SUPPLEMENTS USED IN PREVENTION OF PREECLAMPSIA AND FOR LABOR PREPARATION

Historically, a number of supplements have been used for preeclampsia and preparation for labor. This Whole Health tool highlights some of those which are most commonly used, focusing on the research related to their use.

PREECLAMPSIA PREVENTION

Note: Please refer to the Passport to Whole Health, Chapter 15 on Dietary Supplements for more information about how to determine whether or not a specific supplement is appropriate for a given individual. Supplements are not regulated with the same degree of oversight as medications, and it is important that clinicians keep this in mind. Products vary greatly in terms of accuracy of labeling, presence of adulterants, and the legitimacy of claims made by the manufacturer.

CALCIUM

A systematic review of 12 trials (total number of participants = 15,206) found that calcium supplementation decreased the risk of pregnancy induced hypertension and preeclampsia.[1] The effect was greatest in high-risk groups (e.g. those with prior history of preeclampsia) and those with a low baseline calcium intake, which is, unfortunately, a large number of women in the United States. Calcium, as well as magnesium, is essential for maintaining a healthy blood pressure and can prevent leg cramps women experience in the latter half of pregnancy. Calcium is considered safe for use in pregnancy. A dietary history that assesses intake of calcium-rich vegetables and dairy products can provide helpful information. All calcium intake from diet and supplementation should be taken into consideration, so as to avoid excessive intake. The Institute of Medicine recommends 1000 milligrams daily as the recommended intake, with 2500 milligrams daily as the upper limit of intake from all sources.[2]

Dose: Start a dose of 600 milligrams per day and increase dietary intake.

VITAMIN D

Hyppönen has reviewed the evidence suggesting that the immunomodulatory properties of vitamin D may play a key role in maintaining immunological tolerance in pregnancy.[3] There is some evidence that women who develop preeclampsia have lower 25-hydroxy vitamin D levels when compared with controls.[4,5] The incidence of preeclampsia is also higher in dark-skinned women who live in northern latitudes[6] because they typically have a higher prevalence of hypovitaminosis D than is found in light-skinned women. In a 2007 study, blood samples from 1,198 pregnant women indicated that low vitamin D early in pregnancy was associated with a two-fold increased risk of preeclampsia.[7] While more
research needs to be done, the evidence suggests that screening women in the first trimester for vitamin D deficiency is warranted.

Women can increase vitamin D by obtaining non-burning sun exposure daily and by eating foods high in vitamin D, such as mushrooms, milk, fish, and egg yolks. Due to the common use of sunscreen and high amounts of time spent indoors, even women who live in sunny parts of the country may be deficient in vitamin D. A good rule of thumb is that 1000 International Units (IUs) of D3 taken orally will raise serum vitamin D levels by about 8-10 points.

**Dose:** Because of a huge variability in both sun exposure and dietary intake, it is perhaps best to individually dose supplementation based on a 25-OH vitamin D level.

**CHOCOLATE (THEOBROMA CACOA)**

What pregnant woman does not want an excuse to eat more chocolate? A study of 1,681 pregnant women found those who reported eating chocolate five or more times a week, or who had the highest levels of theobromine (a compound in cocoa) in their cord blood, had the lowest risk of preeclampsia. The scientists speculate that flavonoids in chocolate may provide cardiovascular protection.[8] This is an interesting correlation, especially given our growing understanding of the effects of dietary flavanols on vascular nitric oxide, which can benefit blood pressure control. [9]

**Dose:** As chocolate can be high in calories, it is probably best to encourage women, if they enjoy chocolate, to eat 1-2 ounces of dark chocolate (70% cacao or greater) three to four times per week. For the blood pressure lowering effects, the dose is a fourth of a regular chocolate bar (70% cacao or greater) daily.

**OMEGA-3 FATTY ACIDS**

Omega-3 fatty acids have potential beneficial effects on preeclampsia. Higher blood concentrations of arachidonic acid in preeclamptic women were noted more than 20 years ago, and high-dose omega-3 fatty acid intake has been shown to reduce maternal thromboxane A2 synthesis and enhance maternal refractoriness to angiotensin II. However, despite some promising early observational data, there is little evidence from randomized, placebo-controlled trials of a significant effect on the incidence or severity of preeclampsia.[10] Adequate omega-3 fatty acid intake is important during pregnancy and the postpartum period; however, the data for use in preeclampsia prevention is unclear.

Of note, several studies have looked at a link between omega-3 intake and brain and eye development in the fetus. One large systematic review found that higher docosahexaenoic acid (DHA) intake in pregnancy prolonged the gestation in high risk pregnancies, increased birth weight, and enhanced visual acuity and problem solving in the child.[11] Preliminary findings from one small randomized-controlled trial suggested that maternal omega-3 supplementation during pregnancy may reduce the risk of allergic disease in the child and may reduce the risk of preterm birth.[12] Another review looked at five randomized-
controlled trials and found that omega-3 supplementation during pregnancy decreases the risk of childhood asthma in the offspring.[13] More research is needed.

Good dietary sources include cold-water fish, nuts, ground flax seed, avocado, and vegetables. Although cold-water fish are a good source of omega-3 fatty acids, the pregnant mother should avoid fish high in mercury. Information on fish safety can be found at U.S. Food & Drug Administration

**Dose:** 1000 milligrams omega-3 fats (DHA + EPA) daily

**PARTUS PREPARATORS: SUPPLEMENTS TO PREPARE FOR LABOR**

It is important to stress to women that their bodies know how to give birth. There is no substance that needs to be ingested or used topically in order to have a successful delivery. That being said, there is a rich tradition of the use of herbs and foods to aid labor preparation, and many women may inquire about their use.

