TABLE III. Epinephrine Activity in Isolated Rabbit Ear Associated with Administration of 50 μg of *E. coli* Endotoxin.

Exp.	Tests before endotoxin		Tests after endotoxin*						Flow, cc/min.	Perfusion pressure, cm H_2O
	Dose	Response, mm H_2O	Dose	Response, mm H_2O	Dose	Response, mm H_2O	Dose	Response, mm H_2O		
1 E	.01	15.0	.01	7.0	.01	17.0			2.3	50
2 E	.001	2.5	.001	.0	.001	.5	.001	1.0	3.0	47
3 E	.01	124.5	.01	86.5	.01	94.0			3.0	45
4 E	.001	21.0	.001	19.0	.001	9.5	"	10.0	2.0	45
1 D	"	16.5	"	16.5	"	19.0			3.0	42
2 D	.01	109.0	.01	151.0					3.0	50
3 D	.0001	1.5	.0001	.5	.0001	.5	.0001	.0	3.1	37
1 N	.01	8.0	.01	8.0	.01	5.5	.01	12.0	3.1	50
2 N	"	7.5	"	5.0	"	6.0			2.0	92
3 N	.001	2.0	.001	2.0	.001	3.0	.001	3.5	2.8	40

* All doses were given within 13 min. after administering the endotoxin.
Doses are given in μg. E, ether; D, decaptitation; N, nembutal

of endotoxin was observed only to a slight extent in the presence of barbiturate, and not at all when ether or decapitation without anesthesia was employed to prepare the ear for perfusion, leads us to question whether the effect described by Zweifach, Nagler and Thomas is actually a direct potentiating action of epinephrine. We have no explanation as to how endotoxin might antagonize a barbiturate effect. 2) One point is noteworthy, our preparations in general had a much lower control epinephrine threshold than those reported for the perfused rabbit ear by above mentioned workers. 3) Our results are entirely uniform in showing that no reversal of epinephrine action after the large doses of endotoxin occurred, even with barbiturate anesthesia. We have no explanation to offer for this failure to confirm Zweifach *et al.*

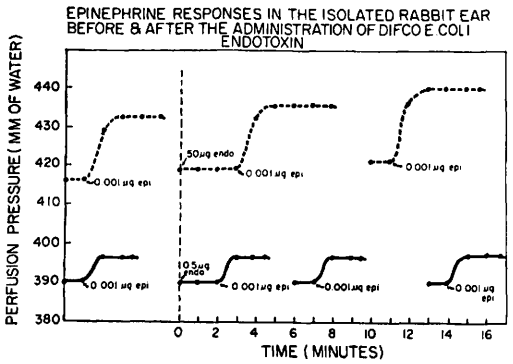

FIG. 1.

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Post Seizure Mortality Following Electroshock Convulsions in Certain Strains of Mice. (24603)

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Many phenomena associated with electrically-induced convulsive seizures in mice have been studied by investigators. Such factors as seizure threshold and experimental modifications thereof, seizure pattern, characteristics of postictal recovery period and effect of anticonvulsant substances on these various phases have been well described (1-5, and oth-

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ers). In spite of wide use of mice in such studies, little attention has been given to the fact that certain strains of mice are highly susceptible to a post seizure lethal effect of electroshock convulsions. Stone *et al.*(6) reported that among various strains of mice there was wide variation with respect to mortality following electroshock seizures. In that study a series of electroshock seizures was elicited in the same animal over several days. However, preliminary investigation showed us that multiple seizures were not required to induce death. In susceptible strains a single seizure may result in immediate fatal outcome. In view of this finding, as well as the fact that mortality in mice following electroshock seizures has not been well characterized, it was of some interest to study this phenomenon in more detail.

