doses of strychnine, promin, dinitrophenol, sulfanilamide, atabrine, and other drugs have been recognized for years.[8-11] Similar results have been observed following toxic doses of diethylstilbestrol[8] and desiccated thyroid.[12-14] In the present experiment toxic effects of alpha-estradiol were similarly modified by dietary means.

Findings indicate that the effects of alpha-estradiol feeding in the immature rat were dependent on the diet employed. On the synthetic ration (diet A_2) ovaries appeared infantile both in weight and microscopic appearance. Similar results were obtained with animals fed additional B vitamins or yeast (diets B_2 and C_2). Oral administration of desiccated whole liver, however, resulted in a significant increase in ovarian weight with ovaries resembling histologically those of the normal rat. On alpha-estradiol-free rations ovaries did not differ significantly in weight or microscopic appearance on any of the diets employed. Available data indicate that the beneficial effects of liver on ovarian development in the immature alpha-estradiol-fed rat were not due to any of the known B vitamins. This is indicated by the fact that ovaries remained infantile on diet B_2 although this ration contained all known members of the vitamin B complex in amounts exceeding their presence in the liver-containing diet D_2. It is suggested, therefore, that desiccated whole liver contains some factor(s) other than the known B vitamins whose requirement is increased following prolonged feeding of alpha-estradiol.† In previous work with smaller doses of alpha-estradiol yeast was also found to promote ovarian development in the alpha-estradiol-fed rat.[1] Such was not the case, however, under conditions of the present experiment.

Summary. Desiccated whole liver counteracted the inhibition of ovarian development observed in immature rats fed massive doses of alpha-estradiol. The protective factor in liver was distinct from any of the known members of the vitamin B complex. It was not present in significant amounts in yeast.

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† The unknown nutrient may be part of an enzyme system concerned with estrogen inactivation. It is possible that prolonged feeding of alpha-estradiol increased requirements for this factor on diets A_2, B_2, and C_2 to the point that a deficiency occurred, interfering with estrogen-inactivation and resulting in impaired secretion of pituitary gonadotropins.[15]

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The Ability of the Cat to Withstand Repeated Electrically Induced Convulsions.

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In carrying out electro-shock therapy on psychotic patients it is frequently observed that some fail to immediately respond to the electrical stimulus with a major convulsive seizure. At times, especially in attempting to establish the convulsive threshold for a particular patient, it becomes necessary to induce 3 or 4 minor responses before the

desired major reaction becomes evident. In other patients, especially in those who are markedly disturbed, it has been observed that a single convulsion may fail to induce adequate sedation. The safety of repeated convulsions in such overly-disturbed patients has, therefore, been considered. Since a survey of the literature has failed to disclose the tolerance of animals to repeated electrically-induced convulsions and because of a fear of the consequences of repeated electrical stimulation this procedure had to be deferred.

Because of a need for such information it was deemed advisable to study this problem experimentally.

For this purpose 11 adult cats (exact ages unknown) were subjected to repeated electrical stimulation at approximately five-minute intervals. In 8 animals (Group A) this procedure was continued until each animal expired. The other 3 cats (Group B) were permitted to recover after having been subjected to a prolonged series of convulsions. On the basis of experience with patients submitted to electroshock this procedure was deemed entirely painless both at the time the convulsions were induced and after the convulsions were over.

The apparatus used to deliver the current was similar to that employed on patients. This utilized the 60-cycle 120-volt house current and consisted of a *step-up and step-down transformer* operated by an electrical timing switch. These were so designed that the duration of the current flow and voltage could be varied by the operator (Lektra Laboratories, New York). The lower voltage range was especially calibrated thus permitting a more accurate determination of the voltage required for the small animal used. The duration of the stimulus was maintained at a constant of 0.2 seconds. The electrodes used were especially constructed to better conform to the small animal head (Lektra Laboratories, New York). In each instance the convulsion was induced by the minimal convulsive dose and this had to be gradually increased in each animal as the experiment progressed.

Results. These have been tabulated in Tables I and II. From Table I it may be

TABLE I.
Tabulation of Data in Electrically-induced Convulsions in the Cat. Stimuli were repeated at 3.5-5.5-minute intervals and the duration of each stimulus was 0.2 seconds.

	Group A (Expired)									Group B (Survived)		
Cat Number	8	15*	16*	19	20*	21*	22*	24*	Avg	17*	18*	23
Wt in lbs	7¾	5¼	4¼	4¼	4¾	6½	5¾	5		8	7	5
Major reactions	30	64	60	46	53	49	75	87	58	40	49	95
Minor reactions	26	20	31	2	9	8	12	7	14.4	22	4	10
Duration of experiment, hr and min.	4-40′	5-50′	6-56′	4-44′	5-23′	5-0′	7-40′	8-19′	6-4′	5-25′	5-17′	9-0′
Initial voltage	80	90	50	40	40	40	40	40	52.5	50	50	40
Terminal voltage	140	150	190	80	90	80	140	150	127.5	120	80	160
Initial amperage (in ma.)	160	100	100	57	57	50	57	44	78.12	71	71	50
Terminal amperage (in ma.)	166	333	475	133	103	177	311	300	278.25	228	160	355
Coulombs (Q = IT)	1.83	3.65	5.24	0.91	0.99	1.30	3.20	3.23	2.54	1.85	1.22	4.28
Q/lbs	0 24	0.70	1.22	0.22	0.21	0.20	0.55	0.65	0.50	0.23	0.17	0.85

* Brain material available.

