Results. The following strains of virus proved to be resistant to the action of DCA. The negative sign before the figures in parentheses indicates that the virus gave a higher titer in the presence of DCA than in the control. GD VII strain of mouse encephalitis (0.0, −0.8, −0.6, −0.6), FA strain of mouse encephalomyelitis (−0.3), Coxsackie virus (0.3, −0.8, −0.3), MEF_1 strain of human poliomyelitis (−1.0, −0.5), Mengo strain of EMC (0.1, 0, −1.0, 0). It is of interest to note that the agents in the DCA resistant group, as a rule, give a slightly higher titer in the presence of DCA than they do in the controls.

The finding that viruses could be divided into bile salt resistant and susceptible groups has been of great value as a preliminary step in identification. In the attempted isolation of viruses by the inoculation of mice, on numerous occasions, strains of encephalomyelitis virus of mice have been accidentally obtained. Being resistant to the action of DCA, this virus can be readily distinguished from the arbor viruses. In recent years, more and more arbor viruses (*e.g.*, Sindbis) pathogenic for infant mice only have been isolated. These can be readily distinguished from the Coxsackie group because the former are susceptible and the latter resistant to the action of DCA. Of unusual interest is the finding that the Mengo strain of EMC is resistant. This agent has been isolated on several occasions from mosquitoes and was for some time considered to be arthropod-borne. However, extensive experiments have shown that this agent does not multiply in the mosquito and no successful experimental transmission by bite has been obtained. Infection with this agent leads to a viremia and, consequently, it is not surprising that at times mosquitoes will be caught in nature apparently infected with this agent. In many of its characteristics the Mengo virus is closely related to the polio group of agents. It is of interest here to recall that Kerr(2), by means of the complement fixation test, has shown an immunological relationship between the Mengo virus and the GD VII strain of mouse encephalomyelitis.

Susceptibility to DCA is not an exclusive property of the arbor group of viruses. Agents such as influenza A and lymphocyte choriomeningitis are readily inactivated.

Summary. All arthropod-borne viruses at present under study in the Rockefeller Foundation Virus Laboratories, New York, have been shown to be readily inactivated by a 1:1000 dilution of sodium desoxycholate. The only viruses discovered to date which are resistant to the action of this bile salt are strains of human poliomyelitis, mouse encephalomyelitis, Coxsackie and encephalomyocarditis viruses.

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Maze Performance, Emotionality, Audiogenic Seizure Susceptibility in Rats and Mice Treated with 2-Dimethylaminoethanol (23484)

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The intimate relationship of acetylcholine to the transmission of impulses in the nervous system has led to the expectation that changes in the metabolism of this substance must have pronounced effects upon various facets of behavior. This expectation has given rise to a number of investigations with confirming results. For example Ginsburg and Hovda(1) and Ginsburg and Huth(2) have described a negative relation between susceptibility to audiogenic seizures and several parasympathomimetic substances. Acetylcholine and

eserine reduced the incidence and fatality of such attacks. Prostigmine also reduced the number of fatalities. In addition they report a central decrease and peripheral increase of free acetylcholine following seizures in a very sensitive strain of mice. Rinaldi and Himwich(3) have stated that acetylcholine and di-isopropyl-fluorophosphate (D.F.P.) stimulate the "mesodiencephalic activating system" and that D.F.P. produces signs of anxiety and restlessness in human subjects. Krech *et al.* (4) describe reliably higher cholinesterase activity in the visual and somesthetic cortex in strains of rats which had been bred to select predominantly visual cues in maze learning. Such animals learned mazes more quickly than those depending primarily upon kinesthetic information. Dimethylaminoethanol (DMAE) has been studied by Pfeiffer *et al.* (5) as a possible tertiary amine precursor of acetylcholine. If DMAE acts as a precursor it might be expected to produce behavioral alterations similar to those attributed to acetylcholine. The studies reported here form a part of a larger program initiated by Pfeiffer to investigate the pharmacology, physiology, and behavioral effects of substances which may produce rather long lasting muscarinic stimulation of the brain and which may possess ameliorative properties in mental disease. In all, 7 experiments involving 2 genera, were performed. Three were concerned with the possible effects of DMAE on maze performance, 3 with emotionality, and one with seizure susceptibility.

