

## Caffeine consumption: advice, physiology, and evidence

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A series of articles that are aimed at reviewing the guidelines (or sections thereof) and the underpinning evidence for counselling pregnant and postnatal women around food and drink. Every month the series will examine the current guidelines for a particular dietary staple, examining how evidence has informed the guideline and revealing where guidance is lacking or conflicting and suggesting how this might influence practice.

### Introduction

Caffeine is consumed in almost every geographic and cultural group, including pregnant women<sup>1</sup>. Many beverages and some food and medications contain caffeine including coffee, tea, coke-based products, energy drinks and chocolate. The amount of caffeine in products varies as Table 1 demonstrates. Therefore, the effects, side effects, recommendations for pregnancy and lactation are important for women to know and midwives to discuss with them.

Product	Amount	Caffeine	
Instant coffee	1 cup (8 ounces)	65mg	
Brewed coffee	1 cup (8 ounces)	95mg	
Espresso (coffee shot)	1 shot (1.5 ounces)	65mg	
Tea (black)	1 cup	47mg	
Tea (green)	1 cup	28mg	
Tea (decaffeinated)	1 cup	2 mg	
Chocolate	1 ounce	24mg	
Regular/ Diet coke	1 can	40mg	
Medications: headache or migraine relief	Varies: Anadin original or extra Beechams cold and Flu remedies Benylin cold and flu remedies Hedex extra Lemsip Max	25-65 mg	

Table 1. Amount of caffeine in beverages and chocolate and medications

The main source of caffeine for adults in the European Union is coffee<sup>2</sup>. In moderation coffee is considered beneficial to health with some studies citing a reduced risk of endometrial and liver cancer, lower risk of developing type 2 diabetes, lower risk of heart disease and stroke<sup>1</sup>. A moderate coffee consumption is typically classed as 3-5 cups per day- but depending on which preparation is used, this can vary from 195-475mg per day (see Table 1). People tend to adjust their caffeine consumption based on individual effects or

sensitivity<sup>3</sup>. So, someone who feels jittery is likely to consume less caffeine than another person who feels more alert.

### **Advice**

In non-pregnant adults 400 mg of caffeine per day is considered safe with advice to limit the consumption in one sitting to 200mg<sup>2</sup>. The 200mg dose is about 3mg/kg based on an adult weighing 70kgs. Doses higher than 300mg per day have been found to have negative effects such as anxiety, restlessness, insomnia, and increased heart rates<sup>1</sup>. The advice on caffeine consumption in pregnancy from reputable sources including the NHS website<sup>4</sup>, European Food Safety Authority<sup>2</sup> and Royal College of Midwives<sup>5</sup> is that pregnant women should limit their caffeine consumption to 200 milligrams per day.

In August 2020, two reputable UK newspapers reported on coffee consumption in pregnancy. They were reporting on the publication of the same study, but the overarching headlines were starkly different. One headline said there was, 'No safe level of coffee drinking for pregnant women', the other, seemingly in direct contradiction stated, 'Having some caffeine in pregnancy is fine'. The RCM Expert Clinical Advisory Group published a briefing in 2020 to counter this controversy<sup>5</sup>. Our article expands on the advice bringing together the physiological effects of caffeine in pregnancy and for the fetus, so that readers have a comprehensive understanding of this to support the conversations they have with women.

### **Physiology**

Caffeine exerts a wide range of effects on the body both positive and negative<sup>3</sup>. These include the stimulation of the central nervous system that increase alertness, better concentration, energy, and cognition. However, it can cause sleep disturbances, nervousness, jitteriness, and irritability. It raises the blood pressure by vasoconstriction and heart rate slightly and is also a diuretic.

The small intestines absorb caffeine rapidly dissolving it into the body's water and fat molecules within 45 minutes of consumption. It is distributed in all body fluids including the umbilical cord blood, amniotic fluid, and breast milk. It crosses the blood-brain, and placental barriers and in men the blood-testicular barrier too<sup>3</sup>.

Caffeine is metabolised by the liver and excreted in urine. It can remain in the blood from 2-9 hours depending on an individual's metabolic speed. The half-life, which is how long it takes for a substance to reduce within the plasma by half, is approximately four to five hours. However, there is marked variation in how individuals metabolise caffeine; some of the differences are genetic other environmental<sup>6</sup>. These include age, sex, hormones, weight, smoking and diet. For instance, daily coffee drinking and smoking are associated with increased clearance<sup>2</sup>, in other words the caffeine is metabolised faster. Oral contraceptives and being female are associated with reduced clearance<sup>2</sup>. Food in the gut can also delay caffeine absorption<sup>1</sup>.

