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Anyone for GM decaff?

Visiting a coffee shop demands great attention to detail. To the volume required have to be added decisions from a menu that reads like the instructions for performing a symphony, and even bean variety is negotiable. At home, in the office, and in most restaurants the options are far simpler. “Decaff or regular?”, for example. Coffee is a complex beverage, chemically speaking. A mug of office black abandoned before a summer vacation will evaporate gently to leave an alarming fatty sludge, and the diterpenes cafestol and kahweol are under scrutiny in chemoprevention. However, because of the caffeine, a substance with known pharmacological effects, the epidemiological focus with coffee is often on this ingredient. The old notion that coffee is associated with pancreatic cancer has faded,¹ but the drink has been studied in the context of, for example, heart attacks, gallstones, cirrhosis, cognitive function, memory loss, and rheumatoid arthritis—with both positive (association) and negative (protection) results. A 1990 study hinted that, in respect of coronary heart disease, increasing consumption of decaffeinated coffee might increase risk.² Anyone tempted to use the decaffeinated drink as a control for normal coffee should read a recent paper by Ai Kubo and her colleagues.³

Health examinations for a prepaid healthcare organisation in northern California in the mid-1980s included a very simple question about coffee consumption, permitting other baseline demographic and medical information to be analysed in respect of coffee use. Consumption was recorded as regular only, decaffeinated only, both, or none, without the inquisition demanded at Starbucks today. Respondents saying “both” (about a quarter) were ignored in the analyses, and another complication is that those declaring “decaff only” would almost certainly have been former drinkers of proper coffee.

The study aimed to identify life styles that might complicate the use of decaffeinated coffee as a control, and the potential confounders revealed can only with the greatest difficulty be corrected for by the usual trick of statistical adjustment, for they point both ways. Drinkers of decaffeinated coffee may make this choice because of their medical history, and they may even have been advised by a doctor to avoid caffeine. Or they may feel well and want to stay that way, seeing decaff as a healthy option. We might also expect drinkers of real coffee to smoke or drink alcohol more often than their decaffeinated peers do. But drinkers of decaff were, for example, significantly more likely than both drinkers of regular coffee and non-coffee-drinkers to reply “yes” to the question “Do you now have heart trouble?”. For control purposes in a cardiovascular study this is no good. On the other hand, if one accepts that diets low in salt or fat, vegetarianism, vitamin pills, exercise, and other lifestyles protect health, such a study might be distorted in the other direction because such habits were more prominent in those drinking coffee from which the caffeine had been extracted.

Caffeine is removed by industrial processes, which do not exactly enhance the flavour. Plant geneticists have a different answer. They have learned a lot about the multistep biosynthesis of caffeine from xanthosine and about the caffeine content of different coffee beans.⁴ Arabica (*Coffea arabica*) is the most popular and its caffeine content is about 1%. For the truly sleepless night *C. canephora* is the one (Robusta 1.7%, Guarini 2.4%) while the wimpish *C. eugenioides* (0.4%) is too bitter for a naturally low-caffeine product. Now, via last week’s *Nature*, comes the prospect of coffee plants genetically modified to be low in caffeine.⁵ Shinjiro Ogita and colleagues report up to a 70% reduction in the caffeine content of *C. canephora* in which the enzyme theobromine synthase had been repressed by RNA interference. Their next target is the market leader, Arabica.

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- 2 Grobbee DE, Rimm EB, Giovannucci E, Colditz G, Stampfer M, Willett W. Coffee, caffeine, and cardiovascular disease in men. *N Engl J Med* 1990; **323**: 1026–32.
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- 5 Ogita S, Uefuji H, Yamaguchi Y, Koizumi N, Sano H. RNA interference: producing decaffeinated coffee plants. *Nature* 2003; **423**: 823.

Child survival

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Our series on Child survival begins today with Robert Black and colleagues describing the epidemiology of a worldwide public-health disaster—that every year, more than 10 million children do not live to reach their fifth birthday. The first four articles in the series provide a technical basis for a new approach to child health, moving from the epidemiology of child deaths to an assessment of how many of these deaths could be prevented with currently available interventions, whether delivery systems can achieve high coverage with these interventions, and how to ensure that the poorest children receive interventions that in general they are the most in need of. The fifth paper addresses what needs to be done to turn this situation around in terms of leadership, health systems, resources, and public awareness. We hope that the series will lead to debate on how to initiate and sustain momentum in child health without creating new bureaucratic structures or provoking political infighting. The authors of the series make no rash promises, but commit to organising meetings every 2 years to check progress on child survival and hold people accountable if none has been made. As the authors point out, this proposal alone is not enough “but is a long-term commitment to change and improve the state of child health”. We hope that this series will encourage others to join them in this endeavour, and as a start invite our readers to join in the debate (e-mail: debate@lancet.com), some of which will be published on our website (<http://www.thelancet.com>). The question now remains “whether we shall have the will to do what needs to be done”.¹

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- 1 Editorial. The world’s forgotten children. *Lancet* 2003; **361**: 1.