Hypoxia at Normal Atmospheric Pressure As a Cause of Congenital Malformations in Mice.* (22862)

FRANCIS J. CURLEY AND THEODORE H. INGALLS (Introduced by F. J. Stare)
Department of Epidemiology, Harvard University School of Public Health, Boston, Mass.

In view of the finding that pregnant mice (1,2,3), rabbits(4) and rats(5) may be made to produce malformed progeny following exposures to low atmospheric pressures of only a few hours duration, and because the interpretation was advanced that these congenital defects were late manifestations of hypoxia the following study was undertaken to test the validity of this assumption. If the results were indeed due to hypoxia then correspondingly low concentrations of oxygen molecules at normal atmospheric pressure should be able to produce similar effects. In the following experiment, therefore, pregnant mice were made hypoxic at normal atmospheric pressure; and this report describes what effect that treatment had on the unborn progeny.

Methods and materials. The 22 white mice used were in their 10th day of pregnancy, a critical time for development of normal or abnormal embryonic ribs and vertebrae(2). Twelve of these mice were kept one or two at

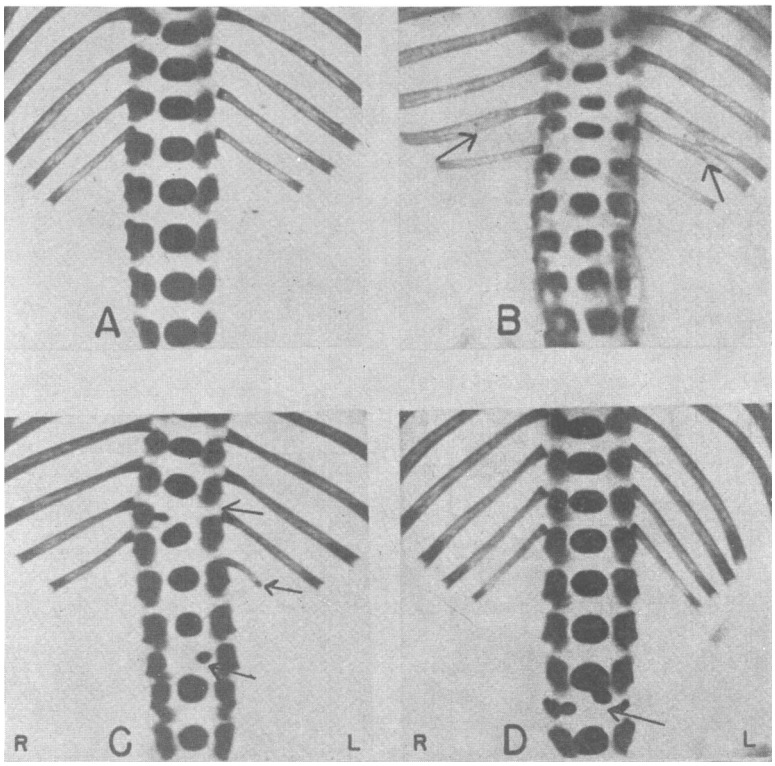

FIG. 1. Malformed vertebrae and ribs in mice on 19th day of gestation, after hypoxia on 10th day. A. Normal vertebrae and ribs—10th thoracic to 4th lumbar segments. B. Total fusion of ribs 11 and 12 on right side of thorax; partial fusion of opposite ribs. C. Ablation of 12th rib and vertebral transverse process on left—hypoplastic, extra 14th rib on same side; hemivertebra of 12th thoracic and 3rd lumbar segments. D. Hemivertebra and fusion of 3rd and 4th lumbar centrums.

* Aided by grants from Assn. for Aid of Crippled Children, United Cerebral Palsy; Amer. Heart Assn. and Mass. Lions Eye Research Fund.

a time for 2 hours in a bell jar of 3.5 liters capacity through which was flowed from bottom upwards a mixture of dry nitrogen and air containing 6% oxygen. A dental anesthesia machine was used to mix the gases and provide constancy of flow which was at a rate estimated at more than 1 liter per minute. A Hay's gas analyzer having graduated measurements of 0.2% was used to measure oxygen and carbon dioxide percentages at inlet and exhaust orifices of the bell jar. Carbon dioxide concentration never reached a measurable level and oxygen concentration remained at six percent; humidity, however, was not standardized in this apparatus. A nitrogen-oxygen mixture at sea level (atmospheric pressure, 760 mm mercury) containing 6% oxygen gives approximately the same concentration of oxygen molecules as exists in the atmosphere at 30,000 feet above sea level (atmospheric pressure, 226 mm mercury). As with mice exposed to low atmospheric pressure(2), test mice upon return to room air showed no immediate ill effects from the exposure and appeared well throughout pregnancy.

The 10 remaining mice were kept as controls under usual laboratory conditions. Fetuses were removed from mothers by section during the 19th day of gestation, and skeletal systems were stained with alizarin red for examination after clearing of soft tissues with potassium hydroxide.

Results. Exposure of pregnant female mice on 10th day of pregnancy for 2 hours to a 6% oxygen-94% nitrogen mixture at normal atmospheric pressure (760 mm of mercury) resulted in malformations of the kind found after exposure to a low atmospheric pressure—226 mm of mercury, which in respect to number of oxygen molecules per unit volume of air is the equivalent of 6% oxygen in nitrogen at sea level. Hemivertebrae, ablations and fusions of ribs and vertebrae (Fig. 1) were found in 26% (15 of 57 young) of the progeny of 12 females. None of 52 young from control animals kept in ordinary atmosphere at sea level showed similar defects.

Summary. Pregnant mice kept for 2 hours during the 10th day of gestation in a gas chamber containing 6% oxygen in nitrogen at normal atmospheric pressure produced progeny having malformed ribs and vertebrae.

1. Ingalls, T. H., Curley, F. J., and Prindle, R. A., *Am. J. Dis. Child.*, 1950, v80, 34.

2. ———, *New Eng. J. Med.*, 1952, v247, 758.

3. Murikami, U., Kameyama, Y., and Kato, T., *Ann. Rep. Research Inst. of Environmental Med.*, Nagoya Univ., 1955.

4. Degenhardt, K. H., *Durch O_2, Z. Naturforschg,* 1954, 9B, 530.

5. Werthemann, A., Reiniger, M., and Thoelen, H., *Z f. Path. u. Bakt.*, 1950, v13, 756.

Received October 17, 1956. P.S.E.B.M., 1957, v94.

Transcapillary Exchange of S^{35}-Labeled l-Methionine in the Human Forearm.* (22863)

RENATO D. KOVACH, EDWARD D. FREIS, HAROLD W. SCHNAPER AND LAWRENCE S. LILIENFIELD†

Cardiovascular Research Laboratory, Georgetown University Medical Center, and Veterans Administration Hospital, Washington, D.C.

Previous reports from this laboratory have been concerned with the transcapillary exchange of water and electrolytes in different vascular areas of the body(1,2). A technic was described utilizing the forearm vascular bed where the transcapillary exchange of labeled substances could be studied in some detail. Observations could be extended over a

*Supported in part by research grants from the N.H.I., U.S. Public Health Service.

† Helen H. Millenson Memorial Fellow, Metropolitan Heart Guild, Washington, D. C.