Caffeine passes through the placenta and both the pregnant woman and fetus have a reduced capacity to metabolise caffeine, so it remains in their systems for longer, especially

in the third trimester (up to 15 hours). Some of this reduction is due to the increased presence of progesterone and oestrogen hormones. This affects the half-life. At the end of pregnancy, the half-life of caffeine is three to four times longer than before pregnancy<sup>2</sup>. This means the concentration of circulating caffeine in the pregnant woman's and fetal blood circulation would be higher than a non-pregnant woman due to this with the same caffeine consumption. Within a couple of weeks after birth the caffeine clearance has returned to pre pregnancy rates but if women are breastfeeding the limit of 200 mg per day is still recommended.

After drinking 200 mg caffeine, blood flow within the villi of the placenta reduces by 25%. This physiological response relates to the evidence of reduced birth weight that follows. With higher consumptions of caffeine, the placental blood flow is likely reduced further, thus having a greater impact on the fetus reaching its potential birth weight.

The body can develop a tolerance to regular ingestion of caffeinated products which can reduce its stimulant effects unless higher amounts of caffeine are consumed<sup>1</sup>. A rapid withdrawal of caffeine, like other substances, can cause headaches, irritability agitation and fatigue. These symptoms take about a week to subside. Therefore, reductions in caffeine intake may be best if they are incremental rather than rapid. Conversations about caffeine consumption are as important for couples trying to conceive as they are for pregnant women because as stated above caffeine crosses all barriers and reduction is recommended. The advice is to limit the caffeine consumption to 200mg a day for men and women planning a pregnancy.

The RCM briefing<sup>5</sup> indicates that only two of several links between caffeine consumption and adverse pregnancy outcomes are supported by the evidence base. These are high caffeine consumption (above 300 mg per day) and spontaneous abortion or miscarriage<sup>7</sup> and high caffeine intake and low birth weight<sup>6</sup>. Although a newer paper also observed links with stillbirth and high caffeine consumption<sup>8</sup>. The links and evidence will be explained here.

### **Miscarriage risk**

Lyngso et al<sup>7</sup> analysed 27 case controlled and cohort studies that provided sufficient data on the effects of caffeine consumption and spontaneous abortion. The source of caffeine consumption was defined as coffee or caffeine from multiple sources. The literature that was included ranged from 1986- 2015 (16 studies were pre-2000), from several countries which included low and high caffeine intakes in their populations. They included a variety of samples from the smallest: 58 women with a history of recurrent miscarriage or 67 women planning a pregnancy to 86,282 pregnant women. The majority of included studies were controlled for maternal age, some also controlled for cigarette or alcohol use, previous miscarriage, gravidity, and determinants of socioeconomic status including educational level or employment. A few also considered whether women had nausea in the first trimester and its intensity<sup>7</sup>. The reason these confounding variables are important is because they are independent variables for miscarriage (age, smoking, previous miscarriage) or theoretically preventative. The link between nausea and successful pregnancies theorises those women reduce their caffeine intake due to nausea. A viable pregnancy may produce more

symptoms of nausea, and this may cause an aversion to coffee. Coffee intake is also associated with decreased hormones, specifically oestrogen and human chorionic gonadotrophin and may impact on cell development and placental blood flow and it may be these effects which cause the miscarriage.

The evidence from the pooled results is that high rates of caffeine consumption are associated with an increased risk of miscarriage<sup>7</sup>. This relative risk is significantly increased above the 300mg threshold compared to no caffeine/ coffee or 100 mg per day. The relative risk of miscarriage with 300mg of caffeine per day is 1.37 increasing to 2.32 with 600mg caffeine per day<sup>7</sup>. This means the risk of miscarriage with higher consumptions of caffeine increases. One of the criticisms of this study, and others, is that women self-report caffeine intake. This is seen as less reliable and a potential source of bias, however, one could argue that women are likely to report consumption accurately.

