may be associated with symptoms of IBS, CVS, atopic dermatitis, fibromyalgia, and chronic fatigue (6).

The diagnosis of a mitochondrial-based disorder is supported by a matrilineal family history, with his mother Susannah and her mother Sarah both having chronic illness for most of their later lives. Susannah's brother Tom suffered headaches, abdominal pain, and seasickness, and had marked cold sensitivity. As well as Susannah and Tom, Sarah had two other children who were probably afflicted. Richard died in infancy with a gastrointestinal complaint; Mary Ann was of short stature and retarded. She suffered from epilepsy, episodes of blindness, and paralysis. She died at the age of eight with symptoms typical of the MELAS syndrome.

An A3243G mitochondrial DNA mutation explains the illnesses of Darwin, of his mother, his maternal uncle, his maternal grandmother, and other relations. Whitehead *et al.* postulate that IBS and its comorbidity disorders may have shared pathophysiological mechanisms (3). It is proposed that mitochondrial dysfunction may be one such mechanism.

CONFLICT OF INTEREST

The author declares no conflict of interest.

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Shanahan's Response to Hayman Regarding Darwinian Dyspepsia

Fergus Shanahan, MD[1]

This letter underwent AJG editorial review.

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To the Editor: I am grateful to Dr Hayman; he and I agree on much. In my article (1), I focused on those facts which are accepted and well documented concerning Darwin's illness, and of course, on the words of the great scientist himself. This led me to refute many earlier suggestions and to the conclusion that Darwin's illness was IBS (irritable bowel syndrome) with some of the co-morbidity that frequently accompanies that condition. Hayman concurs, but goes further, suggesting that Darwin may have had an underlying mitochondrial A3243G mtDNA mutation. While one cannot conclusively refute nor confirm this, the supporting facts are slim and some of the evidence cited can be dismantled. For example, Hayman is confident that Darwin's "eczema has been reliably diagnosed as atopic dermatitis." I contest this; the evidence is weak or speculative (2,3). For example, there is no evidence that Darwin had pruritus; he never used the word *itch* in his detailed health diary, nor did any of the 20 doctors he consulted describe anything consistent with such a skin lesion. Furthermore, atopic eczema would have been far less common particularly in adulthood in the 19th century than it is today. Darwin's illness was characterized by symptoms with a remarkable absence of signs. Although a proportion of patients with IBS-like symptoms might have mitochondrial DNA mutations, the facts of Darwin's well-documented illness don't call for this diagnosis. If the great scientist carried a mitochondrial DNA mutation, he displayed and recorded few, if any, of the signs of it. It is more likely that he had a common presentation with something ordinary, than an uncommon presentation with something extraordinary. Darwin said it best: "False facts are highly injurious to the progress of science because they often endure long; but false views, if supported by some evidence, do little harm …" (4).

CONFLICT OF INTEREST

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Ten-Year Outcome of Radiofrequency Thermal Ablation for Hepatocellular Carcinoma: An Italian Experience

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To the Editor: We read with great interest the article by Shiina *et al.* recently published in the American Journal of Gastroenterology and reporting the outcome of radiofrequency thermal ablation (RFTA) for hepatocellular carcinoma (HCC) at a single Institution in Japan (1). We commend the authors for reporting the results

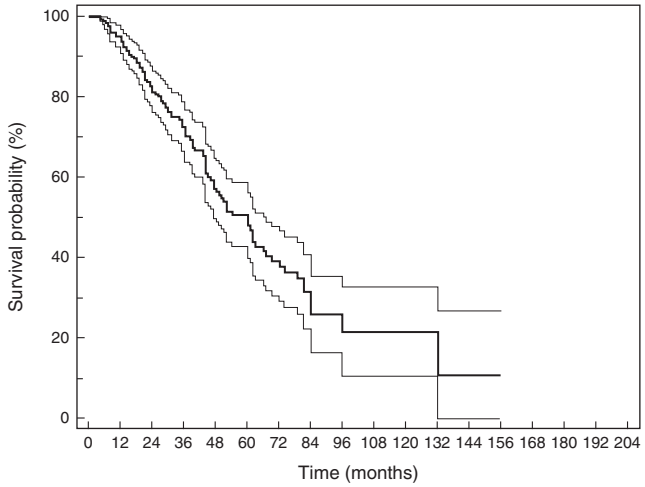

Figure 1. Kaplan–Meier survival curves (thick line) with 95% confidence intervals (thin lines) of the 277 study patients.

of this procedure in such a large population, and for providing important information regarding prognostic factors and predictors of tumor recurrence. We feel that these results may help refine selection criteria for treatment, and better understand the course of patients after RFTA. As these results were obtained in a very specialized institution, with a volume of at least 900 RFTAs per year, we deemed it of interest to evaluate the characteristics and outcome of RFTA in a population of patients with HCC seen in Italy. We felt that comparison of results may be useful for a more thorough selection of patients in the future, and to evaluate whether the very good results obtained by Shiina *et al.* may be generalizable to other clinical settings with different and various expertize in RFTA. In order to carry this out, we analyzed the Italian Liver Cancer (ITA.LI.CA) database, which includes 3,027 HCCs seen at 11 Italian centers from 1987 to 2008 and whose characteristics have previously been described (2). We included patients who underwent RFTA as primary treatment for HCC ($n=277$, 9.2%) and evaluated their main clinical and oncological characteristics, and overall survival. We observed that our population of patients who underwent RFTA was quite similar to the Japanese one. In particular, mean age (69.1±8.5 vs. 68.3±8.6 years), the proportions of Child-Pugh class A patients (76.2 vs. 74.2%), and of patients with HCC ≤3.0 cm (71.9 vs. 76.0%) were not significantly different between the Italian and Japanese patients, although in our series fewer patients had chronic hepatitis C virus infection (66.1 versus 74.4%, $P=0.007$), mean tumor size was larger (3.2±2.9 vs. 2.5±1.0 cm, $P<0.001$), and more patients had one HCC alone (76.5 vs. 58.5%, $P<0.001$). The 1-, 3-, 5-, 7-, and 10-year survival rates in our series were 94.0, 70.4, 48.0, 26.0, and 10.8%, and tended to be lower as compared with the respective figures in the Japanese series (96.6, 80.5, 60.2, 45.1, and 27.3%) especially after the first 5 years of follow-up. **Figure 1** shows the Kaplan–Meier survival curve and 95% confidence intervals for survival of our 277 HCC patients treated with RFTA.

What can be inferred by this comparison of Eastern and European patients with HCC treated with RFTA? It is likely that in order to obtain the best survival results with the use of this technique, a careful selection of patients is of fundamental importance. The poorer survival rates observed in our series are likely owing to the inclusion of patients in whom the results of RFTA were expectedly not satisfying. In fact, although we treated more patients with a single lesion, the mean diameter of the treated lesions was significantly larger than the one reported in the Japanese series, and well above the 2.0–2.5 cm threshold where the prevalence of the two main negative prognostic factors for incomplete ablation and recurrence—satellite nodules and microvascular invasion—sharply increases, thus providing an explanation for the decrease in survival observed after the fifth year of follow-up (3,4).

Noteworthy, the updated Italian Association for the Study of the Liver (AISF) recommendations for the management of HCC suggest that RFTA may be considered the treatment of choice for patients with early HCC, and we feel that the study by Shiina *et al.* should serve to call attention to adequate patients selection and great technical expertize as prerequisites of utmost importance for reaching such important long-term survival results (http://www.webaisf.org/media/16110/raccomandazioni-aisf-per-hcc.pdf).

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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