

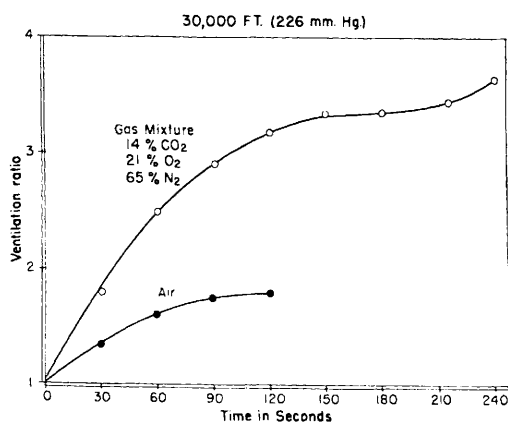


FIG. 1.

Ventilation ratios of subjects breathing air of normal composition and a gas mixture containing 14% carbon dioxide, 21% oxygen, 65% nitrogen, at a simulated altitude of 30,000 feet.

throughout the duration of consciousness in these experiments.

Doubtless there are many interacting factors involved in the explanation of these results. Carbon dioxide through its influence on cerebral blood vessels may influence the supply of oxygen to the brain. It seems plausible from theoretical consideration presented by Fenn *et al.*(5), that the more important factor is the high ventilation rate caused by the increased carbon dioxide and resulting in an increased partial pressure of oxygen in alveolar air, when nitrogen is a component of the inspired air. Consequently,

carbon dioxide increases tolerance to altitude when breathed with normal air and does not do so when breathed with pure oxygen. Further experiments are necessary to place these factors in their proper relationship.

Summary. The addition of certain amounts of carbon dioxide to ambient air at low barometric pressures of 225 mm Hg. and 179 mm Hg increases the duration of useful consciousness in human subjects. This effect is more pronounced at lower simulated altitudes than at higher altitudes.

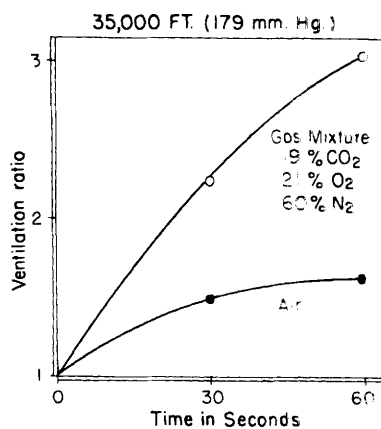


FIG. 2.

Ventilation ratios of subjects breathing air of normal composition and a gas mixture containing 19% carbon dioxide, 21% oxygen, and 60% nitrogen, at a simulated altitude of 35,000 feet.

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Nutritional Hydrocephalus in Infant Rats.* (18416)

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Hydrocephalus in infant rats as a result of inadequate nutrition of the mother has been reported by Richardson and Hogan(1) and

by Richardson and DeMottier(2). Recently Hogan *et al.*(3) reported that folic acid decreased the incidence of the abnormality and

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1. Richardson, L. R., and Hogan, A. G., *J. Nutrition*, 1946, v32, 459.

2. Richardson, L. R., and DeMottier, J., *Science*, 1947, v106, 644.

3. Hogan, A. G., O'Dell, B. L., and Whitley, J. R., *Proc. Soc. Exp. Biol. and Med.*, 1950, v74, 293.

TABLE I. Incidence of Hydrocephalus in the Young Born to Hydrocephalic Parents.

Mating	Diet	No. females	No. litters	No. of young		
				Born, No.	Hydrocephalic No.	%
Hyd. M x Normal F	Basal	4	6	32	3	9.48
Hyd. M x Normal F	Stock	2	6	36	0	0
Hyd. M x Hyd. F	"	2	3	25	0	0
Normal M x Hyd. F	"	1	2	20	0	0

that the addition of crude folic acid antagonist to the basal diet of the mother increased its incidence in young.

Two hydrocephalic males and females each were reared to maturity in this laboratory, and litters were obtained by mating these animals to each other and to normal animals. Studies have been carried out also on the effect of folic acid and APF concentrates in the diet of the mother on the incidence of hydrocephalus in the young. The results of these studies are described in this report.

Experimental. A. Basal diet and care of animals. The composition of the basal diet was the same as that described by Richardson and Hogan(1) with the exception that 4% of Wesson Oil was used instead of lard and Labco Vitamin-free casein was used as a source of protein. The females received the experimental diet from weaning. Five females and a male were kept in a 3 unit Wabmann cage with 2 mesh galvanized wire cloth on front and bottom. When a female was pregnant as shown by a marked increase in weight, she was transferred to a 2 unit cage with 3 mesh wire cloth. Shredded paper was used as a source of bedding for 4 to 5 days after the birth of the litter. The laboratory was controlled so that the temperature did not go above 82° or below 75°F.

