TABLE II. Effect of Coprophagy Prevention and Menadione Supplementation on Hemorrhagic Syndrome and Hypoprothrombinemia of Vit. K Deficiency in the Rat (10 Days).

Diet	Oral supplement/rat/day	No. of hemorrhagic deaths	Plasma prothrombin time, sec. (mean and spread)	Coprophagy, %
Soy protein		1	32 (14- 66)	38
Idem	5 μg vit. K_3	0	14 (13- 18)	29
" , coprophagy prevented		4	92 (63-120)	
Idem	*Idem*	0	15 (14- 16)	

Table I, besides being very low in Vit. K, also appears to lead to low fecal consumption by the rat in comparison to usual casein-synthetic diet and therefore produces a severe Vit. K deficiency in 10 days. 5 μg of menadione/rat/day were adequate for maintenance of normal plasma prothrombin time and completely protected the rats from hemorrhage.

Summary. A diet is described which produces a severe Vit. K deficiency in the rat in less than 10 days. The deficiency was manifested by prolonged plasma prothrombin times and hemorrhages. Daily menadione supplementation protected rats from the deficiency. Coprophagy appeared to be the means by which Vit. K synthesized by the intestinal microflora becomes available to the rat.

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Convulsant Effects of Mikedimide (3,3, Methylethyl Glutarimide) in Monkeys.* (24983)

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Mikedimide‡ (3,3, methylethyl glutarimide) has been recently introduced as a central analeptic with strong antagonism to barbiturates (1). Similarities in some of its actions in humans to those of pentamethylenetetrazole (Metrazol) (2-4) led to these investigations of its effects on a) normal, b) epileptic, and c) brain-operated non-epileptic monkeys.

Method. Tests were performed on 19 *Macaca mulatta* weighing 3-5 kg. In the first group of 11 monkeys, 5 had been made chronically epileptic by application of alumina cream to cerebral cortex (5) and 6 were unoperated normal controls. Mikedimide (0.5%) was injected intravenously "rapidly," *i.e.*, within 1-3 minutes at 1-4 ml/min, at intervals of 12 to 14 days. Clinical observations and electroencephalographic recordings were made for at least 30 minutes following injection; when clinical convulsive seizures occurred, sodium phenobarbital was promptly administered intravenously. Threshold convulsant doses were considered to be the least quantity which induced clinical convulsions. Thresholds for clinical convulsions to intramuscular Metrazol were also determined. In a second

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group of 8 monkeys the effects of rapid intravenous injection of standard challenge test dose of 4 mg/kg Mikedimide were ascertained. Six of this non-epileptic group had been operated 4 to 13 months previously at which time various metals (tantalum, silicon, platinum, silver, cadmium or mercury) had been implanted in the motor cortex of both cerebral hemispheres; the remaining 2 monkeys were normal unoperated controls.

Results. Tonic clonic generalized clinical convulsions occurred in normal unoperated monkeys following rapid intravenous injection of 5-9 mg/kg Mikedimide (5, 5, 6, 6, 9, 9 mg/kg), while epileptic monkeys similarly treated had thresholds of 0.75-2.7 mg/kg, (0.75, 0.75, 1, 2, 2.7 mg/kg). In all cases, intravenous sodium luminal injected soon after onset of seizures promptly controlled them.

Thresholds for clinical convulsions of intramuscular Metrazol exceeded 40 mg/kg in all normal monkeys, whereas in epileptic monkeys threshold doses ranged from 12 to 24 mg/kg (12, 12, 16, 24, 24 mg/kg). Epileptic monkeys with lowest thresholds to intravenous Mikedimide had lowest thresholds also to intramuscular Metrazol.

None of the 6 brain-operated non-epileptic monkeys nor 2 additional normal monkeys showed clinical convulsions following rapid intravenous injection of a test dose of 4 mg/kg Mikedimide.

Discussion. In monkeys, rapid intravenous injection of Mikedimide in adequate dosage may induce clinical convulsions which can be readily controlled and terminated by intravenous barbiturates. Since threshold dosages for clinical convulsions were much lower for epileptic than for normal monkeys, use of an intermediate dose (4 mg/kg intravenously) should induce clinical convulsions in epileptic but not in normal monkeys. Mikedimide compares quite favorably with other agents similarly used such as intramuscular Metrazol, intramuscular and intravenous picrotoxin and intravenous semicarbazide (aminourea). Intravenous Mikedimide produces seizures usually within a minute following injection and threshold convulsant doses in epileptic monkeys seem to parallel those to intramuscular Metrazol. We believe, therefore, that Mikedimide may be used advantageously in evaluation of epileptic status of monkeys and should prove a valuable and reliable addition to the battery of pharmacologic tests developed for this purpose.

Summary. 1) Rapid intravenous injection in monkeys of adequate doses of Mikedimide (3, 3, methylethyl glutarimide) induced clinical convulsions which were readily controlled by intravenous barbiturates. 2) Thresholds for clinical convulsions were lower in epileptic than in normal monkeys. 3) A challenge dose (4 mg/kg) is suggested as one capable of producing clinical seizures in epileptic but not in non-epileptic monkeys.

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