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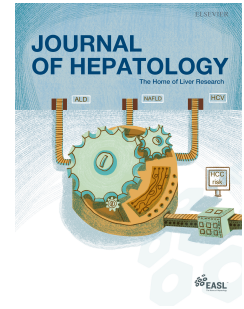
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Holding opposing ideas and the half-life of truth

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Dear Editor,

In a stimulating editorial in this issue of Journal of Hepatology [1], Vincent Di Martino contrasts our current study [2] with previous ones on methotrexate hepatotoxicity. It is worthwhile revisiting the key observations from our previous studies and rehearsing interpretations that were made in these articles. The first of our cohort studies questioning 'are serial liver biopsies justified?' involved 121 liver biopsies from 66 individuals and found 'advanced hepatic fibrosis with low-dose methotrexate therapy to be much less frequent than previously reported' [3]. None in this study developed cirrhosis or discontinued treatment on the basis of liver biopsy findings. The putative hypothesis that was put forward regarding the mechanism consistently stressed the interaction of the drug with the host and environmental factors [4, 5]. Another study based on data from United States Organ Procurement and Transplantation Network involving 158,904 adults who had been listed for, and/or received liver transplantation concluded that the 'burden of end-stage methotrexate-related liver disease to be exceedingly small, suggesting the need for reappraisal of current hepatotoxicity surveillance guidelines' [6]. The discussion section in this article started with a quote that 'Methotrexate hepatotoxicity and the premature reporting of Mark Twain's death: both greatly exaggerated' [6]. In another article, we pointed out that 'evidence base published to date overwhelmingly supports the notion that features of the metabolic syndrome such as diabetes and obesity accentuate the risk of methotrexate related liver disease' [7].

It was Francis Scott Fitzgerald, one of the great American writers of 20th century who wrote about 'holding two opposing ideas in mind at the same time and still retain the ability to function'. The 'null hypothesis' proposes that no relationship and significance exists in a set of observed variables and measured phenomena. A scientist's craft is to question, and loyalty rests with the observations; it is essential to recognise that truth is contextual rather than absolute.

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