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Coffee is one of the most commonly consumed beverages around the world, but for many years, its effects on health have been disputed within the medical community. In recent decades, modern research has dispelled most of the myths surrounding coffee's effects on health. This work has also provided insightful information about the possible health benefits of coffee consumption. Most reviews of scientific literature conclude that for adults who consume a moderate amount of coffee (three to four cups per day), there is very little evidence of health risks and even some evidence of health benefits (Higdon and Frei 2006; Floegel and others 2012). A recent, widely publicized study found that drinking coffee is inversely associated with risk of death (Freedman and others 2012). Many other studies address the potential beneficial health effects of drinking coffee. The mechanisms behind these positive health effects have yet to be elucidated, and continue to be an active area of research in the health community. The following health topics are perhaps the most discussed in association with coffee intake.

Important Considerations

Confounding factors - which have been historically problematic in coffee studies - have led to several studies attributing coffee to illnesses like cancer. Smoking and caffeine are strongly associated, and heavy smokers consume more caffeine than non-smokers (Zavela and others 1990; Schreiber and others 1988b). At this point, the general population is aware that smoking impacts health negatively and causes cancer, and because of this awareness, there is a stigma against smoking. Therefore, in studies involving humans, people lie about their smoking habits. Self-reporting can also be a problem with other confounding factors, especially with behaviors related to health, such as alcohol consumption, exercise, and diet.

A common problem in many of the studies discussed here is the difficulty in measuring coffee or caffeine 'exposure'. This may be the root of inconclusive results reported by some researchers. A cup of coffee was often assumed to provide 85-100 mg of caffeine (Higdon and Frei 2006). However, we know this amount can vary significantly depending on mug size (Bracken and others 2002; Schreiber and others 1988a), coffee species, cultivar consumed (McCusker and others 2003), and brewing method. Also, we have learned that individuals metabolize coffee at different rates, which stems from individual genetics and undoubtedly results in inconclusive research (Carrillo and Benitez 2000).

Mental Performance

There is abundant evidence of the effects of coffee on alertness and attention. From decades of work on this topic we now know that caffeine blocks adenosine, which wards off the tired sensation and can result in increased attention or cognitive performance (Carrillo and Benitez 2000; Ribeiro and Sebastião 2010). This effect has the additional benefit of elevating the mood of coffee drinkers, although some believe this is only a result of the alleviation of withdrawal symptoms (James and Rogers 2005; Addicott and Laurienti 2009). We also know that the extent of these effects is partially mediated by human genetics (Yang and others 2010; Retey and others 2007). Since this is a widely accepted topic, and more related to physiology than health, this report will not elaborate further. Below is an extensive reference list of these topics for further reading.

Improvement in alertness/sleep disruption

(Hameleers and others 2000)
(Glade 2010)
(James 2011)
(Lieberman and others 2002)
(Lorist and Tops 2003)
(Mets and others In Press)
(Philip and others 2006)
(Quinlan and others 2000)

(Ribeiro and Sebastião 2010)

(Roehrs and Roth 2008)

Attention/cognitive performance

(Adan and Serra-Grabulosa 2010)

(Brunyé and others 2010b)

(Brunyé and others 2010a)

(Glade 2010)

(Lieberman et al. 2002)

(Ribeiro and Sebastião 2010)

(Serra-Grabulosa and others 2010)

Positive Mood effects

(Addicott and Laurienti 2009)

(Cropley and others 2012)

(Dawkins and others 2011)

(Haskell and others 2005)

(Higdon and Frei 2006)

(James 2011)

(James and Rogers 2005)

(Lorist and Tops 2003)

(Quinlan and others 1997)

(Smith 2009)

Neurodegenerative Disorders

There is evidence that certain deteriorative neurological disorders, including age-related cognitive decline, dementia, Alzheimer's and Parkinson's diseases are inversely correlated with coffee consumption. The mechanisms for these are active areas of research, and thought to be related to the adenosine blocking effects of caffeine. Work on Alzheimer's disease suggests that caffeine can limit the specific peptide that accumulates in Alzheimer's patients, and others have speculated that this mechanism can be transferred to other types of cognitive impairment (Santos and others 2010; Abreu and others 2011). More research is needed to provide concrete conclusions.

