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Health Effects Research
Laboratory
Research Triangle Park NC 27711

Research and Development

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Project Summary

Fetotoxic Effects of Nickel in Drinking Water in Mice

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Nickel chloride was administered in drinking water to pregnant mice from the 2nd through the 17th day of gestation at nickel doses of 0, 500, or 1000 ppm. Fetal or maternal toxicity was not seen after administration of 500 ppm of nickel. However, the higher dose caused spontaneous abortions, loss of fetal mass in survivors, and loss of maternal mass. The oral route of administration via drinking water was at least 2.7 times less effective than parenteral routes in producing fetal effects.

This Project Summary was developed by EPA's Health Effects Research Laboratory, Research Triangle Park, NC, to announce key findings of the research project that is fully documented in a separate report of the same title (see Project Report ordering information at back).

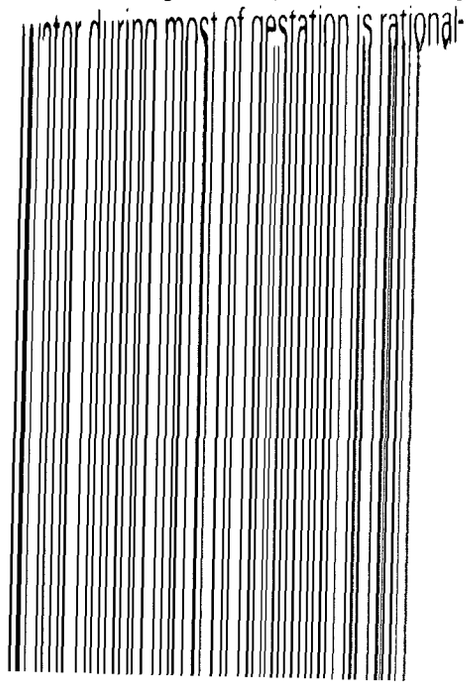
Introduction

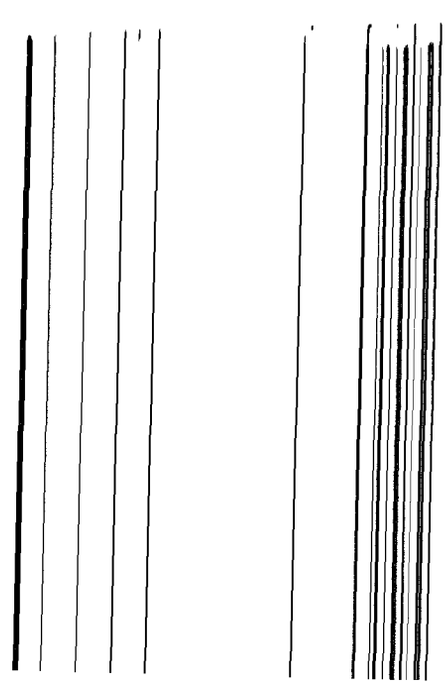
This report summarizes the work done to examine a soluble nickel salt for its efficacy to cause fetotoxic effects in mice. Administering the compound in drinking water during most of gestation is rational-

dam was killed by suffocation with CO_2 gas and weighed. The uterus was removed and counts were made of dead (resorbed and newly dead) and live fetuses. The live fetuses were removed, examined for gross abnormalities, blotted dry, and weighed. Two of every three fetuses were fixed in Bouin's solution, and the third fetus was preserved in alcohol.

Pregnancy rates and other incidental data were analyzed using contingency tables. Unless stated otherwise, all data were analyzed using the litter as the experimental unit.

The rate of water consumption in mice was 160 ml/kg body mass/24 h estimated by observations of bred mice gang-caged from the 14th through the 18th day of gestation. During 24 h of this study, the consumption of nickel at concentrations of 500 and 1000 ppm in water was estimated to be 80 and 160 mg/kg body mass, respectively. For the period of administration (2nd through 17th day of gestation), the total consumption of nickel at concentrations of 500 and 1000 ppm was estimated to be 1280 and 2560 mg/kg body mass, respectively.





tive for producing nickel toxicity A wide range and high incidence of terata in fetuses of mice administered 4.6 mg of $NiCl_2$/kg body mass IP once between the 7th and 11th day of gestation has been observed. On the basis of the ratio of effectiveness of an oral vs. an injected dose, a 4.6 mg IP dose would be equivalent to a 60 mg oral dose.

In our study, we could not induce a wide range and incidence of terata after we administered nickel in 1650 mg/kg orally daily (1000 ppm in drinking water). Only decreased fetal body mass was observed. Any higher dose was so toxic for both dam and conceptuses that the frequency did not continue Therefore, our 160 mg/kg dose is the closest response to a 4.6 mg/kg IP dose that we could achieve. As the calculated oral equivalent of 4.6 mg/kg IP is 60 mg/kg, our 1000 ppm dose is 2.7 times less effective. Therefore, such calculations do not adequately account for the observed differences.

The variation in results may depend on some other factor in the route of administration which decreases the effectiveness of low but continuous oral intake compared to high single parenteral route. It appears, therefore, that the fetal effects of nickel poisoning may be overestimated by experiments using parenteral methods.

Conclusions

The oral dosage of nickel required to produce fetal toxicity or teratology may have been overestimated when based on studies using parenteral administration. A factor as large as 2.7 times may be needed to correlate the effects of parenterally administered nickel with those of orally administered nickel.

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The complete report, entitled "Fetotoxic Effects of Nickel in Drinking Water in Mice," (Order No. PB 83-225 383; Cost: $7.00, subject to change) will be available only from:

National Technical Information Service
5285 Port Royal Road
Springfield, VA 22161
Telephone: 703-487-4650

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