for 20 days has been shown to be even more effective in ovariectomized female rabbits in our laboratory as evidenced by the more pronounced overlapping of the adjacent mammary glands at their peripheries. These glands were comparable to the mammary glands of pseudo-pregnant rabbits routinely prepared preliminary to lactation studies in our laboratory.

Summary. 1. Daily injection of 9 μg of estradiol benzoate for 20 days induced extensive development of the mammary duct system of male rabbits with negligible lobule formation. 2. With male rabbits pretreated with estrogen to develop the duct system, the daily injection of 15 μg of estradiol benzoate combined with 1 mg of progesterone (synergistic ratio 1:67) induced the extensive development of the lobule-alveolar system as indicated by the DNA content and by visual examination of whole mounts of the glands. 3. These observations indicate that the optimum synergistic ratio of the ovarian hormone in lobule-alveolar development in the rabbit differs widely from the ratio of 1:1000 or more observed in the mouse, rat and dog.

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Convulsant Effects of Semicarbazide in Epileptic Monkeys.* (22409)

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Semicarbazide (amino-urea) has been described as a potent convulsant and its action in normal monkeys has been reported(1). The present investigation was undertaken to study the comparative effects of its administration to chronically epileptic as well as normal monkeys.

Method. Semicarbazide was injected by the rapid intravenous route at intervals of one or more weeks to a group of 8 *Macaca mulatta* (3.5-6.0 kg). Five monkeys of this group had been made chronically epileptic by application of alumina cream to the brain (2), and 3 were unoperated normal controls. Each monkey was observed for periods up to 6 hours following injection. Clinical observations and electroencephalographic studies were made.

Results. Threshold convulsant dosages which provoked clinical motor seizures in the 3 normal monkeys were 80, 80, and 60 mg/kg respectively. Time of onset of clinical seizures was approximately 3 hours after intravenous injection in 2 monkeys and 4 hours in the third (60 mg/kg).

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Epileptic monkeys had threshold convulsant dosages of 10 or less, 20, 20, 30, and 30 mg/kg. Time of onset of clinical seizures varied from 2 to 3½ hours. Focal onset of clinical seizures was sometimes evident in this group. Shortening of the latency period for motor convulsions occurred in the epileptic group when suprathreshold dosages were used. Thus in epileptic monkey #757 latency was progressively reduced from 2 hours with a threshold dose of 20 mg/kg to 15 minutes with a dose of 90 mg/kg. Repeated tonic

