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Reciprocal translocations in somatic and germ cells of mice chronically exposed by inhalation to ethylene oxide: implications for risk assessment.

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Abstract

Groups of male B6C3F1 mice were exposed by inhalation to 0, 25, 50, 100 or 200 p.p.m. ethylene oxide (EO) for up to 48 weeks (6 hours/day, 5 days/week). Animals were sacrificed at 6, 12, 24 and 48 weeks after the start of the exposure for analyses of reciprocal translocations in peripheral blood lymphocytes and germ cells. The frequency of the total chromosomal aberrations in the peripheral blood lymphocytes was significantly increased at the 100 and 200 p.p.m. exposure concentrations at the 12-week time point, at 50, 100 and 200 p.p.m. at the 24-week time point and at all EO concentrations at the 48-week time point. The frequency of stable reciprocal translocations, which can be used as biomarkers, was increased ($P < 0.05$) at 100 and 200 p.p.m. at the 12-week time point, at 100 and 200 p.p.m. at the 24-week time point and at 50, 100 and 200 p.p.m. at the 48-week time point. No statistically significant increase could be observed in translocation frequencies at the 6-week time point in the peripheral blood lymphocytes. The exposure-response curves were non-linear when the frequencies of translocations were plotted against EO exposure durations or against EO exposure concentrations. There was no effect of exposure concentration rate on reciprocal translocation frequency. Reciprocal translocations induced in spermatogonial stem cells (observed at the spermatocyte stage) showed significant increases in translocation frequencies over controls at all EO concentrations at 48 weeks. However, increases were small and they did not occur in a dose-responsive manner. The statistically significant increase observed at 12 weeks in the spermatocytes was equivocal. This study provides low-level chronic exposure somatic cytogenetic data generated in mice that can be used to support the shape of the tumour dose-response in rodents and humans The germ cell cytogenetic data are discussed in terms of its relevance for a threshold response for genetic effects at low exposures.

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Publication Types, MeSH Terms, Substances, Grant Support

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