403-8.
- ²⁶ Labbe, L., Abolfathi, Z., Robitaille, N.M., St-Maurice, F., Gilbert, M. and Turgeon, J. 1999. Stereoselective disposition of the antiarrhythmic agent mexiletine during the concomitant administration of caffeine. Therapeutic Drug Monitor. 21(2):191-9.
- ²⁷ Abernethy, D.R. and Todd, E.L. 1985. Impairment of caffeine clearance by chronic use of low-dose oestrogen-containing oral contraceptives. European Journal of Clinical Pharmacology. 28(4):425-8.
- ²⁸ Patwardhan, R.V., Desmond, P.V., Johnson, R.F. and Schenker, S. 1980. Impaired elimination of caffeine by oral contraceptive steroids. The Journal of laboratory and clinical medicine. 95(4):603-8.
- ²⁹ Rietveld, E.C., Broekman, M.M., Houben, J.J., Eskes, T.K. and van Rossum, J.M. 1984. Rapid onset of an increase in caffeine residence time in young women due to oral contraceptive steroids. European Journal of Clinical Pharmacology. 26(3):371-3.
- ³⁰ Ader, D.N., South-Paul, J., Adera, T. and Deuster, P.A. 2001. Cyclical mastalgia: prevalence and associated health and behavioral factors. Journal of Psychosomatic Obstetrics and Gynaecology. 22(2):71-6.
- ³¹ Russell LC. 1989. Caffeine restriction as initial treatment for breast pain. Nurse Practitioner. 14(2):36-7,40.
- ³² Boyle CA, Berkowitz GS, LiVolsi VA, Ort S, Merino MJ, White C, Kelsey JL. 1984. Caffeine consumption and fibrocystic breast disease: a case-control epidemiologic study. Journal of the National Cancer Institute. 72(5):1015-9.
- ³³ Jensen, T.K., Henriksen, T.B., Hjollund, N.H., Scheike, T., Kolstad, H., Giwercman, A., Ernst, E., Bonde, J.P., Skakkebaek, N.E. and Olsen, J. 1998. Caffeine intake and fecundability: a follow-up study among 430 Danish couples planning their first pregnancy. Reproductive Toxicology. 12(3):289-95.
- ³⁴ Florack, E.I., Zielhuis, G.A and Rolland, R. 1994. Cigarette smoking, alcohol consumption, and caffeine intake and fecundability. Preventative Medicine. 23(2):175-80.
- ³⁵ Wilcox, A., Weinberg, C. and Baird, D. 1998. Caffeinated beverages and decreased fertility. Lancet. 2(8626-8627):1453-6.

-
- ³⁶ Pollard, I., Murray, J.F., Hiller, R., Scaramuzzi, R.J. and Wilson, C.A. 1999. Effects of preconceptual caffeine exposure on pregnancy and progeny viability. The Journal of Maternal-Fetal Medicine. 8(5):220-4.
- ³⁷ Lochen ML, Rasmussen K. 1996. Palpitations and lifestyle: impact of depression and self-rated health. The Nordland Health Study. Scandinavian journal of social medicine. 24(2):140-4.
- ³⁸ Shirlow, M.J. and Mathers, C.D. 1985. A study of caffeine consumption and symptoms: indigestion, palpitations, tremor, headache and insomnia. International Journal of Epidemiology. 14(2):239-48.
- ³⁹ Rosmarin PC. 1989. Coffee and coronary heart disease: a review. Progress in Cardiovascular Diseases. 32(3):239-45.
- ⁴⁰ Gowda, R.M., Khan, I.A., Mehta, N.J., Vasavada, B.C. and Sacchi, T.J. 2003. Cardiac arrhythmias in pregnancy: clinical and therapeutic considerations. International Journal of Cardiology. 88(2-3):129-33.
- ⁴¹ Narod, S.A., De Sanjose, S. and Victora, C. 1991. Coffee during pregnancy: a reproductive hazard? American Journal of Obstetrics and Gynecology. 164(4):1109-14.
- ⁴² McGowan, J.D., Altman, R.E. and Kanto, W.P. Jr. 1988. Neonatal withdrawal symptoms after chronic maternal ingestion of caffeine. Southern Medical Journal. 81(9):1092-4.
- ⁴³ Devoe, L.D., Murray, C., Youssif, A. and Arnaud, M. 1993. Maternal caffeine consumption and fetal behavior in normal third-trimester pregnancy. American Journal of Obstetrics and Gynecology. 168(4):1105-11.
