and LD_{100} pentylenetetrazole, as shown in Fig. 2. The effectiveness of Miltown in this respect again confirms Berger's data with mice(3). However, methadone isomers and high doses of morphine and codeine significantly potentiated pentylenetetrazole toxicity, while the low doses of the latter 2 drugs were protective.

Discussion. The results of these experiments show clearly that MEM, unlike morphine, codeine, and methadone isomers, is devoid of a central excitatory action in non-toxic doses in the 3 species studied. It is for this reason that MEM significantly protects against pentylenetetrazole convulsions and fatalities, while morphine, codeine, and the methadones potentiate these effects. However, we have found that smaller doses of these latter compounds, in contradiction to the data of Hazelton and Koppanyi(4,5), are also protective against the effects of pentylenetetrazole; these doses probably produce only C.N.S. depression without a simultaneous stimulatory action.

Summary. (1) In non-toxic doses MEM shows no C.N.S. excitatory effects in mice, rats, and dogs. (2) In doses which do not induce loss of righting reflex, MEM prolongs hexobarbital hypnosis. (3) MEM, unlike morphine, codeine, and some methadone isomers, significantly blocks the convulsant and toxic effects of pentylenetetrazole.

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Frequency of t^w Alleles in a Confined Population of Wild House Mice.* (22460)

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The T locus in mice represents a complex locus in which 11 reported alleles, many of them proven to be different from others, have been derived from laboratory stocks. Many populations of wild mice have also been shown to contain recessive mutants at the T locus. Some of these wild alleles have been shown to be different from those found in laboratory stocks(1). The dominant allele, T, is homozygous lethal and when present in heterozygous condition, T +, with the normal allele causes a variable shortening of the tail (Brachury = short tail). In addition to T there is a series of recessive alleles, t^n, each of which when present with T (as T/t^n) produces the tailless phenotype. The recessive alleles, t^n, may be homozygous lethal or viable. When viable, the males of the genotype, t^n/t^n, are usually sterile. Viable female mice of the genotype, t^n/t^n, are usually fertile. It is relatively simple to discover whether a mouse has the genotype $+/t^n$ or $+/+$. The animal in question is mated to a Brachy ($T/+$). If the animal in question is $+/+$ only two types of offspring are obtained: normal tailed and Brachy, in approximately equal numbers. Should the mouse in question, however, be $+/t^n$, then 3 classes of offspring are found; namely, normal tailed, Brachy and tailless. This latter group has the genotype, T/t^n. Provided that sufficient numbers of offspring are obtained from a test animal, it can be classified as $+/+$ or $+/t^n$. In males the procedure is greatly aided by the phe-

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nomenon of "segregation ratio abnormality" in which $+/t^n$ male mice usually produce many more t^n sperm than $+$ sperm. As a result many male mice that are $+/t^n$ have tailless offspring in their first litters(2). In practice, new t alleles have been numbered in the order of their discovery. It may later be found that some of the numbered t alleles are indistinguishable from each other and the higher numbered line is then discarded. For such t alleles as are discovered in wild populations of mice, the superscript "w" is added to indicate their origin, hence t^{w1}, t^{w2}, etc.

The present paper is concerned chiefly with the problem of determining the frequency of heterozygotes in a population known to possess t^w. This population is descended from wild mice caught in the suburbs of New York and Philadelphia in 1943-44 and since maintained as a small (125-250 individuals) laboratory population by Dr. Howard A. Schneider of the Rockefeller Institute for Medical Research, New York. It has undergone moderate in-breeding (usually by half-sibling matings, with avoidance of full sibling mating) (3). Dr. Schneider has kindly supplied the samples tested.

Previous studies. The first sample (R – 1) tested (January 1952) consisted of 10 males of which 8 produced test offspring. Of these, 5 proved to be $+/t^w$. Two different alleles were found: t^{w1}, homozygous lethal; t^{w2}, homozygous viable. Males t^{w2}/t^{w2} proved to be sterile; t^{w2}/t^{w2} females were fertile(2). A second sample (R – 2) of 6 males and 21 females was tested beginning August 1952. Four males and 11 females gave test progenies. Of these 2 males and 4 females proved to be $+/t^w$ and again both alleles t^{w1} and t^{w2} were present.

Present study. A further sample (R – 3) from this confined population consisting of 68 females and 70 males was obtained in June 1955. These were mated with Brachys ($T/+$) and tested individually. Thirteen females (19%) and 26 males (37%) gave no litters after 4 months of testing by fertile mates, a sterility rate of 28% compared with 33% previously found(4).