B. Observations on the offspring of hydrocephalic parents. During the course of the investigation 2 hydrocephalic males and females each were reared to maturity. These 4 hydrocephalic rats were born at about the same time, and they were used to study the effect of heredity as well as diet on the incidence of hydrocephalus. These data are summarized in Table I. After a total of 15 litters were produced the 2 males and one female were killed, and autopsy showed that they

TABLE II. Effect of Diet of Mother on Incidence of Hydrocephalus in Infant Rats.

Group No.	Supplement	Young observed		
		Born, No.	Hydrocephalic No.	%
1	None	1604	120	7.48
2	Folic acid*	1254	2	0.15
3	Merck APF No. 3†	890	18	2.02
4	Folic acid*			
	Merck APF No. 3†	761	1	0.13
5	Folic acid*			
	Lederle APF 1.0%	288	2	0.69
6	Folic acid*			
	Liver "L" 3.0%	719	0	0.00

* 0.2 mg per 100 g diet.

† 2 g per k of diet.

had severe hydrocephalus. The other female was mated to a normal male and produced 2 additional litters of normal young. This female weaned 3 litters containing 24 normal young. She was killed and autopsy showed that she had severe hydrocephalus.

C. Folic acid, APF concentrates, liver extracts, and the incidence of hydrocephalus. Data showing the effect of folic acid, liver "L," an APF concentrate and combinations of folic acid and APF concentrates in the diet of the mother on the incidence of hydrocephalus in the offspring are given in Table II. There it is seen that both folic acid and the APF concentrate decreased the incidence of hydrocephalus. When the mothers received both folic acid and an APF concentrate, the incidence was essentially the same as when they received folic acid alone. None of the young from mothers which received folic acid and liver "L" developed the abnormality.

D. Folic acid antagonist and hydrocephalus. Fifteen females were reared from weaning on the basal diet supplemented with 2 g of APF concentrate No. 3 per kilo. At the time the

females were mated, 10 mg per kilo of a crude methyl folic acid antagonist were added to the diet. A total of 25 litters containing 125 young were born within the first 5 month period. Six litters containing 29 young were weaned. One young had hydrocephalus. No additional litters were produced within a second 3-month period, and the observations were discontinued. The folic acid antagonist under these conditions decreased the number of litters produced per female but it did not increase the incidence of hydrocephalus.

Discussion. Only a small number of animals were available for studies on reproduction with hydrocephalic rats, but the observations have special significance for two reasons. First, as far as the author is aware no studies on reproduction in animals or man with any type of hydrocephalus have been reported previously. The data show that rats were able to produce and rear normal young when they received a stock diet, even though both parents had severe hydrocephalus. When they received a basal diet low in folic acid, the incidence was about the same as when normal parents received this diet. Second, the possibility that heredity may be a factor in producing this type of hydrocephalus has never been eliminated. The data available, although not conclusive, suggest strongly that heredity has very little or no influence. The observations of Hogan *et al.*(3) that the addition of folic acid to the diet of the mothers decreased the incidence of hydrocephalus was confirmed. The incidence was less also when Merck's APF concentrate was added, and the activity of the concentrate did not appear to be due to the folic acid which it supplied. The basal diet and the concentrate were assayed for folic acid by the procedure described by Flynn(4) and the folic acid content was increased very little by the addition of 2 g of the concentrate per kilo of diet.

The increase was from 0.090 to 0.096 μg per gram. Further evidence that the activity of the concentrate was due to some other factor, is shown by the fact that the addition of crude methyl folic acid to the diet containing the APF concentrate did not increase the incidence of hydrocephalus. Schaefer *et al.*(5) have reported that either folic acid or vitamin B₁₂ afforded some protection of rats against renal damage, and both vitamins appeared capable of replacing each other for normal hemoglobin production. A similar effect of vit. B₁₂ on hydrocephalus could account for the folic acid antagonist not increasing the incidence of hydrocephalus when the diet contained the APF concentrate.

Conclusions. Mature hydrocephalic parents were capable of producing young and when they received a stock diet none of the offspring were hydrocephalic even though both parents had severe hydrocephalus. In studies on the effect of folic acid and APF concentrates on the incidence of hydrocephalus, 7.48% of the young born to female rats, receiving a purified diet low in folic acid developed the abnormality. The incidence was decreased to 0.15% by the addition of 100 μg of folic acid per 100 g of diet. It was 2.02% when the diet contained 2 g of Merck's APF concentrate No. 3 per kilo. When both folic acid and Merck's or Lederle APF concentrates were added, the incidence was essentially the same as when folic acid alone was added. None of the young from parents that received liver "L" was hydrocephalic. When 10 mg of crude folic acid antagonist were added to the basal diet which contained Merck's APF concentrate, the number of litters per female were decreased, but there was no increase in the incidence of hydrocephalus.

5. Schaefer, A. E., Salmon, W. D., Strength, D. R., and Copeland, D. H., *J. Nutrition*, 1950, v40, 95.

4. Flynn, L. M., *J. Assn. Offic. Agr. Chem.*, 1950, v33, 633.

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