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Effect of Feeding Moderate Levels of Commercially Agenized Flour
to Dogs.*

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During the past 18 months many questions have been raised concerning the role of nitrogen trichloride-treated flour (agenized) in the etiology of human epilepsy. Shortly after Erickson *et al.*¹ suggested that wheat gluten might be important in the causation of human epilepsy, a report by Mellanby² showed that epileptiform convulsions in dogs could be consistently induced when the animals were fed rations which contained high amounts of flour treated with nitrogen trichloride. These observations were later confirmed by Silver *et al.*³ and Newell *et al.*⁴ and the studies were extended to other animals. In all these experiments the rations fed to dogs contained large amounts of flour (70-84%). These

flours were treated with nitrogen trichloride in amounts which ranged up to 15 times more than the treatment normally given flour consumed by human beings.

The use of agene as a maturing agent has increased steadily during the past 25 years. In 1945, 85% of the flour used in this country was treated with nitrogen trichloride. Because of the wide use of wheat products, it was decided to place a series of dogs on a diet which contained an amount of flour approximately equal to that used in the average American diet. This flour was treated with nitrogen trichloride at commercial levels commonly used by the milling industry.†

The following ration was used: flour 30, sucrose 49, casein 10, corn oil 5, salts IV 4, whole liver substance 2. Oral supplements of 0.75 mg thiamine, 0.75 mg riboflavin, 0.5 mg pyridoxine, 0.25 mg pantothenic acid, 1 mg nicotinic acid and 70 mg choline per kilo of body weight and 6 drops of halibut liver oil were administered twice weekly. Three dogs, 19, 23 and 30), were placed on ration F-89 which contained flour treated with 1.2 g nitrogen trichloride and 7 g benzoyl peroxide‡ per cwt. of flour. Two other dogs, (241 and

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¹ Erickson, T. C., Gilson, W. E., Elvehjem, C. A., and Newell, G. W., *Proc. Assn. Research in Nervous and Mental Dis.*, 1946, **26**, 164.

² Mellanby, E., *Brit. Med. J.*, 1946, **2**, 885.

³ Silver, M. L., Johnson, R. E., Kark, R. M., Klein, J. R., Monahan, E. P., and Zevin, S. S., *J. Am. Med. Assn.*, 1947, **135**, 757.

⁴ Newell, G. W., Erickson, T. C., Gilson, W. E., Gershoff, S. N., and Elvehjem, C. A., *J. Am. Med. Assn.*, 1947, **135**, 760.

† We are indebted to Dr. H. K. Parker of Wallace and Tiernan Company for the flours used in these experiments.

244), were started on ration F-89A which contained flour treated with 2.25 g of nitrogen trichloride and 7 g of benzoyl peroxide† per cwt. of flour.

Dogs 19 and 23 have been on ration F-89 for 63 weeks (14½ months) and dog 30 has been fed the same ration for 55 weeks (12½ months). Dogs 241 and 244 have been fed ration F-89A which contains 30% flour treated with the higher level of nitrogen trichloride, for 52 weeks (12 months). All of these animals have eaten well, gained weight and remained healthy. At no time has there ever been any indication of running fits or epileptiform convulsions.

Before this experiment was begun characteristic electroencephalographic brain wave patterns (E.E.G.s) of dogs 19, 23 and 30 were obtained.§ Four tantalum electrodes were implanted into the skull above the dura of each animal in the manner described by

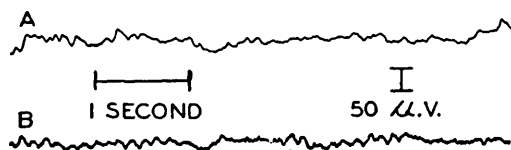


FIG. 1.

A—Control electroencephalogram of dog 30 before experiment.

B—Electroencephalogram of dog 30 after 6½ months on a ration which contained 30% of commercially agenized flour.

Newell *et al.*⁵ Normal E.E.G. records were obtained for each of these animals. Six to 8 months after these experiments started tantalum electrodes were implanted in all 5 dogs. A week later several E.E.G. records were taken and all the animals showed normal electroencephalograms. In Fig. 1 short sec-

tions of the record from one electrode lead of dog 30, characteristic of the entire record of this dog and of the other dogs, are presented to show the similarity of the E.E.G.s before the feeding tests began and during the period of testing. Previous experiments, in which dogs have received flour or wheat gluten treated with high levels of nitrogen trichloride, have consistently showed abnormal changes in the E.E.G. records days before running fits or epileptiform convulsions developed.⁵ If any abnormalities had developed in the brain metabolism or physiology of the dogs fed rations containing 30% of flour treated with agene at commercial levels, significant changes in the E.E.G. records should have been readily observed.

It is interesting to note here that the flour used in these experiments when fed to dogs at 84% of the ration, regularly caused running fits and convulsions in 11-62 days.⁴ This difference in flour intake suggests that there is a tolerance level in the dog below which the toxic factor produced by nitrogen trichloride treatment is metabolized or excreted but above which the toxic material accumulates in the animal producing the characteristic convulsive condition. When higher levels of nitrogen trichloride are used to treat flour, smaller amounts of flour induce the convulsions. Radomski *et al.*⁶ have recently shown that dogs fed 0.1 g of nitrogen trichloride treated wheat gluten (6 g NC1₃/kg gluten) per kilo of body weight per day did not develop running fits. These authors translate their results to mean that a dog could consume 25% of his ration in the form of commercially treated flour (1.5 g NC1₃/cwt.) without developing fits.

Summary. These results demonstrate that dogs can be fed a ration containing moderate levels (30%) of commercially agenized flour for long periods of time (12-14½ months) without developing running fits or electroencephalographic abnormalities.

† Previous tests have shown benzoyl peroxide bleached flour to be ineffective in producing fits.⁴

§ We wish to express our thanks to Dr. Henry M. Suckle for his assistance in some of the experiments.

⁵ Newell, G. W., Erickson, T. C., Gilson, W. E., and Elvehjem, C. A., *PROC. SOC. EXP. BIOL. AND MED.*, 1947, **65**, 115.

⁶ Radomski, J. L., Woodard, G., and Johnston, C. D., *Fed. Proc., Abstracts*, 1948, **7**, 250.