Epigenetics is the study of how changes to chromosome structure record and/or transmit changes in the expression of genes. Epigenetic mechanisms act during development to control mechanisms such as cell proliferation and differentiation, tissue formation, organogenesis, and the emergence of physiological function. They also act throughout life to regulate gene expression over the long term. Epigenetic mechanisms respond to a wide range of biological signals, including stimuli from the external and social environments. So, why should this matter to general practice?

We know that poverty and socioeconomic deprivation are directly linked to premature mortality and morbidity. We also know that, despite universal access to free health care, inequitable healthcare outcomes persist in socioeconomically deprived populations. Although some of the disease-causing effects of poverty and deprivation are biologically direct, such as inadequate diet or exposure to alcohol, tobacco, and other toxins, there may also be later-emerging effects, in which epigenetic mechanisms play a part.

**EPIGENETICS ACROSS THE LIFECOURSE**

Although scientific understanding of the mechanisms by which adversity and social inequality lead to health consequences is still developing, it seems likely that processes are involved that regulate the production of inflammatory cytokines and stress hormones such as noradrenaline and cortisol. Together the accumulated effect of these stress-related biological signals is known as allostatic load. It refers to allostatic, the process of restoring physiological set-points after exposure to stressors (which may be environmental or social). Repeated or chronic exposure to stressors appears to erode the capacity of allostatic mechanisms to restore physiological set-points, and so promote survival under duress. Thus, over time, the consequences of prolonged exposure to stressors become more pronounced. By helping us to understand how these processes change, epigenetics provides an explanatory model through which the biological embedding of low socioeconomic status (SES) affects the functioning of a person’s genome.

**AND CAN THEY BE REVERSED?**

Epigenetic mechanisms influence the structure of chromatin, which is the complex formed of DNA and chromosomal histone proteins. Chromatin structure influences the accessibility of DNA to the gene transcription machinery, which drives differentiation of every cell type, all of which have the same DNA, by regulating the expression of different genes. A cell, organ, or person’s phenotype is thus determined not only by genome but also by the epigencode. At present, there are three well-understood mechanisms by which epigenetic factors affect gene expression: DNA methylation, histone modification, and non-coding RNA-mediated pathways. DNA methylation usually results in gene silencing or reduced gene expression. A wide range of histone modifications are known that either increase or decrease the amount of gene transcription, depending on the modification. Finally, microRNAs (miRNAs) are a class of non-coding single-stranded RNAs of 19–25 nucleotides in length, which regulate gene expression by binding to complementary sequences within messenger RNAs (mRNAs), blocking mRNA translation and/or promoting mRNA degradation.

Although there is abundant information about how these epigenetic mechanisms are deployed extensively in somatic tissues, their roles in the transgenerational transmission of chronic diseases risks, via the germ line, are less well understood. One likely explanation of how epigenetic changes may be passed from one generation to another is that, during pregnancy, the foetal germ cells that will give rise to the
mother’s grandchildren are exposed to the same environmental factors as both the mother and the somatic tissues of the fetus. Epigenetic modifications could thus be acquired by fetal germ cells during gestation, the functional impacts of which may not emerge until later life.11

As epigenetic mechanisms are regulators of gene expression, it is important to ask whether, once applied, they are reversible. This appears to be the case: for instance, there is accumulating evidence that mind–body therapies designed to reduce stress-related arousal and promote coping are associated with reductions in expression of genes for proinflammatory cytokines.12

WHAT ARE THE IMPLICATIONS OF EPIGENETICS FOR PRIMARY CARE?

The GP core curriculum emphasises the need to understand the physical health of our patients in combination with the psychological, socioeconomic, and cultural dimensions of health. If the epigenome is modifying gene expression, as a direct — but sustained or delayed — response to environmental stressors, then the need to move from the primacy of a biomedical model to an integrative holistic approach becomes particularly important. An epigenetic explanatory model allows us to see how many of our patients from socioeconomically deprived backgrounds are disadvantaged not only by the immediate lack of access to material, nutritional, and educational support that are conducive to the development and expression of capabilities for flourishing, but also by the cumulative biological embedding of their ongoing social deprivation.”

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