1. *T-Maze performance in mice.* Two groups of male Swiss Albino mice (average weight 25 g) were trained to run a 3-unit elevated T-Maze learned one segment at a time. The length/unit was 12 inches and the paths were 1.5 inches wide. Learning was defined as achieving a proportion of correct responses significant at the one per cent confidence level. This criterion differs from the usual one involving a specific proportion of correct responses on an arbitrarily designated number of trials. It was used to minimize overlearning. The incentive for learning was food preceded by 23 hours' fasting. The experimental group received 1.0% DMAE administered intravenously; the control group received no pharmacological treatment. Performance in this as well as all subsequent experiments was evaluated by non-parametric statistical procedures. Two group comparisons were evaluated by means of the Mann-Whitney U test: three or more groups by the Kruskal-Wallis H test.

The *results* indicated that performance was superior in the control group (median trials to criterion: 30 *vs.* 35). This difference was significant at the .01 level ($U = 28$, $m/n = 12/11$). The experimental animals were meanwhile noted to be hyperactive and difficult to handle. The significance of this for the maze data will be discussed later.

2. *Serial-maze performance in mice.* Several weeks after Exp. 1 the 2 groups described above were tested on a 4-unit enclosed serial maze (LRLR). The alleys were 3.5 in. wide and 16 in. long. Criterion of learning was a conventional two consecutive errorless trials without retracing. For this experiment the drug was administered as 0.05% in drinking water to which the experimental group had *ad libitum* access. The mean daily intake of DMAE was 2.25 mg. This time no difference in trials to criterion was observed (experimental median $= 22.4$; control median $= 20.6$, $U = 58$, $m/n = 12/11$, $P > .05$).

3. *Emotionality in mice.* Two tests of emotionality were run on the mice which had learned the maze problems. These tests were run immediately after learning had occurred in each instance. In the Stone stove-pipe maze (an L-shaped enclosed opaque alley with long arm 36 inches, base 12 inches, and short arm 24 inches) emotionality is indicated by the time required for the mouse to enter a brightly illuminated goal box. In the Anderson water-wading test, emotionality is indicated by the number of boli passed in a 5-minute period when an animal is placed in an enclosed opaque chamber in water one cm deep at approximately 25°C. Each animal was tested 3 times on each test, individual tests being separated by 48 hours. After Exp. 1 experimentals were more emotional than the controls on both tests. (Median time in stove-

pipe: 270 sec. *vs.* 110 sec., U = 13, m/n = 12/11, P<.001; water wading median number of boli = 2 *vs.* 1, U = 29, m/n = 12/11, P<.025). After Exp. 2 involving oral administration of DMAE, no significant differences were found between the groups.

4. *Serial-maze performance in rats.* Three groups of 4-month-old male and female albino rats (total N = 28), derived from Wistar stock, were trained in a 4-unit enclosed serial maze. They were trained on the first unit to criterion, then on Units 1 and 2, Units 1, 2, and 3, and finally on Units 1, 2, 3, and 4 to criterion. The criterion was the proportion of correct responses significant at the one per cent significance level. One group served as the control (C), the other 2 as experimental groups. These latter were placed on the drug regimen shortly after weaning. One (E_1) received 0.1% solution of DMAE in water for *ad libitum* oral intake, the other (E_2) a 1% solution. Both E Groups were continued on the drug throughout the maze-learning period. This was approximately 109 days for E_1 and 189 days for E_2. The average daily fluid intake for C, E_1 and E_2 was 20.1 ml, 18.0 ml, and 16.0 ml respectively.

Performance in the maze problem was measured by the following scores: (a) median trials to criterion, (b) median total errors to criterion, (c) median total time to criterion, (d) median errors per trial, (e) median time per trial. No significant differences were found between the control group and E_1 (the 0.1% dose group); E_2, however, gave, on the average, poorer performance than either C or E_1 on trials to criterion, total errors and errors per trial. No difference in performance times was noted. The median performance scores were as follows: median trials to criterion: C = 125, E_1 = 130, E_2 = 165; median total errors: C = 33, E_1 = 32, E_2 = 90; median errors per trial: C = .28, E_1 = .35, E_2 = .51; median total time: C = 1743″, E_1 = 3647″, E_2 = 5843″; median time per trial: C = 15″, E_1 = 24″, E_2 = 30″. The animals in group E_2 were observed to have frequent spontaneous clonic convulsive attacks, often rather severe. These seizures occurred both in the home cage and in the maze and probably account for the poorer performance of E_2.

