Australian Government
Department of Veterans' Affairs

Literature reviews of effects of fuel and solvent exposure on human male reproductive outcomes

Lay summary

February 2019

Royal Australian Air Force (RAAF) personnel may be exposed to aviation fuel (jet fuel) and a range of solvents. At the request of the Department of Veterans' Affairs (DVA), researchers at Monash University conducted literature reviews of the scientific evidence regarding whether occupational exposure to jet fuels and specified solvents of most relevance to the military were associated with adverse reproductive outcomes in men.

The literature examined was restricted to human studies in English during the search periods: January 2000 - April 2018 for jet fuels and January 2000 – June 2018 for specified solvents. The key outcomes assessed were the associations between exposure to jet fuels and/or ten specified solvents and the risks of adverse reproductive health in men:

- adverse reproductive outcomes: hypogonadism / primary testicular failure, androgen (testosterone) deficiency, impaired semen quality, reduced reproductive success (infertility, involuntary childlessness, not achieving desired family size, increased time-to-pregnancy, low fecundity, use of assisted reproductive technologies, adverse pregnancy outcomes or reduced fertility in female partners), altered reproductive hormone levels (testosterone, oestradiol, luteinising hormone (LH), follicle stimulating hormone (FSH))
- adverse sexual outcomes (erectile dysfunction, libidosexual dysfunction and psychosexual dysfunction).

The solvents included in this review were ethyl acetate, ethyl benzene, toluene, xylenes, acetone, isopropanol, methyl ethyl ketone (MEK), propylene glycol monomethyl ether (PGME), white spirit and trichloroethylene (TCE). This solvent list was that used previously for the female reproductive outcome review undertaken by Monash University in 2018 and adopted without modification. Combinations of solvents, e.g. benzene, toluene, ethylbenzene and xylene (BTEX) were considered for inclusion because the constituents were of interest in this review.

For jet fuels, eight eligible records were identified. Of these, five were scientific research publications and three were publicly available government agency or independent medical scientific advisory committee reports or toxicological profiles (herein referred to as reports).

One study reported adverse sexual health effects (i.e. erectile dysfunction and poor sexual function) in exposed male personnel compared with unexposed comparison groups. However, the participants were potentially exposed to a range of solvents in addition to jet fuel and the study was conducted many years after the exposure. Further assessment in this group found

no association between male exposure to jet fuels and miscarriage or stillbirths or difficulties in getting pregnant in partners of exposed men compared to partners of unexposed men. The findings of a cross-sectional study suggested that exposure to jet fuels could be associated with alterations in some reproductive hormone levels in men (i.e. FSH) but limited information was reported and the health implications are unclear. A prospective cohort study found that very low exposures to jet fuels and/or solvents was not associated with adverse effects on semen quality in aircraft maintenance personnel. Very limited evidence was available from a case control registry-based study suggesting increased risk of birth defects in babies born to mothers whose male partners worked in the gas and petroleum industry compared to those who did not work in this industry. However, the number of babies with birth defects was very small and the fathers could potentially be exposed to various chemicals in addition to fuel. No additional relevant studies to include in the review were identified through the reports.

The data limitations included the small number of studies, studies with a small number of participants or cases and low power to detect statistically significant differences in adverse reproductive outcomes, limitations in exposure assessment or in health outcome assessment such as self-reported exposure and health outcomes, possible recall bias, and co-exposure with solvent(s) or other chemical(s), which made it difficult to attribute any health effect to fuel exposure. More substantial high quality evidence is needed to draw firm conclusions.

For specified solvents, 34 eligible records consisting of 18 publications (from 14 primary studies) and 16 reports were identified. The most commonly assessed exposures were toluene, xylene and TCE; the evidence base for other specified solvents was very limited.

Ten publications reported outcomes related to fertility and/or fecundity. The exposures varied across these studies and only three publications reported outcomes assessed in relation to a single specified solvent exposure; two reported on TCE and one on toluene. In the other publications, exposure to several solvents and associations with reproductive outcomes were reported.

Of the six publications that investigated an association between specified solvent exposure and semen profile, sperm motility was reported in five; a significant decrease in sperm motility was reported in three and two reported no association with sperm motility. Co-exposure to several solvents including benzene, toluene and xylene was identified in all three studies that reported a reduction in sperm motility. The other two publications reported no association of TCE or PGME with sperm motility.

Five publications from four cross-sectional studies reported endocrine profiles. Four publications reported serum levels of FSH, LH and testosterone. Exposure to toluene was investigated in three publications and TCE in two.

In TCE exposed workers, the studies found that the mean serum FSH, LH, and testosterone levels decreased with the number of years' exposure up to a total of seven years of exposure, FSH levels were lower in those with greater than seven years of exposure, but the study did not include an unexposed comparison group.

The evidence for an association between exposure to toluene and reproductive hormone outcomes was equivocal; two publications reported no significant associations with FSH, LH and testosterone levels in the exposed group compared to the unexposed group. However, one of these studies reported significantly lower levels of FSH and LH in a subgroup of workers less than 40 years old. The third study reported that exposure to toluene was associated with significantly lower levels of FSH, LH and free testosterone.

Four studies (four publications) reported pregnancy outcomes in partners of exposed men. Four reported on spontaneous pregnancy loss. These publications did not report significant associations with pregnancy outcomes in partners of exposed men when the exposed group was compared with the unexposed comparison group. However, one publication conducted a subgroup analysis and found a significant increase in risk of spontaneous abortion in the high toluene exposure subgroup.

Two publications reported on the incidence of birth defects. One publication found a significantly higher risk of congenital defects in the solvent-exposed group based on quantitative model predicted exposure estimates using toluene as a marker, but the numbers were low; based on 37 birth defects (398 pregnancies) in the exposed group and 11 birth defects (302 pregnancies) in the unexposed group. However, it was difficult to establish any clear association between exposure and outcome due to uncertainty in the specific solvent exposures. The other publication did not find any association between toluene or xylene exposure and likelihood of birth defects.

One publication reported adverse sexual health effects (i.e. erectile dysfunction and poor sexual function) in solvent exposed male F-111 Deseal/Reseal (DSRS) personnel compared to non-exposed personnel. However, the participants had been exposed to a wide range of solvents.

The level of available evidence was weak due the limited number of studies and the limitations of study designs. The majority of evidence came from cross-sectional studies and in some studies co-exposure with other solvent(s) or chemical(s) at the workplace made it difficult to ascertain specific exposure-outcome associations. Limitations of individual studies included study designs (including cross-sectional and case control), small numbers of cases of adverse reproductive health outcomes, potentially biased exposure assessment or health outcome assessment. The omission of possibly relevant papers that were published prior to 2000 or after June 2018 and the omission of non-English language papers was partly addressed by including relevant studies found during a reference check of included publications. No key relevant publications were identified by scrutinising the reports that met inclusion criteria and were not included in this review.

The available literature on associations of exposure to jet fuels or the specified solvents with adverse reproductive health outcomes in men is very limited in its extent and quality and in its applicability to men in the Australian military. It is difficult to form conclusions about the association between exposure to jet fuels or specific solvents and adverse reproductive outcomes in men without more high quality evidence.