in monolayer cultures can easily be infected by poliovirus I, whereas cells of the intact membrane and freshly trypsinized amnion cells are for the most part resistant to infection. Silver impregnation of the histologically intact membrane revealed the presence of a well demarcated intercellular matrix. As the trypsinized amnion cells flatten and spread out on the glass surface, this intercellular substance diminishes considerably, the cells demonstrate marked phagocytic activity and they become susceptible to polioviral infection. It is suggested that this matrix prevents penetration of the virus within the cell either by restricting viral adsorption or by restricting phagocytic activity.

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Barometric Pressure and Seizures.* (31649)

EDWIN E. BOLDREY† AND J. GORDON MILLICHAP

Division of Neurology, Children's Memorial Hospital, and Departments of Pediatrics and Neurology, Northwestern University Medical School, Chicago, Ill.

Several factors have been shown to modify the threshold to seizures in animals and man (1), but the possible importance of changes in barometric pressure in explanation of periodic variations in seizure susceptibility has been investigated infrequently. Petersen(2), in an extensive treatise concerning the effects of the weather on disease, reported mortality and draft statistics which pointed to a relation between meteorological disturbances and the precipitation and severity of epileptic seizures. Furthermore, Tille(3) observed that the incidence of febrile convulsions in young children was greater at times of cold weather fronts than during passage of warm fronts.

In previous investigations of barometric pressure and experimental seizures, animals were tested in decompression chambers in which altitudes of 12,500 ft (474 mm Hg) to 25,000 ft (280 mm Hg) were simulated (4,5). Increases in central nervous system excitability and severity of seizures at these low pressures could be explained by changes induced in tissue CO_2 and O_2. The present study was designed to investigate the effect of relatively small changes in barometric pressure on the threshold to seizures so that results might be related more meaningfully to the variations encountered in the normal environment.

Materials and metrods. A pressure chamber constructed of transparent Plexiglass was fit-

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ted with a positive-negative pressure gauge, a valve through which gases could be introduced or removed, and an air-tight door. A hose was attached by one end to the valve on the box and the opposite end was connected to a wall valve for air or for vacuum.

One hundred and thirty-two mice aged 7-8 weeks and weighing 20-39 g were divided at random into 3 test groups and 3 control groups. Each control group was examined at the same time as the corresponding experimental group so as to minimize the possible influence on results of day to day variations in environmental atmospheric pressure. Experimental seizures were induced by subcutaneous injection of pentylenetetrazol (Metrazol) (1).

The animals in 2 test groups were placed in the pressure chamber at 1.5 p.s.i. above or below atmospheric pressure immediately after injection and the third group was subjected to a negative 2.5 p.s.i. pressure for one hour before injection. The increase of 1.5 p.s.i. above atmospheric pressure corresponds to a total pressure of 836 mm Hg and simulates a distance of 2,500 feet below sea level; the decrease of 1.5 p.s.i. is equivalent to 682 mm Hg total pressure and an altitude of 2,900 feet. Control groups were examined at atmospheric pressure. All animals were observed for 20 minutes and a record was made of the number of convulsions, time of onset and grade of convulsion, and those with fatal termination. Convulsions were graded by severity and the classification described by Millichap(6) as follows: grade 5, maximal seizure activity consisting principally of tonic extension of fore- and hind-limbs; grade 4, tonic flexion of all limbs and extension of fore-limbs followed by clonus; grade 3, symmetrical clonic movements with loss of posture; grade 2, catatonia; and grade 1, hyperkinetic behavior. The threshold to major seizures was determined in the first 2 test groups and their controls by observation of the incidence of grade 3 to 5 seizures in subgroups of 5 animals injected with different doses of pentylenetetrazol between 20 and 75 mg/kg. From 4 to 7 subgroups were tested until a convulsive response was obtained in greater than 0% or less than 100% of mice at 3 or more dose levels. The dose necessary to induce convulsions in 50% of animals (convulsive $dose_{50}$) was calculated by the statistical method of Litchfield and Wilcoxon increase or decrease in incidence of seizures thresholds in the first 2 test and control groups. The doses expected to cause seizures in 16% and 84% of control animals, determined from these data, were used in the third test and control groups so that either an increase or decrease in incidence of seizures which might result from the pre-treatment with negative pressures could be evaluated. In all experiments animals were tested only once in order to avoid effects of previous shocking on the seizure threshold.