Method. Electroshock convulsions were induced in mice of various strains by the method essentially similar to that of Swinyard *et al.* (1). In studying susceptibility of different strains to lethal effect of electroshock convulsions, the convulsive stimulus was delivered through saline-wick corneal electrodes. The stimulus, delivered from a Medcraft apparatus, type B2, was supramaximal in intensity (120v) and consisted of alternating current passed for 0.3 seconds. Care was taken to saturate the corneal electrodes with physiological saline at all times. When experiments studying mortality of various strains were conducted on different days, a control group of non-susceptible animals (CF#1) was studied concurrently. In the study of the relation between stimulus intensity and proportion of maximal seizures and mortality, different groups of mice were shocked with currents of varying intensities, such that the proportion of mice exhibiting maximal seizure increased from 0 to 100%. Square wave pulses of 2 msec. duration and frequency of 59/sec. were delivered through corneal electrodes for 0.3 second. The Offner electroshock apparatus, type 736-A, was used. The strains of mice included male and female CF#1 and CFW mice obtained from Carworth Farms, male and female mice of the ICR strain from the Inst. of Cancer Research and reared in these laboratories and male mice of the C57 and DBA strains obtained from Jackson Memorial Labs. Mice weighed between 14 and 26 g at time of experiment.

TABLE I. Post-Seizure Mortality among Various Strains of Mice Subjected to Maximal Electroshock Seizures.

Mouse strain		No. animals dying/No. tested*	% mortality
CFW	♀	31/40	78
"	♂	17/20	85
C57	♂	13/20	65
DBA	♂	18/20	90
ICR	♀	3/20	15
"	♂	4/20	20
CF#1	♀ †	0/70	0
"	♂	0/20	0

* All mice exhibited maximal seizure.
† Concurrent control animals, grouped for simplicity.

Results. Death in susceptible mice as a result of electroshock-induced convulsions occurred immediately after termination of maximal seizure. The apnea present during seizure appeared to be indefinitely prolonged. Autopsy performed when convulsion ceased, revealed that the heart was still beating in an apparently effective manner. Therefore, death may be ascribed to respiratory failure. Non-susceptible mice exhibited all characteristics of seizure pattern of susceptible mice, with the exception that respiration was promptly resumed at the end of the complete extensor phase of the convulsion. Recovery from that point was similar to that described for rats by Page(4) and more recently by Millichap(5).

A study of different strains of mice showed that there was wide variation in susceptibility to acute lethal effect of electroshock convulsions. The data in Table I indicate that DBA, C57 and CFW mice were considerably more susceptible than either the ICR strain or the CF#1 strain. The latter strain is used in this laboratory for routine anticonvulsant testing, and rarely has death followed electroshock-induced maximal seizures. The data in Table I also suggest that a sex difference did not exist with respect to susceptibility of death following electroshock seizures, at least in the particular strains tested.

The stimulus-response relationship between

TABLE II. Effect of Various Stimulus Intensities on Incidence of Maximal Seizure and Mortality in Female CF #1 and CFW Mice.

	CF #1 strain		CFW strain		
Avg current (m.a.)	No. of mice with M.S.* of 10 tested	No. of mice dying/No. with M.S.*	No. of mice with M.S.* /No. tested	No. of mice dying/No. with M.S.*	% mortality of those with M.S.*
4.2	0	0/0	2/40	1/2	50
5.0	3	0/3	10/40	6/10	60
6.0	7	0/7	21/30	13/21	62
7.2	9	1/9	20/20	18/20	90
8.4	10	0/10	20/20	13/20	62
25.1	10	1/10	20/20	17/20	85

* Maximal seizure.

intensity of stimulus and incidence of maximal seizure and mortality for a susceptible strain and non-susceptible strain is shown in Table II. As is to be expected, the data show that, as stimulus intensity was increased, number of mice exhibiting maximal seizure increased. Both the susceptible CFW strain and the non-susceptible CF#1 strain behaved in a quantitatively similar manner in this respect. The incidence of mortality following maximal seizure, however, was much more marked in the CFW strain, since only an occasional death occurred with the CF#1 strain.

The data in Table II also demonstrate that per cent mortality based upon number of mice exhibiting maximal seizure at different stimulus intensities, does not change over the range of intensities studied. Probit analysis showed that there was no significant regression relating per cent mortality of mice with maximal seizure with stimulus intensity ($X^2 = 2.68$, $P > 0.1$, with one degree of freedom). Moreover, no deaths were recorded among mice which did not react with maximal seizure. The data indicate that the risk of dying following electroshock convulsions is related to maximal seizure and not to intensity of stimulus employed. Support for this concept is also given by the observation that the CF#1 strain survived current intensities as high as 400 m.a.(2).