There is a large amount of evidence to support that drinking coffee can help maintain general cognitive function in older individuals. Generally, people of all ages can benefit from the short-term perks of caffeine consumption (Rees and others 1999). Some research suggests caffeine may be related to the longer-term stalling of cognitive decline in women but not men (Arab and others 2011; Johnson-Kozlow and others 2002), or specifically for those women without dementia (Ritchie and others 2007). Other studies have found a link between coffee drinking and reductions in cognitive decline with men (van Gelder and others 2007). Some research has found that coffee drinkers of both sexes who drank coffee at midlife had a lower risk of dementia later in life than those who did not drink coffee (Eskelinen and others 2009). Other studies point to caffeine as linked to the slowing of dementia progression, including the type of dementia that leads to Alzheimer's disease (Cao and others 2012; Gelber and others 2011). However, not all research has resulted in the same conclusion (Hameleers et al. 2000). Overall, a recent review still urged for more work on this topic, as the mechanisms are unclear, and the gender differences found in many studies are yet to be explained. Like other health topics, issues such as caffeine dosage and self-reporting were likely distorting the results (Santos et al. 2010).

Alzheimer's Disease

Alzheimer's disease is one of the most common types of dementia among older people, and is characterized by a progressive decline in cognition, daily functioning, and behavioral alterations, including loss of

short-term memory, language impairment, and disorientation (Santos et al. 2010; Alloul and others 1998). It is estimated that between two and ten percent of Americans and Europeans over 65 years old are affected by this disease (Alloul et al. 1998). In the brain, this has been linked to extracellular plaques containing β -amyloid peptides and neurofibrillary tangles by abnormally broken-up proteins (Arendash and Chuanhai 2010). A large amount of research relates drinking coffee and caffeine consumption with a lower risk of or lessening the progression of the disease (Barranco Quintana and others 2007). Caffeine is shown to reduce these peptides in the brain, and this is the mechanism believed to be causal to this relationship (Arendash and Chuanhai 2010; Arendash and others 2009; Tabaton 2009; Qosa and others 2012; Cao and others 2009; Cao and others 2011; Cao et al. 2012). However, there are other theories as to the specific mechanisms, such as an increased cerebral blood flow, which need to be further investigated (Audenaert and others 2011).

Parkinson's Disease

A large number of studies have also reported an inverse relationship between coffee or caffeine ingestion and risk of Parkinson's disease development (Higdon and Frei 2006; James 2011; Costa and others 2010; Hernán and others 2002). Parkinson's disease afflicts about three percent of the over-65 age group in the US, and there is evidence that this number is growing (Ross and others 2000). It is caused by degeneration in certain cells of the brain stem, which causes a continuous loss of dopamine and creates debilitating physical motor disturbance symptoms (Costa et al. 2010). Some studies have noted a dose-dependent effect, where a higher coffee consumption results in a stronger preventative effect (Ross et al. 2000). However, in women, the results are less conclusive (Ascherio and others 2001; Ascherio and others 2003; Palacios and others 2010). Some hypothesize the mechanism may be related to caffeine blocking the adenosine receptors, which increases motor activity (Fenu and Morelli 1998; Chen and others 2001). However, this area is in need of more research. Interestingly, cigarette smoking has also been often associated with a decrease risk of this disease, but some have suggested that coffee drinking is a confounding factor in these cases, as the two are statistically correlated (Hernán et al. 2002).

Sports Performance

For over 100 years, caffeine was known for its capacity to enhance muscular work (Rivers and Webber 1907). Today, scientific evidence has led to the consensus that any sports-related effects of coffee are due to caffeine. We know that caffeine is rapidly absorbed in the body through the gastrointestinal tract and quickly moves through cell membranes to the bloodstream (Harland 2000; Carrillo and Benitez 2000). Later, it is broken down in the liver. Peak caffeine concentrations have been shown to be about an hour post-ingestion (Harland 2000; Lieberman et al. 2002). Much of the scientific research regarding caffeine and exercise has been conducted with caffeine pills rather than coffee, as it is easier to measure caffeine's direct effects when all other biologically active compounds within coffee are not complicating matters.

