Seizure in experimental animal (right) contrasts with normal gerbil (left).

Animals suited to epileptic research

Gerbils' susceptibility to seizure adds epilepsy to animals' research usefulness

Since its introduction as a laboratory animal, the Mongolian gerbil, Meriones unguiculatus, has provided a valuable set of characteristics and susceptibilities for research into heart and kidney disease (SN: 1/22/66). Some researchers now think that the gerbil's susceptibility to spontaneous seizures may become a useful tool in studies of epilepsy.

To date, no satisfactory animal model has been found for studying the convulsive disorders. Usually seizures must be induced in laboratory animals by using electric shock, sound waves or vitamin deficiencies.

For several years it's been known that certain Mongolian gerbils can undergo mild seizures. After being handled, a susceptible animal may lie passively with limbs extended and body trembling, then resume normal activity within minutes. During these periods of cataleptoid behavior, muscular rigidity sometimes molds the gerbil's body in specific postures or allows the animal to be held in positions that it would not normally tolerate.

More recently, moderate to severe seizures have been observed in some gerbils. This behavior is characterized by a staring appearance of the eye, falling down on the side, muscular spasms, running movements of the legs, and a recovery period during which the gerbil appears dazed. Recovery is rapid and apparently complete; no deaths or aftereffects have been reported.

Dr. Delbert D. Thiessen, Gardner Lindzey and Harold C. Friend, psychologists at the Behavior Genetics Laboratory of the University of Texas, Austin, believe that gerbils exhibit spontaneous seizures more frequently under normal conditions than other experimental animals. Their evidence suggests that the gerbil's convulsive behavior may provide a model system to further medical research on grand mal epilepsy in man.

Dr. Thiessen was pleased to learn that other researchers had witnessed similar seizures. "We thought that the seizures might be a peculiarity of our lab, or of a particular group of gerbils," he explained.

To determine whether the seizures could be controlled, Dr. Thiessen and co-workers identified a group of seizure-prone gerbils and injected half of this

group with an anticonvulsant drug, diphenylhydantoin sodium, and the other half with a control agent. Retesting showed that no seizures occurred in gerbils receiving the anticonvulsant, whereas 70 percent of the control animals were still susceptible.

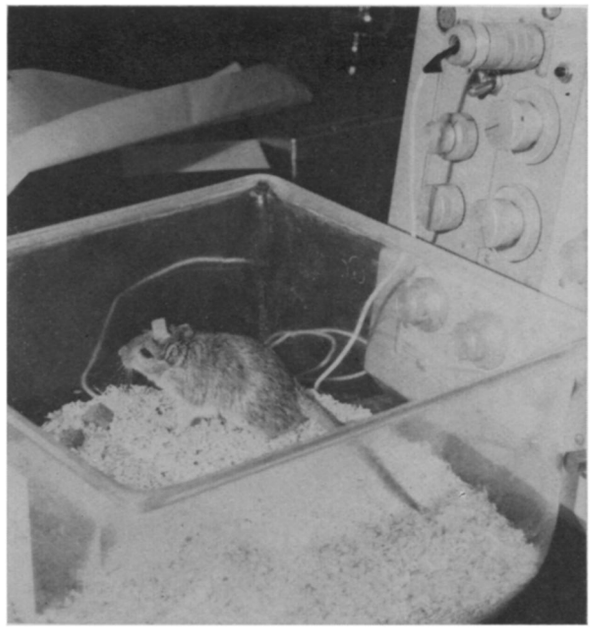
Preliminary results indicate that about 25 percent of the gerbils in some colonies may suffer seizures of varying intensity; males and females appear to be equally susceptible. By contrast, convulsive disorders affect less than one percent of human populations.

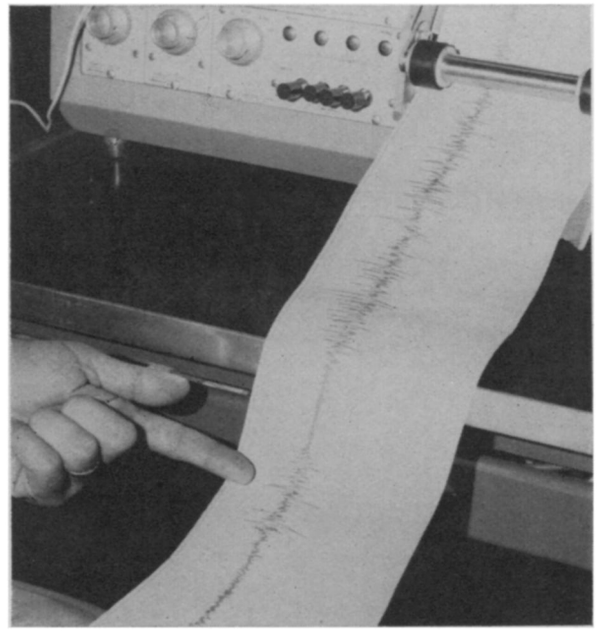
The gerbil's seizures are generally precipitated by environmental changes, including handling, rapid change of temperatures or lighting, exposure to testing devices and confinement in small areas. One experimenter has induced severe seizures merely by lifting the animal's cage a few inches above its normal shelf position. Seizures have been seen occasionally when no apparent stimulus was present.

Employing mazes and arenas of different sizes, shapes and colors, investigators find little distinction among environmental methods of producing seizures, but some adaptation occurs—perhaps because of familiarity with testing conditions.

