

# GSA's 75th Anniversary: Guest Editorial



# A Glance Back at the Journal of Gerontology – Coffee, Dietary Interventions and Life Span

### Eleonora Duregon, MD, PhD, Michel Bernier, PhD, and Rafael de Cabo, PhD\*

Translational Gerontology Branch, National Institute on Aging, National Institutes of Health, Baltimore, Maryland.

\*Address correspondence to: Rafael de Cabo, PhD, Translational Gerontology Branch, National Institute on Aging, National Institutes of Health, Baltimore, MD 21224. E-mail: decabora@grc.nia.nih.gov

In the first issue of Journal of Gerontology in 1946, Sperling and colleagues published "The Effect of Coffee, Human Diets, and Inheritance upon the Life Span of Rats" (1). A lot has changed since then in the field of diet, nutrition, and aging research. However, key questions driving this field remain relevant today such as: How do dietary interventions extend life span? How do we study such interventions in laboratory animals? How translatable are these animal results to human population? What is the role of dietary habits on reproduction and fertility?

The coffee plant is native to Ethiopia, whose fruit can be roasted and brewed to produce coffee. Consumed since the 15th century, coffee has become one of the most popular beverages. Its popularity is mostly due to its stimulant effect on the central nervous system as well as unique taste and aroma. Because of the general acceptance of coffee consumption and the fact that little was known about whether drinking coffee leads to a longer life, Sperling and colleagues set up a longevity study in laboratory rats to understand the contribution of coffee and western-type diet on life span (1). The laboratory of Dr. Clive M. McCay was one of the pioneers in the field of caloric restriction (2) and heterochronic parabiosis between old and young rats (3). In this study, a large cohort of white rats of both sexes were assigned to one of the following three diets: a basal diet (A) designed from human foods proportioned according to those known to be consumed in the 1930's (4); an "improved diet," with increased quantities of whole foods considered "nutritious" (eg, whole milk, liver, carrots); and a third diet (C), which was the basal mixture plus synthetic vitamins. In addition, half of the rats in each group received a "modest supplement of coffee brewed fresh each day" prepared in the so called "usual manner, allowing one tablespoon of coffee per cup," in order to make "the experiment closer to human practices." Both the supplemented diets B and C had a favorable effect on growth based on tibia X rays, although overall life span was not improved. Quite interestingly, females on the basal diet and those receiving synthetic vitamins lived significantly longer with coffee consumption (Figure 1).

From the time this investigation was conducted, the field has dramatically changed its standards in order to improve the reproducibility of the research and maintain optimal laboratory husbandry conditions. Sperling's study was done in one of the top-notch and most influential laboratories focused on nutrition in the United States (1). Today, we would expect all information regarding the strain of rats, exact husbandry conditions (bedding, water, light cycles, etc.) as well as all aspects of veterinary care and diet composition (eg, macronutrients-fat, protein, carbohydrate content-from plant-based and animal origins) to be made available. We know now that the micronutrient composition of whole foods can change considerably in relation to how, when, and where they are prepared. This is also true for coffee as the caffeine content is highly variable depending on how it is prepared (instant coffee can contain from 30 to 90 mg of caffeine per cup) even when the coffee beverage is obtained from the same vendor. The challenges in the reliability and reproducibility of aging intervention studies led to the creation in 2003 of the Interventions Testing Program by the National Institute on Aging at the National Institutes of Health whose mandate was to standardize and test how diets, drugs, or other inventions can prevent or delay disease onset and extend life span in mice (5). The overall approach consists of testing all interventions simultaneously at three different locations using a genetically heterogeneous strain of mice of both sexes and comparable environmental conditions, such as light/dark cycles and temperature. After the initial reports showing differences across sites, the leading investigators made adjustments to obtain the bedding and diets from the same suppliers and shipped from a single source. Additional controls include the incorporation of a pair-fed group of animals to account for possible decrease in food intake associated with the drug or intervention under study (6). Such coordination is key to reduce variability to a minimum and provide statistical power to detect a 10% increase (or decrease) in life span (5).

Numerous studies in humans have now shown favorable effects of coffee in lowering cardiovascular risk factors, including type 2 diabetes, depression, and obesity. Chronic coffee consumption also appears to protect against some neurodegenerative diseases and is associated with improved asthma control and lower risks for liver disease and cancer.



Figure 1. Survival curves generated from the data of Sperling et al. "The Effect of Coffee, Human Diets, and Inheritance upon the Life Span of Rats."

However, there are still many misconceptions about coffee and health that can lead to confusion about whether coffee consumption can be enjoyed as part of a healthy, balanced diet. In this regard, genetics, metabolism, and individual responses to caffeine must be considered as key contributors to the variance between coffee drinkers (7).

To the credit of the authors, the Sperling's paper went even further than reporting survival and included an auxiliary study where coffee was given to female rats as sole source of fluid during lactation. The authors concluded that consumption of large amounts of coffee did not have adverse effects on the growth performance of their progenies for over three generations. Today, we know that there are no contraindications toward moderate coffee drinking (around 400 mg caffeine, up to four cups of coffee per day); however, lower levels are recommended for pregnant women, who are advised to limit caffeine intake to 200 mg from all sources, and in children because of their lower body weight (8).

#### Conclusion

At the time the study of Sperling and colleagues (1) was performed, the design and execution were state-of-the art. Although their reporting of

survival curves is outstanding, by today's standards, the study lacks key information to properly replicate their findings. Nevertheless, the authors achieved remarkable outcomes that have set the stage for extensive evaluation of the health benefits and risks of coffee consumption in a preclinical animal model.

#### Acknowledgments

The authors are supported by the intramural research program of National Institute on Aging, National Institutes of Health (NIA/NIH).

### **Conflict of Interest**

The authors have no conflict of interest to declare.

#### References

- Sperling GA, Loosli JK. The effect of coffee, human diets, and inheritance upon the life span of rats. J Gerontol. 1946;1(Pt 1 4):426–432. doi: 10.1093/geronj/1.4\_part\_1.426
- McCAY CM. Nutritional experiments on longevity. J Am Geriatr Soc. 1958;6:171–181. doi: 10.1111/j.1532-5415.1958.tb00704.x
- McCAY CM, Pope F, Lunsford W, Sperling G, Sambhavaphol P. Parabiosis between old and young rats. *Gerontologia*. 1957;1:7–17. doi: 10.1159/000210677
- Stiebling HK, Coons CM. Present Day Diets in the United States. Yearbook of Agriculture. Washington, DC: United States Government Printing Office; 1939:296–320.
- Miller RA, Harrison DE, Astle CM, et al. An aging interventions testing program: study design and interim report. *Aging Cell*. 2007;6:565–575. doi: 10.1111/j.1474-9726.2007.00311.x
- Gonzalez-Freire M, Diaz-Ruiz A, Hauser D, et al. The road ahead for health and lifespan interventions. *Ageing Res Rev.* 2020;59:101037. doi: 10.1016/j.arr.2020.101037
- Loftfield E, Cornelis MC, Caporaso N, Yu K, Sinha R, Freedman N. Association of coffee drinking with mortality by genetic variation in caffeine metabolism: findings from the UK Biobank. *JAMA Intern Med.* 2018;178:1086–1097. doi: 10.1001/jamainternmed.2018.2425
- Poole R, Kennedy OJ, Roderick P, Fallowfield JA, Hayes PC, Parkes J. Coffee consumption and health: umbrella review of meta-analyses of multiple health outcomes. *BMJ*. 2017;359:j5024. doi: 10.1136/bmj.j5024