It has been extensively supported that caffeine can improve intensity and endurance in aerobic sport, measured by time-to-exhaustion tests (Ganio and others 2009; Gant and others 2010). This can be variable, depending on the individual and their genetics, type of caffeine consumed, and other confounding factors. One study found that endurance was enhanced as little as zero percent and as much as 17 percent (Ganio et al. 2009). Others found an average of 27 percent increase in performance time, regardless of medium or high caffeine dosage (200-300 mg) (Pasman and others 1995; Lieberman et al. 2002). Some research has found evidence that caffeine may improve high intensity, short-term exercise (Astorino and Roberson 2010; Stuart and others 2005; Woolf and others 2008; Anselme and others 1992).

There is mixed evidence of improvements in resistance or strength training, including number of repetitions completed (Woolf et al. 2008; Hudson and others 2008; Hoffman and others 2009; Goldstein and others 2010a). However, not all research on this topic has come up with similar results (Beck and others 2006; Astorino and others 2008). Many studies found no difference in resistance capabilities or found

mixed results (Astorino et al. 2008; Green and others 2007; Hudson et al. 2008; Jacobs and others 2003). Therefore, this area is still under research and no conclusions can be drawn.

All of the above effects are likely due to the adenosine blocking effect of caffeine in the brain, making one seem less tired (Graham and Spriet 1991) and feel less pain (Goldstein and others 2010b; Fredholm and others 1999; Davis and Green 2009). Adenosine has been shown not only to induce tiredness but also muscle pain, therefore, blocking it could possibly reduce one's pain threshold during exercise (Sylvén and others 1988; Pappagallo and others 1993; Sylvén and others 1986; Gliottoni and others 2009). However, not all mechanisms are known, and additional pathways have been suggested, including direct muscle stimulation (Spriet 1995).

Type II Diabetes

Type II diabetes is a chronic disease where there are high levels of sugar (glucose) in the blood. This is caused by a problem with how the body produces or uses insulin in the body, which is needed to move blood glucose into cells. Type II diabetes usually forms over time, and those diagnosed are often overweight, as high levels of body fat can interfere with the way the body uses insulin. In the US, diabetes is the seventh leading cause of death for adults (Centers for Disease Control and Prevention 2011). Globally, it is estimated that the total number of people with diabetes will rise from 171 million in 2000 to 366 million by 2030 (Wild and others 2004).

Recently, it's been established that coffee consumption has an inverse association with type II diabetes (Bidel and others 2006; Bidell and others 2008; van Dieren and others 2009; Huxley and others 2009; Natella and Scaccini 2012; Psaltopoulou and others 2010; Floegel et al. 2012). Recent studies have consistently supported the idea that regular, or 'habitual', coffee drinking is associated with reduced risk of type II diabetes (van Dam and Hu 2005; van Dam and Feskens 2002; Oba and others 2010). There are a few proposed mechanisms behind this association, but no consensus has been reached. This consensus is complicated by the fact that some studies have linked caffeine to increased insulin sensitivity (Graham and others 2001; Keijzers and others 2002). This is an active area of research for health professionals as the incidences of type II diabetes are rising rapidly in the United States (Centers for Disease Control and Prevention 2011).

Most research has found that with more coffee consumption, there is less risk of developing type II diabetes, known to the scientific community as 'dose related' (Greenberg and others 2006; van Dieren et al. 2009; van Dam and Hu 2005; Huxley et al. 2009). One study of Dutch citizens found that the risk of getting the disease was cut 50 percent by consuming seven cups of coffee per day (van Dam and Feskens 2002). A very large study found risk reduced by 54 percent for men and 29 percent for women who drank more than six cups per day (Salazar-Martinez and others 2004). These studies are just a few examples of the very robust risk reduction found in studies of risk for type II diabetes and coffee consumption. There are also studies that suggest only moderate, long-term coffee consumption is associated with a lower likelihood of developing diabetes (Panagiotakos and others 2007; Psaltopoulou et al. 2010).

Several studies have found no significant association between drinking coffee and the risk of diabetes (Reunanen and others 2003; van Dam and others 2004; Saremi and others 2003; Hamer and others 2008). It's possible that these populations did not drink enough coffee, or perhaps they drank the 'wrong' type of coffee, or the studies were plagued by self-reporting errors and confounding factors, such as age or lifestyle choices. Or, perhaps all people do not receive the same level of health benefit from coffee, much like caffeine is metabolized differently depending on genetics (Retey et al. 2007; Yang et al. 2010). We will not be able to answer these questions until the specific mechanisms for this association are elucidated.