Of the fertile animals, 22 out of 44 males (50%) and 36 out of 55 females (65%) produced at least 2 tailless offspring each (usually more) and were diagnosed as $+/t^w$. There was thus found a minimum of 58 heterozygotes out of 99 tested (59%). The results are shown in Table I.

TABLE I. Results of Testing Wild Type Mice by Brachy ($T/+$) Mice.

	Offspring			
	Normal	Brachy	Tailless	
Genotype	$+/+$ or $+/t^w$	$T/+$	T/t^{w2}	Total
22 $+/t^{w2}$ ♂	107	13	80	200
22 $+/+$ ♂	252	237	—	489
26 sterile ♂	—	—	—	—
36 $+/t^{w2}$ or t^{w2}/t^{w2} ♀	150	64	101	315
19 $+/+$ ♀	131	104	—	235
13 sterile ♀	—	—	—	—

Some of the tailless offspring were tested for the presence of t^{w1} and t^{w2}. Of 13 $+/t^w$ animals whose descendants were tested all proved to contain t^{w2} only. In the 2 previous samples, we estimated the relative frequencies of t^w alleles as 25% t^{w1} and 75% t^{w2}. Assuming such frequencies the probability of getting 13 t^{w2} out of 13 tested is less than 3%. Hence t^{w1} had either disappeared or was very rare in the third sample.

The apparent disappearance of t^{w1} from the population may have been either due to a superiority of t^{w2} or to random breeding. This population is reduced each summer from about 250 to approximately 125 animals. It is possible that in one of the reductions between 1952 and 1955 inadvertently only t^{w2}-containing mice were retained. Should this be the case, it would constitute an actual example of *random genetic drift* resulting in the elimination of a gene from a population.

In Table I, the ratio of tailless to tailless plus Brachy offspring, from the cross $+/t^w$ x $T/+$, expressed the proportion of t^w gametes in the $+t^w$ parent. For males the proportion is .86, indicating a preponderance of t^w sperm, such as is usually found in male heterozygotes(5). However, in the case of t^w-containing females the proportion is .61, which seems to indicate an excess of t^w eggs. No definite statement about a possible segre-

gation ratio in females of this population can be made as it was not possible to test each mutant carrying female as to whether she was homozygous or heterozygous for t^{w2}. Much of the excess of t^w eggs may be due to females. homozygous for t^{w2}. Such females are both viable and fertile and when mated to Brachy males can give only normal tailed and tailless offspring.

Discussion. It is interesting to contrast the frequency of t^w-containing individuals in this confined population (59%) with those found in newly caught wild animals. This latter frequency has been estimated as a minimum of 32%(1). Confined populations and wild populations of mice are undoubtedly subject to different selection pressures. It is possible that conditions in a confined population favor t^w-containing individuals more than do conditions in wild populations. Experiments have shown that, in this confined population, male mice heterozygous for a lethal ($+$ t^{w1}) have a higher net relative fertility than $+/+$ males(4).

The lack of adequate samples in previous studies makes it impossible to state whether 59% represents the equilibrium frequency of t^{w2} in this population. The population may still be in a state of flux and t^{w2} may eventually either be eliminated or reach fixation. Prout has considered the possible fates of t^w alleles in a population(6).

Two observations which may be casually related are the relatively high frequency of males that gave no litters and the relatively low frequency of $+/t^w$ males, as compared with females in this population. These phenomena may be due to the peculiar characteristics of t^{w2} homozygotes which, as males, are viable but sterile. Females, homozygous for t^{w2}, are both viable and fertile.

Summary. 1. A sample (R – 3) from a confined population of mice, consisting of 70 males and 68 females, was tested for the presence of t^w alleles. This population is descended from animals caught in the wild. 2. Of 44 tested males, 50% were $+/t^w$; while of 55 tested females, 65% contained t^w. This population has an overall-frequency of 59% t^w containing fertile individuals. The present generation of this population seems to contain only t^{w2}, a viable allele, and $+$. Previously tested generations (R – 1 and R – 2) had contained both t^{w2} and t^{w1}. The latter is a lethal allele. 3. The $+/t^{w2}$ males of this population transmitted t^{w2} gametes to their offspring in excessive numbers, a phenomenon known from other studies and referred to as "segregation ratio abnormality." 4. Discussed is the overall high frequency of t^w-containing individuals found in this population as compared with animals caught in the wild. Also discussed is the disparity between males and females with respect to frequencies of sterility and t^w-containing individuals.

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