### **Birthweight and caffeine consumption**

The link between the maternal circulation and fetal growth or birth weight is well known for conditions such as preeclampsia but perhaps less discussed for caffeine consumption. Two studies will be explored in detail here due to the limited word count of this paper: the CARE prospective study of 2635 women<sup>6</sup> and Chen et al systematic review of 90,747 participants<sup>9</sup>. Their conclusions are similar, higher caffeine consumption is associated with a higher risk of a lower birthweight baby. Details of the other studies that found associations with lower birthweight are cited in the RCM briefing<sup>5</sup>.

The two studies classified caffeine consumption in slightly different ways. Less than 100 mg, 100-199 mg/ day, 200-299mg/ day and over 300mg<sup>6</sup> compared to low consumption (50-149mg/ day), moderate intake (150-349mg/ day) and high (above 350mg/ day)<sup>9</sup>. Despite their differences a higher caffeine consumption is above 300/350 mg and this aligns with the RCM briefing that considers less than 200 mg low consumption<sup>5</sup>. It was interesting that the mean caffeine consumption before pregnancy was 238mg reducing to 139 mg per day in the first 12 weeks<sup>6</sup>. So, women tend to half their caffeine consumption in pregnancy. However, the intake gradually increased to 153mg per day in the third trimester. Furthermore, most of the caffeine came from tea consumption (62%) compared to coffee (14%). These findings suggest that most women's caffeine consumption is low and below the recommended amount.

Caffeine consumption above 200 mg per day was associated with a reduction in birthweight of about 60-70 g, with a greater reduction seen with higher caffeine intakes<sup>6</sup>. In the moderate (150-349g) caffeine intake group birthweight was 33g lower or associated with a 38% risk of lower birth weight, increasing to 69g lower or 60% higher chance when more caffeine was consumed (above 350g)<sup>9</sup>. Each additional cup (which is equivalent to 100mg) was associated with a higher risk of low birth weight<sup>9</sup>. While the reduction in fetal weight may seem small, in a compromised fetus this could be significant.

Remember fetal growth is exponential which means most of the growth is in the last 6-8 weeks. Combine this with the longer lasting effects of caffeine in the maternal and fetal

circulation, especially in the third trimester, with a potential increase in consumption and it is understandable how caffeine has the potential to reduce birthweight.

### **Stillbirth**

The logical conclusion of this line of thinking is that the decreased placental flow that contributes to a reduced fetal weight could be associated with stillbirth. The most recent evidence, published in 2021<sup>8</sup> found an independent association between caffeine intake and late stillbirth, particularly when the intake was above 300mg. This study was interesting because it cited increased intakes of instant coffee, cola and energy drinks. Tea was not associated. The authors considered other constituents in cola and energy drinks (sugar, sugar replacements and taurine) that may be responsible for the association with stillbirth. They reiterate the message that pregnant women should be advised to reduce their caffeine consumption in pregnancy with midwives best placed to share this information with women<sup>8</sup>.

### **Postnatal period**

While most of the research focuses on the effects of caffeine consumption in pregnancy, the advice in the postnatal period if a woman is breastfeeding is to maintain a caffeine consumption of 200mg per day. This is based on the effects for the neonate as caffeine is found in breastmilk and the neonatal clearance of caffeine is low. The neonatal half-life of caffeine is between 65-130 hours due to immature kidneys - to produce urine and immature liver for its metabolism. Furthermore, the first 1000 days from pregnancy to the child's second birthday are accepted as being crucial for optimal child development, so limiting caffeine consumption while breastfeeding is seen as the best advice. If maternal caffeine consumption in pregnancy exceeds eight cups per day the neonate could exhibit withdrawal symptoms.

The last reason some postnatal women may want to maintain a low caffeine consumption is because of its diuretic effect. Women who have pregnancy induced or pre-existing urinary symptoms such as incontinence may find they increase with a higher caffeine consumption.

### **Conclusion**

This article hopes to help you make sense of the headlines and the research behind them so you can have conversations with women to support them make decisions about what is safe and acceptable for them. The advised limit of a maximum of two cups of coffee/200 mg caffeine per day may be considered too high for some women. Therefore, the midwife should tailor the information to the woman and her personal circumstances. For instance, a woman who has had one or more miscarriages may want all the available information on reducing her chances of this happening again. For her a lower caffeine threshold or abstinence may be preferred. It is important to explore with women all the sources of caffeine they consume. For now, the best available evidence recommends a 200 mg per day caffeine threshold is safe for women contemplating pregnancy, during their pregnancy and breastfeeding period<sup>2,5</sup>.

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