There are multiple possible mechanisms for the strong inverse relationship found between coffee intake and type II diabetes. Some think it has to do with caffeine (van Dam and Feskens 2002), others not (van Dieren et al. 2009; Oba et al. 2010). There is also evidence of similar preventative effects with decaffeinated coffee (Greenberg et al. 2006; Salazar-Martinez et al. 2004; Wu and others 2005; Greenberg and others 2005; Natella and others 2002). This may be partially explained by chlorogenic acids, which were

found in some studies to inhibit intestinal glucose absorption, therefore slowing the amount of glucose entering the bloodstream (Higdon and Frei 2006; Clifford 2000). Others propose that the additional energy and exercise performance via caffeine ingestion affects weight gain and therefore the risk of diabetes (Greenberg et al. 2006; Natella et al. 2002; Lopez-Garcia and others 2006). Some simply do not attempt to find a mechanism, noting the possible involvement of the thousands of organic compounds in coffee.

Finally, there is new evidence to suggest that drinking coffee after the onset of diabetes could be beneficial. One study found that coffee might have a potentially positive influence on other health complications due to type II diabetes, such as mortality via heart disease (Bidel et al. 2006). This study found a 21 percent decrease in cardiovascular disease mortality risk in those who drank seven or more cups of coffee per day, as compared to patients who drank two cups or less.

Liver Health

There is evidence that coffee has beneficial effects on the liver, including reducing the risk of liver cancer (see the cancer section of this report), cirrhosis/fibrosis, and fatty-liver disease (Cadden and others 2007; La Vecchia 2005). Drinking coffee has also been linked by scientific studies to the slowing of the progression of hepatitis C or hepatic fibrosis in the liver (Freedman and others 2009; Modi and others 2010).

Chronic injury to the liver can result in an accumulation of a certain extracellular matrix protein in the liver (scar tissue) and this causes hepatic fibrosis/cirrhosis, leading to many complications due to reduced liver function (Gressner 2009). This occurs mainly through hepatitis C or B infections and alcohol abuse. These proteins have been shown to be inversely associated with coffee consumption (Higdon and Frei 2006; Muriel and Arauz 2010; Gressner 2009). There is some evidence that this effect is dose-dependent, as one study showed the number of cups of coffee consumed accounted for >39 percent of the variance seen in severity of liver damage of study participants (Catalano and others 2010). One study went as far as to point out a particular caffeine metabolite, paraxanthine, as the mechanism for breaking up these proteins (Gressner and others 2009). That being said, not all studies have found this inverse relationship between coffee drinking and liver disease (Ong and others 2011). There is some possibility that the disease itself is a confounding factor, as people with cirrhosis tend to decrease their coffee intake because they metabolize caffeine more slowly due to their decreased liver function (Higdon and Frei 2006).

Cancer

There is a bit of an unfortunate history of flawed associations between coffee and cancer due to common confounding factors like smoking and alcohol use. These factors lead to a confusing lack of consistency in the scientific literature on this topic. For example, a review of studies concluded that there was a correlation between coffee drinking and lung cancer, but admitted in the discussion that confounding effects of smoking may still exist (Tang and others 2010). Today, we know that there is no real relationship between coffee and cancer risk in the majority of body sites. There is now ample evidence that coffee consumption is *not* related to the risk of cancers of the stomach (Arab 2010; Botelho and others 2006), breast (Fagherazzi and others 2011; Bhoo Pathy and others 2010; Arab 2010; Larsson and others 2009), kidney or renal cell (Bravi and others 2007a; Lee and others 2007), prostate (Park and others 2010; Jain and others 1998; Hsing and others 1990), esophagus (Tverdal and others 2011; Yu and others 2011), and ovaries (Larsson and Wolk 2005; Steevens and others 2007). There are also a growing number studies that have found coffee drinking associated with a reduced risk of certain cancers (list below), although the exact mechanisms for these are still unknown (Yu et al. 2011; Arab 2010). The mechanisms behind these relationships may or may not differ, depending on the particular cancer site. Anti-oxidant and anti-microbial activity (Ferrazano and others 2009) may all play roles. However, there is still some research that links coffee consumption with specific types of cancer. These are most notably lung and bladder cancer (Arab 2010; Tang et al. 2010; Zeegers and others 2001; Villanueva and others 2006). However, these studies are in the definite minority as research improves and confounding factors are removed more thoroughly from study groups.

