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**AGE AND GENDER DIFFERENCES IN ACUTE TOXICITY
AND BLOOD-BRAIN BARRIER OPENING INDUCED BY
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The age- and gender-related differences in acute toxicity and opening of blood-brain barrier induced by an organophosphate soman were investigated in rats. To assess acute toxicity, young (7 weeks old) and old (12 weeks old) male and female rats were subcutaneously administered with various dose levels of soman. In both male and female groups, young animals ($LD_{50} = 156 \mu\text{g/kg}$ for males; $100 \mu\text{g/kg}$ for females) were relatively resistant (1.25 times) compared to the old ($124 \mu\text{g/kg}$ for males; $80 \mu\text{g/kg}$ for females). In addition, male rats showed 1.55 times higher LD_{50} values than age-matched females. To analyze the permeability of blood-brain barrier during seizures, rats of each group were intravenously administered with 2% Evan's blue solution (3 ml/kg) followed by subcutaneous intoxication with $1.3 \times LD_{50}$ of soman. In order to reduce mortality, HI-6 (125 mg/kg) was pretreated 30 min prior to soman challenge. One hr after soman poisoning, cerebrum was removed after intracardial perfusion with saline, and the dye penetrated into brain tissue was quantified. In comparison with the quantities ($6.9 \pm 1.9 \mu\text{g}$ for males; $2.9 \pm 1.4 \mu\text{g}$ for females) in old rats, relatively large amounts ($11.7 \pm 2.7 \mu\text{g}$ for males; $5.1 \pm 1.5 \mu\text{g}$ for females) of Evan's blue penetrated in young animals. Taken together, it is suggested that blood-brain barrier opening of young male animals is more sensitive to seizures, in spite of higher resistance to acute toxicity of soman than the old, and that the result could be a cautionary note on the vulnerability of blood-brain barrier of the young to epileptiform seizures.

keyword : Organophosphate, soman, acute toxicity, blood-brain barrier