Environmental Genotoxicity: Gene-environment interactions and epigenetic mechanisms.

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Exposures to adverse environmental exposures have the potential to impact on the normal growth and development of children both before and after birth. The precise impact of an exposure depends on the developmental timing of the exposure. Exposures during vulnerable periods of organogenesis may have long-term structural effects. While many organ systems are mature at birth or soon after, the respiratory, immune and central nervous systems have prolonged periods of post-natal maturation; rendering them vulnerable to adverse postnatal exposures. Children are more susceptible to environmental exposures than adults and their dynamic developmental physiology means that they receive a higher “dose” in a given environment. Inherited genetic variations may convey disease susceptibility directly but, more frequently, provide a susceptibility to environmental exposures. There are numerous examples of a given gene variation being either a disease risk factor or a preventative factor depending on the environment. This has been well demonstrated for susceptibility to allergic sensitization and asthma in relation to levels of environmental exposure to microbial products. Environmental exposures may directly cause gene abnormalities; a classic example being tobacco smoke exposure. The list of environmental carcinogens is long and growing and children are exposed to many such agents in the modern environment. Environmental exposures may also alter gene expression through epigenetic mechanisms; a term that is used to describe changes in gene function (or expression) without alterations in gene structure. A variety of mechanisms can be responsible for epigenetic regulation of gene expression; including: methylation of CpG moieties in the gene promoter that results in gene silencing; and acetylation of histones in the nuclear chromatin which prevent gene transcription. Methyl donors in the diet, including folate and vitamin B12 can alter gene expression, with both beneficial and potentially detrimental effects. Tobacco smoke is thought to have some of its detrimental effects via epigenetic mechanisms. A general overview of these issues will be presented.