Reduction of Cancer Risk linked to Drinking Coffee

Liver

(Bravi and others 2007b)
(Cadden et al. 2007)
(Gressner 2009)
(Inoue and others 2005)
(La Vecchia 2005)
(Larsson and Wolk 2007)
(Muriel and Arauz 2010)
(Nkondjock 2009)

Endometrium (uterine)

(Bravi and others 2009)
(Hirose and others 2007)
(Koizumi and others 2008)
(McCann and others 2009)
(Shimazu and others 2008)

Colon and rectum

(Arab 2010)
(Galeone and others 2010)
(Nkondjock 2009)
(Oba and others 2006)
(Tavani and La Vecchia 2004)

Cardiovascular Health

Most studies have found no statistically significant association between coffee and cardiovascular diseases, including coronary heart disease (Sofi and others 2007; Wu and others 2009; Andersen and others 2006). Over the past thirty years, research has been conducted on the effects of coffee and caffeine on cardiovascular health, with mixed results. Some studies have found evidence that links drinking coffee to heart disease and cardiac events (Nilsson and others 2010). Overall it is likely that coffee does contribute a small amount to human cholesterol levels (Wu et al. 2009). This has left health professionals and the public concerned. There are likely confounding factors at play that make it difficult to analyze this complex topic.

Cholesterol

There is evidence that drinking unfiltered coffee can lead to a very small increase in LDL-cholesterol (Jee and others 2001; Grubben and others 2000). Coffee diterpenes (cafestol and kahweol) have been found in certain studies to raise the cholesterol of humans (Gross and others 1997; Ranheim and Halvorsen 2005; Urgert and Katan 1996). One study found that five cups per day could elevate cholesterol by 8-10 mg/dL. However, they also found that filtered coffee retained negligible traces of these cholesterol-raising compounds (Urgert and others 1995; Ranheim and Halvorsen 2005). Other studies have found no relationship between coffee and increasing cholesterol, possibly due to the difficulty of separating coffee brewing methods (Thelle and others 1987; Grubben et al. 2000).

Blood Pressure

There is some confusion about the effect of coffee on blood pressure; a major concern for some coffee drinkers, as blood pressure is a serious risk factor for developing heart disease, stroke, and heart failure. Some research has linked coffee drinking to hypertension (Zhang and others 2011b; Zhang and others 2011a; Jee and others 1999). Other studies have found that this increase is negligible for coffee drinkers (Noordzij and others 2005; Geleijnse 2008). There is a possibility that this research is also confounded by

smoking or physical inactivity (Jee et al. 1999; Wu et al. 2009). However, recent reviews have made clear that drinking filtered coffee has no effect on blood pressure, and may even reduce the risk of hypertension in women (Geleijnse 2008).

Pregnancy

There are as many conflicting opinions as there are scientific studies on the effects of coffee and caffeine on pregnancy outcomes. The lack of clear evidence has made it very difficult for health professionals to advise pregnant women on safe levels of coffee consumption. This is a case where confounding factors are impossible to separate from the consumption of coffee. For example, pregnancy outcomes are dependent on the effects on the body of the pregnancy itself, which are individual and vary greatly over different populations. Pregnant women are also a group which tend to have unreliable self-reporting about smoking, alcohol use, or other 'risky' behaviors (Peck and others 2010). On top of this, due to the difficulty of adequately measuring caffeine ingestion, exposure level within studies is inconsistent and difficult to compare between studies (Bracken et al. 2002). We do know that caffeine metabolism slows during pregnancy, which makes it last longer in the blood. Some authors conclude that caffeine is harmful to the fetus, others that it has no effect. Recent reviews of many studies have concluded that there is still insufficient evidence to link caffeine with adverse fetal, neonatal, or maternal outcomes (Peck et al. 2010; Jahanfar and Sharifah 2009; Brent and others 2011). Most concerns and evidence fall into two categories, spontaneous abortion and fetal health. There are certainly other concerns, none of which have a large amount of evidence behind them and therefore they are not covered in this review.

