EFFECTS OF MONOSODIUM GLUTAMATE ON DEVELOPING MOUSE FETUSES *

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Introduction
The study of congenital malformations by experimental means appears to have been first undertaken in about 1820.\(^\text{(16)}\) A survey of literature reveals that there are approximately 60 methods whereby congenital malformations have been produced in laboratory animals.\(^\text{(8,16)}\) Now that the vast resources of the drug industry and of private and nationalized medicine are to be poured into research in this field, the testing of new drugs or chemicals for teratogenic activity on the mammalian embryo must be revealed.

More recently, the chemical, monosodium glutamate has received a great deal of attention due to its uses and its properties.\(^\text{(1,3,10)}\) In North America, the Chinese restaurant syndrome is believed to be caused by this agent.\(^\text{(6,13)}\) A similar use of this chemical in cooking has been observed in Asian countries. This study was then planned in order to determine whether monosodium glutamate which can produce specific brain lesions and vascular disturbances when injected into Swiss mice,\(^\text{(9,11,12)}\) is also teratogenic to the developing mouse fetuses.

Materials and Methods.
Swiss albino mice were used throughout this experiment. Four young females, age 12 weeks and weighed about 25 gm. and one male of the same age were kept in each cage. These females were examined for the presence of vaginal plugs twice a day. Those showing vaginal plugs were considered to be in day 1 of pregnancy.\(^\text{(7)}\) Males were removed each day and return to mating cages next morning.

Monosodium glutamate (Ajino-moto) in the form of powder was used in this study. It was dissolved in distilled water before use. Since it has been demonstrated that most congenital defects in rats and mice were produced by teratogens given on the ninth day of gestation,\(^\text{(2,14,15)}\) different doses of the chemical were then injected intraperitoneally on day 9 after mating. A series of pilot experiments was run to determine the most effective teratogenic dose. The dose of 500 mg/kg body weight was found to be suitable for this strain of mice. Controls were injected with correspon-

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Controls were injected with corresponding volumes of distilled water.

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Table 1. The Effects of Different Doses of Monosodium Glutamate Injected into Pregnant Swiss Mice on Day 9 of Gestation. All Fetuses Were Examined 8 Days After Infection.

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<th>mg/Kg. B.Wt.</th>
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<th>No.</th>
<th>% Dead</th>
<th>Resorptions</th>
<th>No.</th>
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<th>Total No. of Surviving Fetuses</th>
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<th>% No.</th>
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Swiss mice on Day 9 of gestation. All Fetuses were examined 8 days after infection.
Effects of Monosodium Glutamate

Fig. 1 A monosodium glutamate treated fetus, showing exencephaly.

Fig. 2 Amonosodium glutamate treated fetus, showing encephalocele, aprosopia agnathia.

Each unit of the scale in figure 2 represents 1 mm.

ding volume of distilled water. The females were killed 8 days after the injection, the number of resorption sites and visible fetal anomalies were recorded. Paraffin sections of the abnormal fetuses were recorded. Paraffin sections of the abnormal fetuses prepared for confirmation of the abnormalities.

Results

As a result of one injection of the chemical into pregnant mice, the incidence of resorption sites was observed. However, it was not differ than of the control. The highest incidence of externally visible anomalies was produced by a dose of 5,000 mg/kg. body wt. (Table 1). Therefore, the dose of 5,000 mg/kg. body wt. was considered to be the optimal teratogenic dose for Swiss mice. Only 1.6% of the surviving fetuses was abnormal. The anomalies observed were those involving the cephalic region. There was a definite protrusion of the brain tissue outside the skull in one abnormal fetus (Fig. 1). Another abnormal fetus had extremely malformed facial region (Fig. 2). This was classified as aprosopia. The fetus showing aprosopia also had complete absence of the lower jaw.
Discussion

Although monosodium glutamate has not been tested for its teratogenicity in large number of species, its effects on the developing chick embryo(4) and an infant rhesus monkey suggest the possibility that such chemical might be harmful to other experimental animal species. The low incidence of fetal mortality and abnormality was observed from this experiment. It is interesting to point out that such a low incidence of fetal death and abnormalities may be due to the route of administration which inevitably cause variation in the concentration of the compound, the duration of exposure and the nature of the metabolic by-products reaching the embryo.(5) In new born mice, subcutaneous injection of this chemical, induced acute neuronal necrosis in several regions of developing brain within few hours after treatment.(11,12) This also suggests the direct action of this agent and also indicates the possible role of placental barrier in the prevention of the embryo from this teratogen. Whether the chemical is teratogenic or not is difficult to ascertain from this study. However, according to the excessive and long term use of this compound in cooking, thorough investigations should be made in order to prevent any danger that might occur to the developing human fetuses.

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References