TABLE II.
Comparison of Original Minimal Convulsive Dose (M.C.D.) of Electricity (Q_2) with Total Current Employed (Q_1).

	Group A (Expired)								Group B (Survived)		
Cat Number	8	15	16	19	20	21	22	24	17	18	23
Total coulombs (Q_1)	1.83	3.65	5.24	0.91	0.99	1.30	3.20	3.23	1.85	1.22	4.28
Coulombs of M.C.D. (Q_2)	.032	.020	.020	.010	.010	.010	.010	.008	.032	.014	.010
Q_1/Q_2	57	132	262	91	99	130	320	403	57	87	428

seen that of those animals which expired (Group A), 1 succumbed after 30 convulsions; 1 at the end of 87 convulsions; and that the average number of convulsions was 58.

In addition, a varying number of minor (non-convulsive) reactions was observed—these occurring for the most part between major reactions when the animal failed to respond adequately to the previously effective minimal convulsive dose.

The total duration of treatment in this group varied from 4 hours 40 minutes to 8 hours 19 minutes (average = 6 hours, 4 minutes).

Initial minimal convulsive voltage of 40-90 volts (average = 52.5 volts) was gradually observed to rise to 80-190 volts (average = 127.5 volts) as the experiment progressed.

Initial minimal convulsive amperage of 44-160 ma. (average = 78.12 ma.) was gradually observed to rise to 103-475 ma. (average = 287.25 ma.).

The total current in coulombs (Q) administered to each animal (according to $Q = IT$) was found to vary from 0.91 to 5.24 coulombs (average = 2.54 Q).

In those animals surviving (Group B), it will be observed that one animal had had as many as 95 convulsions; that the total duration of the experiment in this animal was 9 hours; and that the total current administered to this animal was 4.28 coulombs. In spite of such intense treatment the rapidity of recovery, as judged by hopping and placing reactions, gait, feeding habits, preening and general alertness, was truly amazing. After 21 days these cats were behavioristically indistinguishable from untreated controls.

Discussion. It will be observed that in speaking of current intensities these were always designated "currents administered" rather than as "currents received" by the animal. This distinction was made in order to make clear that exact amounts of current received by the animal brain remained unknown since the degree of dissipation along skin and bone was not ascertained.

It must be admitted that the number of convulsions through which these animals survived was surprisingly high especially since

they were experienced in such concentrated form. It is interesting that the oldest appearing cat in the group (No. 8) was first to die. The brain of this animal, like those of all others, showed no evidence of gross pathology. Microscopic studies will be reported later. Electroencephalographic changes were observed, however, as the experiment progressed and these consisted for the most part of a gradual slowing and decrease in voltage. Detailed study of these findings is now under way.

The rise of the convulsive threshold as the experiment progresses is also significant in that it is at first very gradual. Later it increases in accelerated fashion so that in some cases the animal requires 4 times the initial voltage and as much as 7 times the initial amperage before responding with a convulsion. This is probably due to exhaustion, and experiments are now being planned to verify this hypothesis.

The striking fact obtained from this study is that no positive correlation between the amount of electricity applied and the tolerance of the animal could be demonstrated. This lack of correlation can best be appreciated from the tabulated coulomb-body weight ratios (Q/lbs) in Table I. These ratios show a variation of from 0.21 to 1.22 total coulombs per pound body weight in those animals which expired; while the surviving animals showed variations in ratios which were almost as great. This seems to indicate that of those cats which expired some required almost 6 times as many coulombs as others. It, therefore, appears that tolerance of electrical stimulation by a particular animal varies for each animal as an individual. Perhaps the best criterion of the ability of the cat to withstand electrical stimulation is illustrated in Table II. Here, a comparison of the original convulsive quantity of current (Q_2) with the total coulombs used (Q_1) discloses that in those cats expiring this ratio varied from 57 to 403. In the 3 surviving cats these ratios were 57, 87, and 428 respectively. In other words, of all the cats used it required at least 57 times the minimal convulsive coulomb value before any of them died. And in one instance a cat survived 428 times the original minimal convulsive coulomb value.

Summary. Adult cats submitted to repeated stimulations with, whenever possible, minimal convulsive doses of electricity showed an ability to withstand 30 to 87 major convulsions before expiring. Of those cats surviving the experiment one experienced 95 such convulsions. Initial voltage was observed to rise in one instance to approximately 4 times, and initial amperage was observed in one instance to rise to approximately 7 times the original minimal convulsive levels as the experiment progressed. The oldest appearing cat in the group was first to succumb. The brain of this cat, like the brains of all others, showed no *gross* pathological changes. Electroencephalographic changes in the form of gradual slowing and decreasing voltage were observed as the experiment progressed. The surviving cats showed no gross defects in behavior 21 days after the last convulsion.

It is *assumed* that death when it occurred was the result of exhaustion. No correlation between total applied current and tolerance could be ascertained. The striking observation is the unexpectedly high tolerance of the adult cat for repeated minimal convulsive-inducing doses of electricity. This is quantitatively best shown in comparisons between original minimal convulsing coulomb values and total coulombs used. In those cats which expired this total varied from 57 to 403 times the original minimal convulsive quantity. Of the surviving cats one received as much as 428 times the original minimal convulsive coulomb value. These experiments, therefore, point to the relative safety of the minimal convulsive dose of electricity in the cat and suggest a probable greater tolerance in the human than has heretofore been recognized.