“Reverse Causation”

Some think that a natural aversion to coffee and therefore caffeine in early pregnancy is a signal of a healthy pregnancy. Therefore, over time reduced caffeine consumption is found to be associated with a healthy pregnancy, which has caused a 'reverse causation' in the literature. This term is used to describe such errors in causation. The cause of this natural aversion to caffeine is attributed to stronger pregnancy hormones in viable pregnancies that are naturally likely to last longer and to be healthier than pregnancies with less strong hormones (Lawson and others 2002). In the literature this is called 'pregnancy signal'. One study found a 59 percent decrease in caffeine intake in women 4-6 weeks pregnant, which occurred concurrently with morning sickness (Lawson and others 2004).

Preterm Labor, Stillbirth, Miscarriage, and/or Spontaneous Abortion

There are insufficient numbers of comparable studies without confounding factors to conclude a clear link between spontaneous abortions and caffeine intake. Individual research studies have concluded a relationship in specific instances (Greenwood and others 2010), some having inadequate sample sizes (Weng and others 2008; Mongraw-Chaffin and others 2008). Studies that found no increase of risk due to caffeine ingestion (Pollack and others 2010; Zhang and others 2010; Jarosz and others 2012; Savitz and others 2008; Kuczkowski 2009; Browne and others 2007). When the body of research is evaluated; there is not enough of a consensus to draw conclusions (Signorello and McLaughlin 2004; Peck et al. 2010; Brent et al. 2011). Some still recommend moderate consumption during pregnancy, just to be 'safe' (Kuczkowski 2009).

Fetal Health

Although there have been large studies devoted to understanding the relationship between caffeine intake and fetal health, including risk of birth defects and birth weight, there is little evidence of causation via caffeine. For birth defects, estimating early exposure levels would be particularly important, as defects often are formed very early in the first trimester. Due to erroneous self-reporting of exposure, adequate estimation of caffeine ingestion is all but impossible. Also, defects are most commonly documented and measured at birth, therefore defects that result in miscarriage are not included in these types of studies (Peck et al. 2010). This leads to a whole set of literature that is unintentionally biased. Birth weight can also be

easily confounded by factors such as smoking (Balat and others 2003; Klebanoff and others 2002), which makes many studies void the possibility of certainty in their own results.

That being said, some studies have concluded that caffeine ingestion is correlated with low birth weight or birth defects (Orskou and others 2003), but they often present with a very small sample size (Miller and others 2009; Balat et al. 2003) or statistically insignificant conclusions (Schmidt and others 2010). Other studies have found no links to either affliction (Collier and others 2009; Jarosz et al. 2012; Torfs and Christianson 2000; Grosso and others 2001), and most reviews conclude that there is inadequate evidence to draw a conclusion about this relationship (Peck et al. 2010; Brent et al. 2011). However, the association between caffeine intake and birth defects has been null in the majority of recent studies (Peck et al. 2010). It is possible that it's simply difficult to measure the effect of caffeine on fetal health, but it is also possible that the level of caffeine humans consume would never cause these problems. As there are moral obligations to forcing pregnant women to consume semi-toxic levels of caffeine throughout their gestation period, we will probably never know conclusively.

Conclusions

It is important to remember that none of the research conducted on the health effects of coffee have discriminated as to 'specialty' or any other categories of coffee. While we would like to think that specialty coffee is more 'healthful' than other coffees, there is no evidence to support this yet. Some scientists investigating diabetes have addressed coffee brewing methods, and there is some consensus that filtered versus unfiltered coffees have differing levels of cholesterol. Unfortunately, most studies did not report this type of information, probably due to the difficulty on data collection (and perhaps, because they did not know to differentiate). In American studies, one review stated that most studies reflect consumption of drip-filtered coffee (van Dam and Hu 2005). Another article brought up the potential confounding factor of coffee additives, "for example, the ardent coffee enthusiast who drinks seven cups of black coffee without sugar compared with the social coffee drinker who adds full-fat cream and two lumps of sugar to his daily cup." (Tan 2003). However, most studies have not accounted for such additives. The preponderance of research to date has focused on trying to accurately estimate caffeine content. Since this is such a difficult task on its own, research has not gone further into the more specific type of coffee. Perhaps one day the industry can push research in a new direction, one where health professionals are more educated about the products they are investigating. Until then, there is some evidence that drinking coffee is related to health benefits.

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