- ⁴⁴ Tuomilehto, J., Tuomilehto-Wolf, E., Virtala, E. and LaPorte, R. 1990. Coffee consumption as trigger for insulin dependent diabetes mellitus in childhood. British Medical Journal. 300(6725): 642-3.
- ⁴⁵ Salvador, H.S. and Koos, B.J. 1989. Effects of regular and decaffeinated coffee on fetal breathing and heart rate. American Journal of Obstetrics and Gynecology. 160(Pt 1): 1043-7.
- ⁴⁶ McGowan, J., Devoe, L.D., Searle, N. and Altman, R. 1987. The effects of long- and short-term maternal caffeine ingestion on human fetal breathing and body movements in term gestations. American Journal of Obstetrics and Gynecology. 157(3):726-9.
- ⁴⁷ McKim, E.M. 1991. Caffeine and its effects on pregnancy and the neonate. Journal of Nurse Midwifery. 36(4):226-31.
- ⁴⁸ Stavchansky, S., Combs, A., Sagraves, R., Delgado, M. and Joshi, A. 1988. Pharmacokinetics of caffeine in breast milk and plasma after single oral administration of caffeine to lactating mothers. Biopharmaceutics & drug disposition 9(3): 285-99.
- ⁴⁹ Ryu, J.E. 1985. Caffeine in human milk and in serum of breast-fed infants. Developmental pharmacology and therapeutics. 8(6):329-37.
- ⁵⁰ Nehlig, A. and Debry, G. 1994. Consequences on the newborn of chronic maternal consumption of coffee during gestation and lactation: a review. Journal of the American College of Nutrition, 13(1): 6-21.
- ⁵¹ Liston, J. 1988. Breastfeeding and the use of recreational drugs--alcohol, caffeine, nicotine and marijuana. Breastfeeding review. 6(2):27-30.
- ⁵² Bergman, E.A., Massey, L.K., Wise, K.J. and Sherrard, D.J. 1990. Effects of dietary caffeine on renal handling of minerals in adult women. Life Sciences. 47(6):557-64.

-
- ⁵³ Kynast-Gales, S.A. and Massey, L.K. 1994. Effect of caffeine on circadian excretion of urinary calcium and magnesium. Journal of the American College of Nutrition. 13(5):467-72.
- ⁵⁴ Massey, L.K. and Whiting, S.J. 1993. Caffeine, urinary calcium, calcium metabolism and bone. Journal of Nutrition. 123(9):1611-4.
- ⁵⁵ Johnson, S. 2001. The Multifaceted and widespread pathology of magnesium deficiency. Medical Hypothesis. 56(2):163-70.
- ⁵⁶ Gums, J. 2004. Magnesium in cardiovascular and other disorders. American Journal of Health System Pharmacy. 61(15):1569-76.
- ⁵⁷ Morck, T.A., Lynch, S.R. and Cook, J.D. 1983. Inhibition of food iron absorption by coffee. American Journal of Clinical Nutrition. 37(3):416-20.
- ⁵⁸ Hallberg, L. and Rossander, L. 1982. Effect of different drinks on the absorption of non-heme iron from composite meals. Human nutrition. Applied nutrition. 36(2):116-23.
- ⁵⁹ Hurrell, R.F., Reddy, M. and Cook, J.D. 1999. Inhibition of non-haem iron absorption in man by polyphenolic-containing beverages. British Journal of Nutrition. 81(4):289-95.
- ⁶⁰ Korpelainen, R., Korpelainen, J., Heikkinen, J., Vaananen, K. and Keinanen-Kiukaanniemi, S. 2003. Lifestyle factors are associated with osteoporosis in lean women but not in normal and overweight women: a population-based cohort study of 1222 women. Osteoporosis International. 14(1):34-43.
- ⁶¹ Barrett-Connor, E., Chang, J.C. and Edelstein, S.L. 1994. Coffee-associated osteoporosis offset by daily milk consumption. The Rancho Bernardo Study. JAMA. 271(4). 280-3.
- ⁶² Hernandez-Avila, M., Stampfer M.J., Ravnkar, V.A., Willett, W.C., Schiff, I., Francis, M., Longcope, C. and McKinlay, S.M. 1993. Caffeine and other predictors of bone density among pre- and perimenopausal women. Epidemiology. 4(2):128-34.
