Public health implications of epigenetics

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We read with interest the model of epigenetic inheritance developed by Slatkin in *Genetics* (SLATKIN 2009). The problem of missing heritability is one that requires urgent consideration in many complex conditions (RAMAGOPALAN et al. 2008). However, an equally important issue to address is the public health implications of heritable epigenetic marks passed through multiple generations. There is now convincing evidence of multiple environmental factors affecting several consecutive generations, often in complex, sex-specific ways (ANWAY et al. 2005; LI et al. 2003; PEMBREY et al. 2006). Epigenetic alterations have the potential not only to confuse epidemiological identification of the point of initial exposure to environmental factors (OGBUANU et al. 2009) but may also impede attempts to intervene after population-wide exposure to epigenetically active environmental factors.

The transgeneration rate of decay in epigenetic marks is currently unknown although it is likely that these do change over the course of a lifetime (ECKHARDT et al. 2006; FRAGA et al. 2005). We used the hypothetic values given in Slatkin’s model to illustrate how critical it is for public health officials to act as rapidly as possible to limit exposure to prevent widespread and long-lasting epigenetic changes. This model assumes that public health actions result in zero exposure to the causative environmental factor, meaning that the population frequency of the epigenetic mark ($\pi$) decays at a constant rate between generations ($\alpha$). This means that, after exposure is limited, the population frequency at any particular frequency ($\pi_{t+1}$) depends upon the population frequency in the previous generation ($\pi_t$) and $\alpha$:

$$\pi_{t+1} = (1 - \alpha) \pi_t$$

As can be seen in the accompanying figure, this could conceivably lead to high frequencies of epigenetic marks long after population exposure ceases. This is critically dependent both upon the value of $\alpha$ and how long after exposure public health measures are instituted. It is
critical that longitudinal studies are conducted as soon as possible to determine the true rate of epigenetic decay to understand the implications of epigenetics for public health.

**Figure: Intervention at different time points after exposure to an epigenetically active environmental factor.** Using Slatkin’s model of epigenetic inheritance with the probability for epigenetic alteration at a hypothetical locus (β) initially 0.2 and the probability of transgenerational loss of the epigenetic mark (α) 0.05 as described (SLATKIN 2009). Time is measured in generations (for human populations ~25 years) and exposure occurs when t=0. The vertical axis is the population frequency of the epigenetic mark. Intervention to limit exposure (modeled as β becoming 0) occurs after different generations following exposure (see legend). Note that these figures are arbitrary as α and β have never been experimentally determined.
Literature Cited