5. *Emotionality in rats.* The rats used in Exp. 4 were given emotionality tests after completion of maze training. Again, 2 tests were used: the Stone stovepipe maze, and the Anderson water-wading test. No significant differences were found between C and E on either test, although the medians rank from low to high emotionality in the expected direction (C, E_1, E_2). The median values for the several groups were as follows: water-wading: C = 4, E_1 = 3.5, E_2 = 5; Stone test: C = 51, E_1 = 81, E_2 = 300.

6. *Susceptibility to audiogenic seizures in mice.* Four groups of mice, one control and 3 experimental (total N = 20), were tested for susceptibility to audiogenic convulsions before and after administration of DMAE. They were all males of an inbred strain (A strain) with an average weight of 30 g on the day of first test. Tests consisted of 2-minute exposures to noise (average 101 db, range 90 to 104 db) on alternate days. Prior to administering DMAE to the experimentals, all animals were given a sequence of 5 tests. The 3 experimental groups were then placed on *ad libitum* oral intake of 0.01%, 0.10%, and 1.0% solutions of the drug respectively. They were maintained on this until the experiment was completed. The average daily intake was 0.6, 5.4, and 40.0 mg respectively. Two weeks after onset of drug administration, a second series of 5 tests was begun. Seizure susceptibility was ascertained by the following measures: (a) frequency index: this is the proportion of tests on which a running or epileptiform attack was observed; (b) intensity index: this is a weighted score derived from the total number of running and convulsive attacks; (c) latency of first running attack; (d) latency of first convulsion; (e) duration of running prior to convulsion; (f) total time in convulsion. After the groups were matched, the changes in susceptibility from the first to the second test sequence were compared. No significant differences were found between the control group and the experimentals on the frequency index, the latency of first epileptoid fit, or the total con-

vulsion time. Significant differences ($P = .02$ or less) were found between experimentals and controls on the intensity index, the latency of first running attack and the duration of running prior to the epileptoid sequence. At the end of sequence 2 the experimentals were almost without exception more susceptible than their matched controls. Meanwhile no significant differences were found among the three experimental groups. The controls showed the commonly observed decrease in susceptibility with increasing age and repeated tests. In contrast, the experimentals retained their initial sensitivity or showed a slight increase in sensitivity. Thus on the second sequence of tests, the experimentals showed more intense attacks, went into the running attacks sooner, and ran for a shorter period before displaying the epileptiform seizures.

Discussion. Animals receiving DMAE tended to show increased emotionality as indicated by the Stone and Anderson tests. This finding is in agreement with the observations of Jenny,* Grob, *et al.*(6), and Killam and Killam.* Jenny reported that rats given daily doses of DMAE became more irritable, difficult to handle, and exhibited markedly increased muscular tension as well as spontaneous seizures. Grob showed that the administration of D.F.P. produced symptoms of restlessness and anxiety in human subjects, while Killam and Killam found that DMAE increased the amount of cortical low voltage fast activity and reduced the threshold at which reticular stimulation produced a cortical EEG pattern characteristic of the arousal response.

These findings indicate a correlation between the increased emotionality and irritability produced by DMAE in our animals and stimulation of the brain stem reticular formation. Our finding of increased sensitivity to audiogenic seizures might also be expected in light of the above mentioned reports.

The performance decrements exhibited by rats maintained on daily 1% solutions of DMAE is interpreted as secondary to increased emotionality and to the occurrence of spontaneous epileptiform seizures during testing. We have no evidence to indicate that learning capacity *per se* is adversely affected. Our data indicate that when hyper-emotionality disappeared the animals exhibited no performance decrement.

Summary. Rats and mice when given 0.1% and 1.0% solutions of 2-dimethylaminoethanol (DMAE) to drink for prolonged periods showed either a decrement or no improvement in maze performance. They exhibited increased emotionality as measured by the Stone and Anderson tests. Rats given 160 mg/day were subject to frequent spontaneous epileptiform seizures. Inbred (A-strain) mice when tested for susceptibility to audiogenic seizures showed more intense attacks with shorter latent periods while on DMAE. The decremental effect of DMAE upon maze performance was interpreted as a secondary effect of increased emotionality and/or epileptiform seizures. The facilitatory effect upon audiogenic seizure susceptibility is interpreted as due probably to stimulation of the brain stem reticular formation.

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