Seizure incidence remains relatively constant if rest periods are allowed between them. The incidence is believed to be dependent upon the degree of the animal's arousal. Supporting evidence is that gerbils—largely nocturnal in their activity—have more seizures at night than during the day.

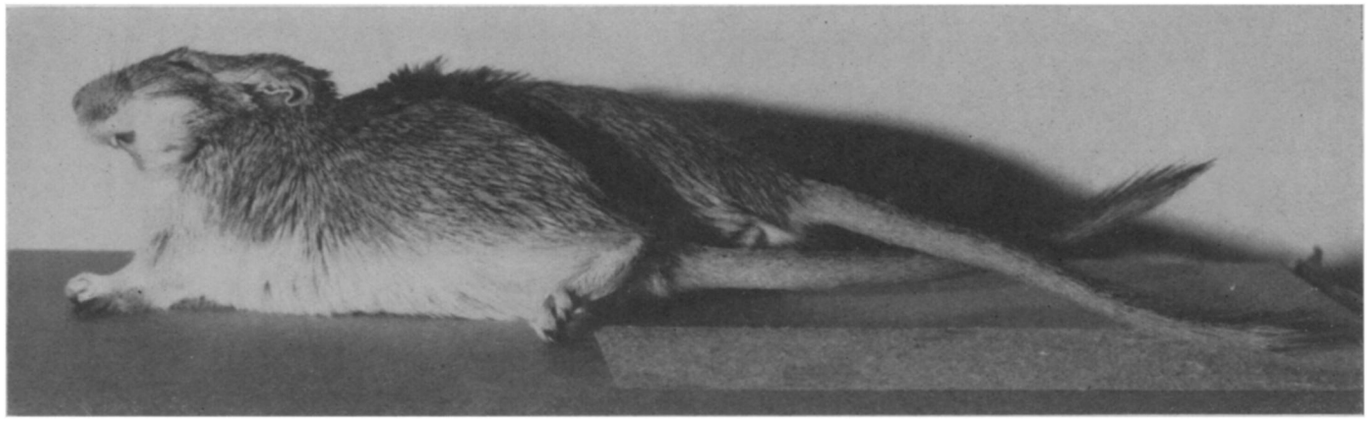
The cause of the seizures is unknown. "Our first hypothesis was that these seizures were nutritional in origin—probably a vitamin B deficiency," says Dr. Victor Schwentker, executive director of The West Foundation, Brant Lake, N.Y. A mammalian geneticist, Dr. Schwentker introduced gerbils to the United States for medical research.





Spikes in readout from electrodes implanted in gerbil's skull (left) indicate convulsions. Gerbils have epileptoid seizures (bottom).

Photos: D.G.R.



During studies at the University of California, Davis, gerbils showing seizure activity were given massive doses of supplementary vitamins. Initial results indicate that nutrition is not a causal factor.

Knowing that complete nutritional determination will require years, Dr. Schwentker experimented with cage space requirements to learn whether overcrowding might cause endocrinological changes that could lead to erratic behavior. Using data from a large colony of gerbils at Tumblebrook Farm, Inc., he concluded that space probably is not a critical factor. *(See p. 18)*

In what seems to be a first with gerbils, associate physiologist Betty Herndon of Midwest Research Institute, Kansas City, Mo., has spent nine months obtaining electrocorticogram (ECoG) data. Surgically implanted electrodes on a plastic socket attached to a gerbil's skull permit normal activity without discommoding the animal. A recording lead carries electrical potentials from the brain for amplification and recording. Normal behavior produces small-amplitude wave traces, but convulsive seizures show up as contrasting spikes. These studies may help to localize areas of the brain involved in seizure activity.

Dr. Cheng-Chun Lee, head of pharmacology and toxicology at MRI, believes that gerbils could be used for screening anticonvulsant drugs. "This might require many gerbils, and it would be desirable if an even larger percentage were susceptible," he adds.

Some scientists think that a greater susceptibility may be achieved through selective breeding of gerbils. One investigator reports a high percentage of susceptibility in five successive generations of gerbils.

In the November 1966 issue of EXPERIMENTAL NEUROLOGY, pathologists Seymour Levine and Hushang Payan reported that gerbils deserve a place in laboratories of neurological research. Both doctors are now studying the effects of abnormal blood flow and possible cell damage in the gerbil's brain. Dr. Payan cautions against attaching too much significance to brain studies in laboratory rodents, but he notes that, compared with the laboratory rat, the vascular system of the gerbil's brain appears to be more similar to man's.

One investigator who has not observed seizures in his gerbil colony and has expressed skepticism about the phenomenon is Dr. Sigmund T. Rich, director of the research animal facility at the center for the health sciences, University of California at Los Angeles. He plans to enlist the aid of researchers at UCLA's Brain Research Institute so that more can be learned about the reported seizure syndrome. From selected gerbils received by Dr. Schwentker, he hopes to observe offspring that will exhibit this behavior. "If such is the case, and we can develop a strain of animals with a high percentage of seizures," Dr. Rich comments, "they will indeed become valuable in many areas of neurological research."

Do some gerbils actually have a form of idiopathic or true epilepsy? The reported seizure activity, apparently normal behavoir between seizures, and limited genetic findings imply that they do. But skepticism is likely to prevail until more evidence is obtained.

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