- ⁶³ Mikuls, T.R., Cerhan, J.R., Criswell, L.A., Merlino, L., Mudano, A.S., Burma, M., Folsom, A.R. and Saag, K.G. 2002. Coffee, tea, and caffeine consumption and risk of rheumatoid arthritis: results from the Iowa Women's Health Study. Arthritis and Rheumatism. 46(1):83-91.
- ⁶⁴ Rapuri, P.B., Gallagher, J.C., Kinyamu, H.K. and Ryschon, K.L. 2001. Caffeine intake increases the rate of bone loss in elderly women and interacts with vitamin D receptor genotypes. American Journal of Clinical Nutrition. 74(5):694-700.
- ⁶⁵ Harris, S.S. and Dawson-Hughes, B. 1994. Caffeine and bone loss in healthy postmenopausal women. American Journal of Clinical Nutrition. 60(4):573-8.
- ⁶⁶ Verhoef, P., Pasma, W.J., Van Vliet, T., Urgert, R. and Katan, M.B. 2002. Contribution of caffeine to the homocysteine-raising effect of coffee: a randomized controlled trial in humans. American Journal of Clinical Nutrition. 76(6):1244-8.
- ⁶⁷ Urgert, R., van Vliet, T., Zock, P.L. and Katan, M.B. 2000. Heavy coffee consumption and plasma homocysteine: a randomized controlled trial in healthy volunteers. American Journal of Clinical Nutrition. 72(5):1107-10.
- ⁶⁸ Grubben, M.J., Boers, G.H., Blom, H.J., Broekhuizen, R., de Jong, R., van Rijt, L., de Ruijter, E., Swinkels, D.W., Nagengast, F.M. and Katan, M.B. 2000. Unfiltered coffee increases plasma homocysteine concentrations in healthy volunteers: a randomized trial. American Journal of Clinical Nutrition. 71(2):480-4.

-
- ⁶⁹ van Meurs, J.B., Dhonukshe-Rutten, R.A., Pluijm, S.M., van der Klift, M., de Jonge, R., Lindemans, J., de Groot, L.C., Hofman, A., Witteman, J.C., van Leeuwen, J.P., Breteler, M.M., Lips, P., Pols, H.A. and Uitterlinden, A.G. 2004. Homocysteine levels and the risk of osteoporotic fracture. *New England Journal of Medicine*. 350(20):2033-41.
- ⁷⁰ McLean, R.R., Jacques, P.F., Selhub, J., Tucker, K.L., Samelson, E.J., Broe, K.E., Hannan, M.T., Cupples, L.A. and Kiel, D.P. 2004. Homocysteine as a predictive factor for hip fracture in older persons. *New England Journal of Medicine*. 350(20):2042-9.
- ⁷¹ Park, Y.J., Paik, H.Y., Kim, Y.J., Hong, S.S., Kim, M.J., Yoon, J.W. and Moon, S.H. 2003. Association of Diet with Menopausal Symptoms in Korean Middle-aged Women. *Taehan Kanho Hakhoe chi*. 33(3):386-94.
- ⁷² Hollander, L.E., Freeman, E.W., Sammel, M.D., Berlin, J.A., Grisso, J.A. and Battistini, M. 2001. Sleep quality, estradiol levels, and behavioral factors in late reproductive age women. *Obstetrics and Gynecology*. 98(3):391-7.
- ⁷³ Lucero, M.A. and McCloskey, W.W. 1997. Alternatives to estrogen for the treatment of hot flashes. *The Annals of Pharmacotherapy*. 31(7-8):915-7.
- ⁷⁴ Ascherio, A., Chen, H., Schwarzschild, M.A., Zhang, S.M., Colditz, G.A. and Speizer, F.E. 2003. Caffeine, postmenopausal estrogen, and risk of Parkinson's disease. *Neurology*. 60(5):790-5.
- ⁷⁵ Lindahl, B., Johansson, I., Huhtasaari, F., Hallmans, G. and Asplund, K. 1991. Coffee drinking and blood cholesterol--effects of brewing method, food intake and life style. *Journal of Internal Medicine*. 230(4):299-305.
- ⁷⁶ Salvaggio, A., Periti, M., Miano, L., Quaglia, G. and Marzorati, D. 1991. Coffee and cholesterol, an Italian study. *American Journal of Epidemiology*. 134(2):149-56.
- ⁷⁷ Aro A, Pietinen P, Uusitalo U, Tuomilehto J. 1989. Coffee and tea consumption, dietary fat intake and serum cholesterol concentration of Finnish men and women. *Journal of Internal Medicine*. 226(6):127-32.
