Teratogenic Effects of Hyperbaric Oxygen.* (29425)

VERGIL H. FERM (Introduced by G. Margolis)
Department of Pathology, Dartmouth Medical School, Hanover, N. H.

During an investigation of the effects of hyperbaric oxygen on gestation in the golden hamster, a small but significant number of the fetuses were found to have severe congenital malformations. This report will thus serve to identify hyperbaric oxygen as a method for experimental induction of mammalian congenital malformations and also warn of its possible effects on human embryonic development. Reduced atmospheric pressure and oxygen tension have produced congenital malformations in mice(1,2), and rabbits(3), but not in the rat(4). These effects have generally been attributed to hypoxia.

Methods. Mature virgin female golden hamsters (*Cricetus auratus*) were bred under direct observation to obtain accurately timed matings(5). Fifty-three pregnant hamsters in the early stages of gestation (Table I) were placed in a 22 cubic foot hyperbaric chamber (Vacudyne Co., Model AC-24-5) which was then flushed with 100% oxygen for 3 minutes. When 12 or more animals were treated at one time a connecting chamber of about 15 cubic feet was used. Soda lime to extract carbon dioxide was added to the chamber at the start of each run. Pressures were then elevated over a 10 minute period to 30, 40, or 45 lb/in^2 (about 3.0, 3.6, and 4.0 atmospheres; room pressure = 0 lb/in^2= 1 atmosphere) for 3 or 2 hours with 100% oxygen. At the end of this time, the animals were decompressed as follows: for 45 lb/in^2—15 min at 15 lb, 1 hour at 10 lb, 3 hours at 5 lb; for 40 and 30 lb/in^2—10 min at 15 lb, 20 min at 10 lb, 3 hours at 5 lb.

Results. Twelve of the 53 treated maternal animals showed signs of convulsions, loss of consciousness, and vertigo within the first hour of treatment. Eleven animals were sacrificed at the end of 24 hours when signs of nervous system involvement did not disappear. The remaining animal recovered quickly and showed no further signs during the remainder of the experimental period. Decompression produced no additional signs of stress in the maternal animals. Forty-one animals survived the treatment without apparent ill effects.

The pregnancies were terminated on either the 13th or 14th day of gestation (normal gestation 16 days) and the fetuses recovered. Resorption sites were recorded at this time. Gross malformations noted in the recovered fetuses were: umbilical hernia, exencephaly (Fig. 1), hare-lip, spina bifida, and a peculiar hypoplasia of the lower extremity (Fig. 2). Most of the defects were found within only a few litters (Table I).

Discussion. Two possible explanations for these findings are: oxygen toxicity and increased pressure. It is not possible from these data to separate the teratogenic nature of these factors, nor to estimate their relative effects. The resorption rate was not as great as might be expected from other teratogenic experiments in the hamster(5,6,7), although the length and degree of treatment ap-

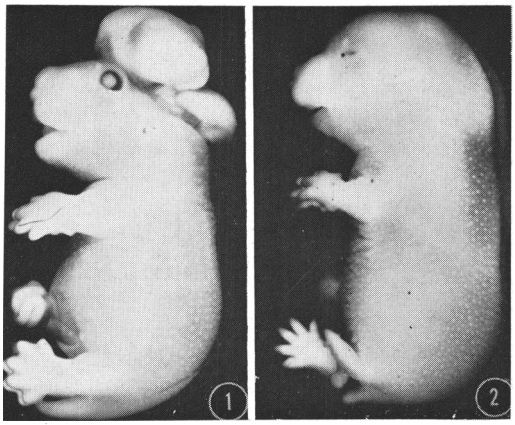

FIG. 1. 13-Day-old hamster fetus from mother exposed to 40 lb/in^2 of 100% oxygen for 3 hr on 6th day of gestation. Marked exencephaly. × 3.6.

FIG. 2. 14-Day-old hamster fetus from mother exposed to 40 lb/in^2 of 100% oxygen for 3 hr on 8th day of gestation. Note marked deformity of left hind extremity. This fetus also had a severe right-sided cleft lip and palate noted only by hypoplasia of the mandible in this lateral view. × 3.6.

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TABLE I. Effect of Hyperbaric Oxygen on Maternal Mortality, Fetal Resorption, and Gross Congenital Malformations in Golden Hamster.

Day of gestation treated	Mothers treated (No.)	Mothers surviving (No.)	Fetuses surviving (No.)	Fetuses resorbed (No.)	Fetal resorption rate (%)	Fetuses malformed (No.)
8*	5	5	60	2	3	0
8†	15	13	139	20	12	3
8‡	5	4	42	13	24	2
7*	6	6	66	2	3	0
7†	6	5	63	3	5	2
7‡	8	5	62	4	6	9
6†	4	4	44	3	6	1
6‡	4	2	26	0	0	0

* 30 lb/in² for 3 hr. † 40 lb/in² for 3 hr. ‡ 45 lb/in² for 2 hr.

proaches the maximal maternal stress since about one-fourth of the mothers succumbed to this insult. None of the malformations noted here have been found in any of the animals run at 30 lb/in² for 3 hours or in any offspring of over 300 hamster pregnancies used as controls in other teratogenic experiments in this laboratory. Repeated attempts by this author to produce experimental malformations in the golden hamster by reduced atmospheric pressure equivalent to 18,000 ft elevation for 12 hours have been unsuccessful. With the increasing use of hyperbaric oxygen therapy in medical practice, attempts should be made to study this teratogenic effect in other species and to determine the relative roles of increased oxygen tension and increased atmospheric pressure in embryonic development.

Summary. Pregnant golden hamsters in early stages of gestation were exposed to hyperbaric oxygen at 3.0, 3.6, and 4.0 atmospheres for periods of 3 and 2 hours. One-fourth of the mothers developed central nervous system signs during treatment and were sacrificed. A small but significant number of fetuses recovered late in gestation had severe gross congenital malformations, consisting of umbilical hernias, exencephaly, spina bifida, and limb defects.

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Additional Rhinovirus Serotypes. (29426)

V. V. HAMPARIAN,* M. B. LEAGUS AND M. R. HILLEMAN
Division of Virus and Cell Biology Research, Merck Institute for Therapeutic Research, West Point, Pa.

The rhinoviruses(1) are presently believed to be a principal cause for common cold in adults and a frequent cause for certain upper and lower respiratory tract illnesses in children. The rhinovirus group includes all agents know previously as JH-2060(2), ECHO 28 (2), coryzavirus(3,4), rhinovirus(5), murivirus(6), ERC agents (ECHO 28-rhinovirus-coryzavirus group)(4), and enterovirus-like viruses(7). Family relationship is based on

* Present address: Dept. Pediatrics, Ohio State University School of Medicine, Columbus, Ohio.