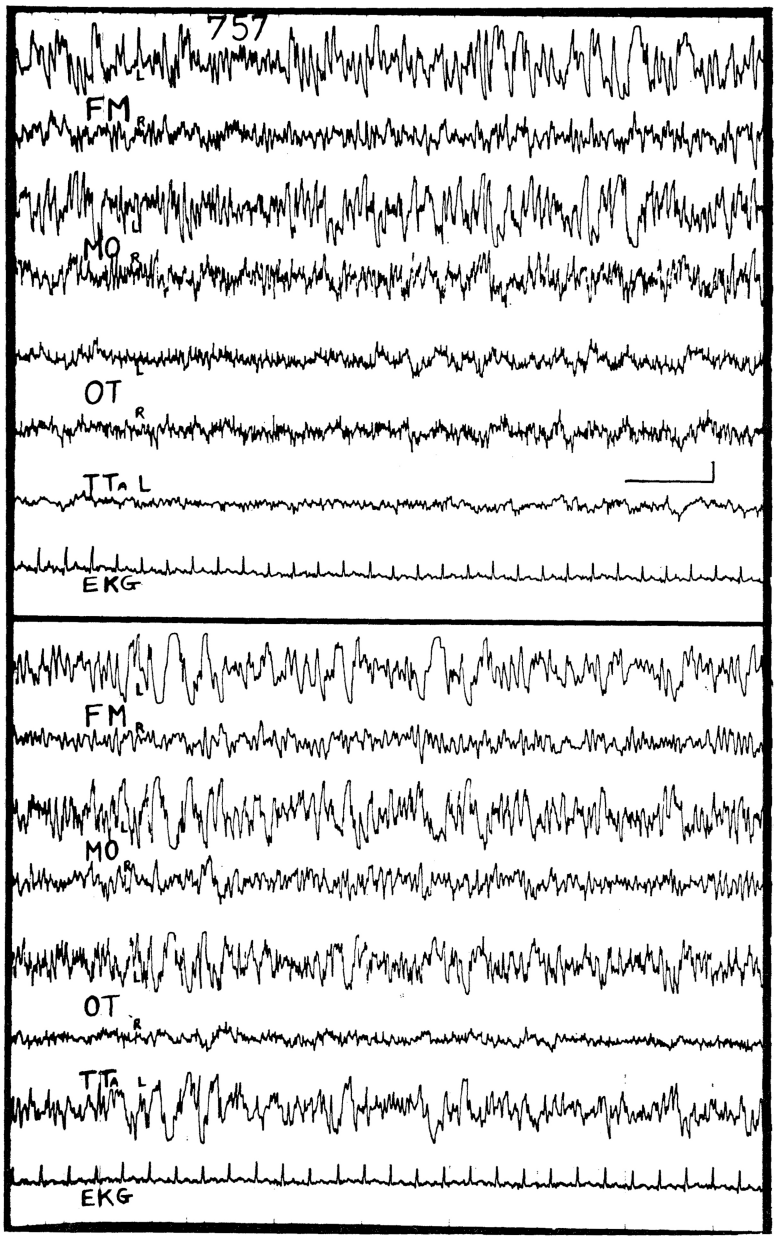

FIG. 1. Electroencephalograms before (top) and 36 min. after (bottom) intravenous inj. of 80 mg/kg semicarbazide in epileptic monkey demonstrating spread of spike, sharp, and slow waves in left cerebral hemisphere which occurred 30 sec. before clinical motor seizure. L = Left; R = Right; F = Frontal; M = Motor; O = Occipital; T = Temporal; Ta = Anterior temporal. Calibration: 1 sec. (horizontal), 50 microvolts (vertical).

clonic seizures occurred particularly with the larger doses.

Electroencephalographic changes accompanied motor seizures, and in epileptic monkeys sometimes briefly (up to ½ minute) preceded the onset of clinical seizures (Fig. 1). Significant detectable changes were otherwise not evident; increased muscle artefact potentials became more prominent after injection when the animals appeared to become more restless. Clinical seizures were accompanied by diffuse spike convulsive patterns.

Summary. (1) Threshold convulsant dosages to rapid intravenous injection of semicarbazide were significantly lower in chronically epileptic monkeys than in normal unoperated controls. (2) Clinical seizures following intravenous injection of threshold convulsant doses of semicarbazide occurred after a latent period of 2 to 3½ hours. With suprathreshold doses the latent period was diminished greatly. (3) Use of a test dose of 30 to 40 mg/kg of semicarbazide by rapid intravenous injection is suggested to distinguish epileptic from non-epileptic monkeys since clinical convulsions should be produced within 3 to 4 hours in epileptic monkeys and not in non-epileptic normals.

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Histopathology of Amino Acid Deficiencies. V. Isoleucine.* (22410)

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The indispensability of isoleucine for growth in rats was demonstrated by Womack and Rose(1). Later, in experiments with dogs, several investigators showed that isoleucine was necessary for the maintenance of nitrogen balance(2), the formation of hemoglobin(3) and of plasma protein(4). The essential nature of this amino acid for human nutrition was established by Rose and his coworkers(5). Hegsted, McKibben and Stare (6) and Albanese(7) reported that the isoleucine content of human plasma protein and hemoglobin was insufficient to support normal growth in rats. Histological studies of isoleucine deficiency have not been reported for any species. The present report is the fifth in a series dealing with the histopathological effects of the total omission of an essential amino acid from the diet of rats.

Method. Young male Sprague-Dawley rats were divided into 3 groups. One group of 5 rats (normal-control) received a purified synthetic diet consisting of a mixture of 19 crystalline amino acids, vitamins, sucrose, cottonseed oil and the necessary minerals and salts as described by Rose, Oesterling and Womack (8). A second group of 15 rats (deficient) was fed the same diet, complete in every respect except for the total omission of isoleucine. The caloric value of the missing amino acid was supplied by additional sucrose. A third group of rats was pair-fed the complete diet so that the food consumption of each was no greater than that of its isoleucine-deficient mate. All rats were kept in individual cages and, with the exception of the pair-fed group, fed *ad libitum*. At the end of a 30-day experimental period, all rats, with the exception of 2 deficients, were sacrificed by decapitation without anesthesia. As rapidly as possible, the liver of each rat was removed, a small portion fixed for histological procedures, and the remainder immersed in liquid nitrogen for total glycogen determination by the method

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