Results. Tables I and II show the seizure responses at increased and decreased barometric pressures applied after injection of pentylenetetrazol. The number of animals with seizures in each subgroup was related directly to the dose of pentylenetetrazol as expected, and the incidence of major seizures was similar in both test groups and their controls. The threshold to seizures at —1.5 p.s.i. pressure was not different from the control at atmospheric pressure, and the increase of 6 mg/kg in the threshold convulsive dose of pentylenetetrazol in animals tested at +1.5 p.s.i. pressure was not significant.

The number of animals which died in each test group and its control was almost identical, although the percentage of convulsions leading to death was different in the two pairs. The higher fatality among animals in the experiment shown in Table I is explained by the use of a relatively wider range of doses of pentylenetetrazol. Time of onset of the seizure was the only measure which seemed to show a difference between test and control groups; the incidence of seizures occurring within 5 minutes of the injection was greater in animals tested at +1.5 p.s.i. and —1.5 p.s.i. pressures but the differences were not significant.

Table III shows the incidence of seizures in mice pre-treated with —2.5 p.s.i. atmospheric pressure compared to controls. A dose of pentylenetetrazol (CD_{16}) expected to induce convulsions in 16% of animals in normal conditions was non-convulsant in the 10

TABLE I. Comparison of Pentylenetetrazol Seizures in Mice at Atmospheric and Increased Barometric Pressures.

Barometric pressure	Pentylenetetrazol-induced seizures: Threshold convulsive dose$_{50}$ (mg/kg)	Animals with seizures		Onset within 5 min		Fatal termination	
		No.	%	No.	%	No.	%
Atmospheric	33.0 (27.5-39.6)*	18	(51)	7	(39)	8	(44)
+1.5 p.s.i.	39.0 (32.0-47.6)	16	(43)	12	(71)	8	(50)

* 95% confidence limits.

TABLE II. Comparison of Pentylenetetrazol Seizures in Mice at Atmospheric and Decreased Barometric Pressures.

Barometric pressure	Pentylenetetrazol-induced seizures: Threshold convulsive dose$_{50}$ (mg/kg)	Animals with seizures		Onset within 5 min		Fatal termination	
		No.	%	No.	%	No.	%
Atmospheric	38.0 (31.7-45.6)	10	(50)	5	(50)	2	(20)
−1.5 p.s.i.	37.5 (30.5-46.1)	9	(45)	7	(78)	3	(33)

animals tested and seizure susceptibility was not increased by previous exposure to negative barometric pressures. A dose sufficient to cause seizures in 80% of controls had an effect of similar magnitude in the test animals. Further experiments following pre-treatment with positive pressures were considered unwarranted.

Comment and summary. The present study in mice has failed to demonstrate significant changes in susceptibility, pattern, or severity of seizures in response to moderate increases and decreases in atmospheric pressure. The results suggest that fluctuations in barometric pressure are an unlikely explanation for the periodicity of recurrent seizures in epileptic patients. Further experiments in other animal species with alternative methods of measurement of seizure thresholds might be indicated.

TABLE III. Pentylenetetrazol Seizures in Mice Subjected to a Negative Barometric Pressure for 1 Hour Before Injection.

Pentylenetetrazol* dose (mg/kg)	Animals with seizures: Normal controls	Pre-treated at −2.5 p.s.i.
30	0	0
50	4 (80%)	3 (60%)
Totals	4 (40%)	3 (30%)

* CD_{16} and CD_{81}.

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