

## MUTAGENICITY AND ITS TESTING

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Mutagenesis refers to those processes that cause changes in the genetic material (mutations) in individuals or cells, either spontaneously or by the actions of chemicals or radiation, whereby their successors differ in a consistent and heritable way from their predecessors. Although deleterious effects may not be manifested in certain circumstances for many generations, a proportion of mutagenetic changes will produce these effects in the offspring.

Just as the thalidomide disaster brought about an awareness of teratogenesis, a hitherto unrecognized toxic effect, so the dramatic developments in genetics, particularly at the molecular level, during the past two decades have evolved the new subject of mutagenesis or genetic toxicology. Here the hazard is not merely to the next generation, as in teratogenesis, but to all succeeding generations. Unlike teratogenesis, for which valid human evidence exists, chemical mutagens have yet to be clearly associated with specific human genetic disorders.

Although the burden of spontaneous genetic diseases involves about 2-4% of the population, the full extent of such diseases is unknown. At present, detection of any effects of a mutagenic chemical is unlikely because the background is noisy, an inherent time scale of generations operates and the probable exposure time to significant numbers of new chemicals is about one generation. Clearly, however, the kinds of genetic damage that can be brought about by chemicals in experimental systems are remarkably similar to those observed in spontaneous human disease. In one case, the biochemical defect in the rare sex-linked disease known as the Lesch-Nyhan syndrome has been exploited to form the basis of an in vitro mammalian cell test system for mutagens. Chromosomal anomalies are probably the most clearly definitive form of all human mutations, and some 60 different conditions have been described in fetuses surviving to birth. Similar chromosomal damage can be induced by chemicals in both in vivo and in vitro experimental systems.