Journal of
Environmental & Analytical Toxicology

Chauhan, J Environ Anal Toxicol 2015, 5:2
DOI: 10.4172/2161-0525.1000e104

Editorial Open Access

Germ Cell Toxicity Induced by Environmental Pollutants

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Germ cell toxicity is a fatal hazard that is associated with numerous chemicals as they intervene in some way with normal functioning of the reproductive system of the human males and females. Among the major substances that are toxic to developing reproductive systems some of the chemicals are as follows:

- Heavy metals (lead, mercury, manganese, cadmium, arsenic)
- Organic solvents (benzene, toluene, xylene, vinyl chloride, trichloroethylene, phenols)
- Persistent organic pollutants (POPs) (PCBs, dioxins, DDT, organo chlorine pesticides)
- Hormonally active agents (plasticizers such as phthalate esters)
- Pesticides (organophosphate and carbamate type)
- Cigarette smoke

It induces malfunctioning and adverse effects on sexual function, fertility (adult males and females), development and propagation of toxicity in the offspring. An essential part of the drug development process in the pharmaceutical industry is an assessment of the potential adverse effects of a new drug compound during drug trials and clinical studies. An evaluation of any potential adverse effects of the drug in the pharmacological dose must be carried out in accordance to its benefits in order to get it approved for use by the concerned regulatory bodies. The safety of potential drug compounds is accessed in non-clinical and clinical studies. A range of non-clinical studies are carried out before first administration to humans in phase I clinical trials. Non-clinical assessments continue through-out the development process, with certain studies being carried out before administration of the drug to different groups of people in clinical trials. For example, potential drugs cannot be tested in clinical trials with women of child-bearing age, without a non-clinical evaluation of the potential effects of the drug on fertility and fetal development. Non-clinical safety testing involves in vitro and in vivo toxicology tests (general, reproductive and genetic), and safety pharmacology studies. General regulatory toxicology studies involve administration of the potential drug compound to a range of animal species (usually one rodent rats), for varying lengths of time, and with different doses. The toxicology of the potential drug is evaluated during these studies via monitoring of bodyweight and clinical observations, and at the end of these studies using Histo-pathological analysis of tissue and clinical chemistry. Any potential toxic observed must be evaluated depending on the pharmacological dose and its effects observed. If the potential drug compound causes adverse effects at a pharmacologically relevant dose, depending on the risk: benefit ratio of the potential drug, it may not be developed further, One of the most common target organs leading to cessation of development of a drug is the testis. Early detection of toxicity leading to cessation of development is essential for reducing the number of animals used, and the cost of drug development. Biomarkers are becoming increasingly important in bioscience, particularly in toxicology, and could have a role in early detection of testicular damage, and translation into the clinic for monitoring testicular damage. In toxicology studies, as well as early detection, a profile of testicular damage could also be obtained throughout the period of the study to provide an idea how the damage is caused, rather than just looking at the histo-pathology results of the study. The biomarkers can be identified and measured as a means of providing an 'early warning' of testicular damage in non-clinical toxicology studies. In order to achieve this, germ cell specific proteins shall be identified, and the potential for their leakage from semi-niferous tubules into interstitial fluid and bloodstream shall be investigated in situations in which experimental damage to spermatogenesis has been induced.

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Received January 12, 2015; **Accepted** January 13, 2015; **Published** January 18, 2015

Citation: Chauhan A (2015) Germ Cell Toxicity Induced by Environmental Pollutants. J Environ Anal Toxicol 5: e104. doi:10.4172/2161-0525.1000e104