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Comment on Eskenazi et al.

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I enjoyed the hypothesis of Eskenazi et al. regarding the possible fitness promoting effects of mutant alleles in Huntington disease [1]. As Eskenazi et al. point out, the mutant Huntington disease allele is a plausible candidate for an antagonistically pleiotropic genetic effect as postulated by Williams in his famous proposal regarding the origins of senescence [2]. This is not, however, a novel idea [3,4]. Eskenazi et al. deserve credit for proposing a specific mechanism of enhanced early fitness – increased activity of p53 and consequent better health. In the industrialized world, however, mutant Huntington disease allele carriers do not enjoy better health. The universal clinical experience with these unfortunate individuals is that they actually experience early mortality in part because they suffer more severe consequences of routine chronic illnesses. Huntington disease victims are terrible patients; they miss appointments for preventative medical and dental care frequently and don't take prescribed medications appropriately. Physicians are also less likely to diagnose and treat other medical problems in Huntington disease victims. This latter fact may account for Sorensen et al. describing less cancer mortality in Danish Huntington disease victims [5].

Nonetheless, the idea that some human genetic diseases are examples of antagonistic pleiotropy is intriguing and should be pursued.

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