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Publication

Michael K. Skinner, Mohan Manikkam, Rebecca Tracey, Eric Nilsson, Md. M. Haque and Carlos Guerrero-Bosagna (2013) Ancestral dichlorodiphenyltrichloroethane (DDT) exposure promotes epigenetic transgenerational inheritance of obesity. *BMC Medicine* 11:228.

Summary

Background: Ancestral environmental exposures to a variety of environmental factors and toxicants have been shown to promote the epigenetic transgenerational inheritance of adult onset disease. The current study examined the potential transgenerational actions of the insecticide DDT on obesity and associated disease.

Methods and Results: The F1 generation offspring (directly exposed as fetus) derived from the F0 generation exposed gestating female rats were not found to develop obesity. The F1 generation DDT lineage animals did develop kidney disease, prostate disease, ovary disease and tumor development as adults. Interestingly, the F3 generation (great grand-offspring) had over 50% of males and females develop obesity. Several transgenerational diseases previously shown to be associated with metabolic syndrome and obesity were observed in the testis, ovary and kidney. The transgenerational transmission of disease was through both female (egg) and male (sperm) germlines. The F3 generation sperm epimutations, differential DNA methylation regions (DMR), induced by DDT were identified. A number of the genes associated with the DMR have previously been shown to be associated with obesity.

Conclusions: Observations indicate ancestral exposure to DDT can promote obesity and associated disease transgenerationally. The etiology of disease such as obesity may be in part due to environmentally induced epigenetic transgenerational inheritance.

Highlights

- First transgenerational study with DDT suggesting the 1950s exposure of the North American population may be a factor in today's populations disease.
- That the dramatic increase in the incidence of obesity and metabolic disease over the past 25 years may be in part due to ancestral environmental exposures, like DDT.
- Supports recent studies of the environmental compound induced epigenetic transgenerational obesity, including the plastic compounds BPA and phthalates, hydrocarbon mixture (jet fuel), and tributyltin. However, the frequency of DDT effects are far greater.
- What your great grandmother was exposed to during pregnancy, like DDT, may promote a dramatic increase in the susceptibility in your ability to develop obesity, and you will pass this one to your grandchildren in the absence of any continued exposures.
- That the current policy to use DDT in developing countries for malaria control needs to consider the long term generational impacts on disease as part of the assessment of its continued use.