- ⁷⁸ Green MS, Harari G. 1992. Association of serum lipoproteins and health-related habits with coffee and tea consumption in free-living subjects examined in the Israeli CORDIS Study. *Preventive medicine*. 21(4):532-45.
- ⁷⁹ Happonen P, Voutilainen S, Salonen JT. 2004. Coffee drinking is dose-dependently related to the risk of acute coronary events in middle-aged men. *Journal of Nutrition*. 134(9):2381-6.
- ⁸⁰ Robertson, D., Frolich, J.C., Carr, R.K., Watson, J.T., Hollifield, J.W., Shand, D.G. and J.A. Oates. 1978. Effects of caffeine on plasma renin activity, catecholamines and blood pressure. *New England Journal of Medicine*. 298(4):181-6.
- ⁸¹ Lane, J.D., Adcock, R.A., Williams, R.B. and C.M. Kuhn. 1990. Caffeine effects on cardiovascular and neuroendocrine responses to acute psychosocial stress and their relationship to level of habitual caffeine consumption. *Psychosomatic Medicine*. 52(3):320-36.
- ⁸² Lane, J.D. 1994. Neuroendocrine Responses to Caffeine in the Work Environment. *Psychosomatic Medicine*. 546:267-70.
- ⁸³ Kerr, D., Sherwin, R.S., Pavalkis, F., Fayad, P.B., Sikorski, L., Rife, F., Tamborlane, W.V. and During, M.J. 1993. Effect of caffeine on the recognition of and responses to hypoglycemia in humans. *Annals of Internal Medicine*. 119(8):799-804.

-
- ⁸⁴ Gannon, L., Luchetta, T., Pardie, L., and Rhodes, K. 1989. Perimenstrual symptoms: relationships with chronic stress and selected lifestyle variables. Behavioral Medicine. 15(4):149-59.
- ⁸⁵ Roca, D.J., G.D. Schiller, and D.H. Farb. 1988. Chronic Caffeine or Theophylline Exposure Reduces Gamma-aminobutyric Acid/Benzodiazepine Receptor Site Interactions. Molecular Pharmacology, May;33(5):481-85.
- ⁸⁶ Silverman, K., Evans, S.M., Strain, E.C. and Griffiths, R.R. 1992 Withdrawal Syndrome after the Double-Blind Cessation of Caffeine Consumption. The New England Journal of Medicine. 16(327): 1109-14.
- ⁸⁷ Physicians Desk Reference for Herbal Medicines. Second Edition. Copyright 2000.
- ⁸⁸ Roehl, E. Whole Foods Facts: The Complete Reference Guide. Copyright 1996.
- ⁸⁹ Roberfroid MB. 1997. Health benefits of non-digestible oligosaccharides. Advances in experimental medicine and biology. 427: 211-9.
- ⁹⁰ Biddle, W. 2003. Gastroesophageal reflux disease: current treatment approaches. Gastroenterology nursing : the official journal of the Society of Gastroenterology Nurses and Associates. 26(6):228-36.
- ⁹¹ Kim M, Shin HK. 1996. The water-soluble extract of chicory reduces glucose uptake from the perfused jejunum in rats. Journal of Nutrition. 126(9):2236-42.
- ⁹² Al-Shahib W, Marshall RJ. (2003) The fruit of the date palm: its possible use as the best food for the future? International Journal of Food Sciences and Nutrition. 54(4):247-59.
- ⁹³ Li, J., Kaneko, T., Qin, L.Q., Wang, J. and Wang, Y. 2003. Effects of barley intake on glucose tolerance, lipid metabolism, and bowel function in women. Nutrition. 19(11-12). 926-9.
- ⁹⁴ Lovejoy, J.C., Most, M.M., Lefevre, M., Greenway, F.L. and Rood, J.C. 2002. Effect of diets enriched in almonds on insulin action and serum lipids in adults with normal glucose tolerance or type 2 diabetes. Journal of Clinical Nutrition. 76(5):1000-6.
- ⁹⁵ Haskell, W.L., Spiller, G.A., Jensen, C.D., Ellis, B.K. and Gates, J.E. 1992. Role of water-soluble dietary fiber in the management of elevated plasma cholesterol in healthy subjects. American Journal of Cardiology. 69(5):433-9.
- ⁹⁶ Johnson, S. 2001. The Multifaceted and widespread pathology of magnesium deficiency. Medical Hypothesis. 56(2):163-70.