**BLUE COHOSH (CAULOPHYLLUM THALICTROIDES)**

Blue cohosh has a long history of use as a labor aid. Indigenous North American women used blue cohosh to induce labor or stimulate sluggish, ineffective contractions. It was included in the United States Pharmacopeia as a labor-inducing agent from 1882 to 1905. Today, blue cohosh is found in many formulations marketed to women as partus preparators. Many physicians are unfamiliar with its use, but a survey of nurse midwives in 1999 found that 64% used blue cohosh, often in combination with black cohosh, to augment labor during delivery.[14] While many used blue cohosh, midwives also reported having the least comfort with its use during pregnancy. A significant number reported observing increased rates of meconium, tachycardia in the neonate, and need for resuscitation in the neonate with its use.

There have been a small number of case reports implicating blue cohosh, often in combination with black cohosh and/or other herbs, with myocardial infarction,[15] multi-organ failure, congestive heart failure,[16] and perinatal stroke[17] in infants born to mothers taking the herb several weeks before birth. While the published case reports are not conclusive, blue cohosh contains some potentially dangerous compounds including caulosaponin, a glycoside that has been shown to constrict coronary vessels and likely accounts for its oxytocic effects. It also contains N-methylcytisine, an alkaloid with action similar to nicotine, known to cause coronary vasoconstriction, tachycardia, hypotension and respiratory depression. In vitro studies show that extracts of blue cohosh rhizome (the lateral root) or pure N-methylcytisine (at 20 parts per million [ppm]) induce major malformations in cultured rat embryos.[18] The concentration of N-methylcytisine in dietary supplements containing blue cohosh ranges from 5-850 ppm.[19]

Despite the shortcomings of published case reports, the chemistry and pharmacology of blue cohosh are reasonably well known. The human case reports, as incomplete as they are, paint a picture that is consistent with the evidence provided by in vitro and animal studies.
At this time, it is wise to err on the side of caution and advise pregnant women not to use this plant.

(X) Do not recommend.

**BLACK COHOSH (ACTAEA RACEMOSA; CIMICIFUGA RACEMOSA)**

Black cohosh is probably best known for its use in menopause, though it was traditionally used for rheumatic pain, uterine cramping, and to support mood. The German health authorities also recognize its use for dysmenorrhea. It is unrelated to blue cohosh, but the two herbs are often used in combination as a partus preparator. Studies on other *Cimicifuga* species failed to show teratogenicity in female rats at doses up to 2000 milligrams/kilogram per day; however, similar studies in *Actaea racemosa* have not been published. Both the British Herbal Pharmacopoeia and American Herbal Products Association recommend against the use of black cohosh during pregnancy.[20] It is best to advise patients against its use, as reproductive toxicology studies are needed for this herb. An analysis of 69 cases shows little, if any, supportive evidence for a significant hepatotoxic risk of black cohosh.[21]

(X) Do not recommend.

**RASPBERRY LEAF (RUBUS IDAEUS, R. OCCIDENTALIS)**

Raspberry leaf can be found in many popular "pregnancy teas" in conventional stores across the country. It is often promoted to prevent miscarriage, ease morning sickness, and ensure a quick birth. A survey of 172 certified nurse midwives found that 63% of midwives using herbal preparations recommended red raspberry leaf.[14]

A double blind, placebo-controlled study randomized 192 low-risk, nulliparous women to receive raspberry leaf tablets (two tablets of 1.2 grams per day) or placebo, from 32 weeks gestation until delivery.[22] Raspberry leaf was not associated with any adverse effects in mother or baby, but it has not been shown to shorten the first stage of labor. Clinically significant findings were a shortening of the second stage of labor (mean difference, 9.59 minutes) and a lower rate of forceps deliveries between the treatment group and the control group (19.3% versus 30.4%). No contraindications for use in pregnancy or lactation are found in the literature; therefore, it is considered reasonable for pregnant women to use this plant.

**Dose:** Raspberry leaf tablets 1.2 grams orally daily, or as a tea, 1-3 cups daily

**EVENING PRIMROSE OIL (OENETHERA BIENNIS)**

Evening primrose oil is used widely during the last month of pregnancy by midwives in the Unites States for cervical softening. It is typically administered as two capsules intravaginally at bedtime. Five studies have been done indicating the safety of evening primrose oil, three of which were randomized controlled trials. When used orally as a cervical ripening agent, it has not been shown to reduce the risk of post-dates presentation.[23]
This is not surprising, since oral administration during pregnancy was never a traditional use. More trials assessing efficacy are needed.

**Dose:** Two capsules intra-vaginally at bedtime

**CASTOR OIL**

In one national survey 93% of midwives reported using castor oil to induce labor.[14] Despite this prevalence, there has been little research into the use of castor oil. Only one study looking at safety was included in a recent Cochrane review which, unfortunately, was small and of poor methodological quality.[24] Outcomes which were evaluated in this study included c-section rate, meconium staining of amniotic fluid, and APGAR scores. All women who ingested castor oil had nausea; otherwise, outcomes were no different than for women who did not ingest it. There has been no randomized-controlled trial evaluating the effectiveness of castor oil for induction of labor.

**Dose:** Unknown

**OTHER HERBS**

Many herbs have historically been used to induce labor. These include Blue Cohosh (*Caulophyllum thalictroides*), Cotton Root Bark (*Gossypium herbaceum*), Partridge Berry (*Mitchella repens*), Cramp Bark (*Viburnum opulus*) and Black Cohosh (*Cimicifuga racemosa*). As little to no research has been conducted on the safety of these herbs for labor induction, their use by those without training in herbal medicine is not recommended.[25]

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**REFERENCES**