Discussion. The phenomenon of post-seizure mortality in mice following electroshock convulsions has been mentioned(7-9), but has had little experimental attention. Mention is also made of the fact that certain drugs increased susceptibility of mice to post-seizure mortality. Reserpine(9), for example, increased post-seizure mortality, as has benactyzine(10). The present study demonstrated that post-seizure mortality varies considerably with the strain studied.

Swinyard *et al.*(1) have indicated that post-seizure deaths occur in a majority of mice in which electrode contact has been made improperly. This phenomenon, as observed by Swinyard and coworkers, resembles seizure fatalities reported here. In both instances, death resulted from failure of mice to resume breathing following termination of maximal seizure. Swinyard *et al.* speculated that, in the instance where improper electrode contact was made, severe respiratory depression resulted from current spread to the medulla. It is unlikely that a similar mechanism was involved in experiments reported here because: 1) Extreme care was used to maintain the saline-wick corneal electrodes fully saturated with saline at all times, 2) Concurrent control studies were always made with a resistant strain (CF#1), which rarely died, and 3) As shown above, post-seizure mortality was not directly related to intensity of stimulus, but occurred in constant proportion of those exhibiting a maximal seizure.

It is of interest that strains found most susceptible to post-seizure mortality after electroshock convulsions are identical with those susceptible to audiogenic seizures. The DBA and C57 mice have been widely studied in this latter respect. Moreover, both strains frequently die following audiogenic maximal seizure(11). The CFW strain has also been shown to be, at least in part, susceptible to audiogenic seizures, while both the CF#1 and the ICR strains are resistant (N.P. Plotnikoff, personal communication). Such findings suggest that susceptibility to post-seizure mortal-

ity following electroshock is genetically determined and may be related to factors which render certain strains susceptible to audiogenic seizures.

Summary. An acute lethal effect from electroshock convulsions has been demonstrated to occur among mice of the DBA, CFW and C57 strains, and to a lesser extent the ICR strains. CF#1 mice were rarely susceptible. Death was ascribed to failure to resume breathing and appeared to be dependent upon occurrence of maximal seizure and independent of intensity of current employed to elicit the seizure. The mechanisms involved were not revealed, but attention was directed to the finding that strains susceptible to post-seizure electroshock death are identical to those which are susceptible to audiogenic seizures.

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Gastrointestinal Absorption of Mg^{28} in Rabbits.* (24604)

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In a previous study a tracer dose of Mg^{28} was administered orally to human beings(1). Less than 10% of the radioactivity was recovered in the urine within 72 hours. Fecal excretion within 120 hours accounted for 59 to 88% of administered dose. The low renal excretion of magnesium was thought to be due to poor gastrointestinal absorption. The following study was undertaken to extend these observations in rabbits more clearly to delineate the metabolism of orally administered magnesium.

Material and methods. Domestic rabbits of mixed breeds were placed in individual metabolism cages and fed a stock diet of compressed pellets. Water was given without restrictions, except as indicated. About 200 μcuries of radioactive magnesium, Mg^{28}, contained in 30 to 35 meq of magnesium, was received weekly as acid solution of $MgCl_2$. This material was neutralized with 1N NaOH and the precipitate dissolved in 1N H_2SO_4. A slightly acid solution of $MgSO_4$ containing 5 meq of Mg in 150 ml of distilled water was fed to each rabbit. Radioactivity assays of tissues, urine and feces were made with a well scintillation counter and a scaler. External body surveys were performed with a directional scintillation counter attached to recording counting ratemeter. At least 10,000 counts were made on each sample. All determinations were corrected for physical decay. *Plan of experiments.* Each group of 6 rabbits was treated slightly differently, as follows: (a) In Exp. I, food and water were withheld for 17 hours. Water containing Mg^{28} was then left in feed pans for 24 hours. After

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