The use of powerful bioantioxidants may thus be a promising approach to reducing the mutagenic potential of PAH. Less detrimental genetic consequences may also be expected from PAH if they are liberated into the environment mixed with powerful bioantioxidants.

LITERATURE CITED

1. R. I. Goncharova, T. D. Kuzhir, G. Ya. Dibur, et al., Dokl. Akad. Nauk SSSR, 255, No. 6, 1483 (1980).
2. Yu. V. Pashin and L. M. Bakhitova, Byull. Éksp. Biol. Med., No. 9, 327 (1981).
3. A. Abbondandolo, S. Bonatti, G. Corti, et al., Mutat. Res., 46, 365 (1977).
4. L. M. Calle, P. D. Sullivan, M. D. Nettleman, et al., Biochem. Biophys. Res. Commun., 85, 351 (1978).
5. B. L. Kaul, Mutat. Res., 67, 239 (1979).
6. A. D. Rahimtula, P. K. Zacharian, and P. J. O'Brien, Biochem. J., 164, 473 (1977).

ROLE OF RECESSIVE LETHAL GENES IN SPONTANEOUS EMBRYONIC MORTALITY IN NONINBRED MOUSE AND RAT POPULATIONS IN CUBA

Kh. Kh. Semenov and D. Walker

UDC 612.646.013:612.6.052:575.113.39

KEY WORDS: recessive lethal genes; spontaneous embryonic mortality.

The frequency of recessive genes, lethal in the homozygous state, is a more objective criterion of latent variation, although recessive lethals are a very limited group of variants which cannot give an adequate idea of the general level of genetic variation. Meanwhile, recessive lethal genes are expressed if in the homozygous state and they make a definite contribution to spontaneous embryonic mortality. This latter parameter, a biological characteristic of the population, is very important for research workers who use this feature as an indicator of the genetic and teratologic effect of physical and chemical agents (mutagenesis and teratogenesis). The main method of determining genetic variation is by the use of inbreeding, which leads to an increase in homozygosity which, in turn, favors the manifestation of recessive alleles, hitherto concealed in heterozygotes.

The object of the present investigation was to study the frequency of recessive lethal genes in the genetic pool of noninbred mouse and rat populations in the laboratory animals nursery of the National Scientific Research Center (CENIC), Academy of Sciences of the Republic of Cuba.

EXPERIMENTAL METHOD

Small colonies of noninbred mice and rats from the CENIC Nursery served as test material. A colony of random-bred mice consisted of 240 parents (ratio 2:1) and a colony of rats consisting of 110 parents (ratio 1:1). Two crossing versions were used in the investigation: 1) autobred crossing, 2) inbred or closely related (crossing between sibs). Virgin females aged 2-2.5 months were crossed with males of the same age. In both versions of crosses the females were autopsied on the 15th-17th day of pregnancy and the number of living and dead embryos and the number of corpora lutea in the ovaries were counted. The spontaneous embryonic mortality level was determined as the total number of pre- and postimplantation embryos lost for the autobred crossing group. The frequency of recessive lethals was determined as the difference between embryonic mortality in progenies from sib crossing (F = 1/4) and crossing of unrelated males and females (F = 0), multiplied by 4. Altogether 150 female mice and 112 female rats were used in the experiment. Since parameters of normal ovulation, the level of spontaneous embryonic mortality before and after implantation, and the frequency of reces-

Research Laboratory of Experimental Biological Models, Academy of Medical Sciences of the USSR, Moscow.

(Presented by Academician of the Academy of Medical Sciences of the USSR N. P. Bochkov.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 95, No. 3, pp. 71-73, March, 1983. Original article submitted July 19, 1982.

0007-4888/83/9503-0339$07.50

TABLE 1. Results of Autopsy on Noninbred Female Rats at 15th-17th Day of Pregnancy

Crossing version	Number of females studied	Number of living embryos			Number of dead embryos			Number of implantation sites			Number of corpora lutea	
		absolute	%	confidence interval, percent	absolute	%	confidence interval, percent	absolute	%	confidence interval percent	total	at 10+
Autobred	80	800	91,85	84,6—96,9	71	8,15	3,1%—15,2	871	85,56	78,2—91,6	1018	12,7±0,21
Inbred	32	313	86,94	64,1—99,4	48	13,33	4,0%—36,2	360	85,71	66,1—97,6	420	13,1±0,27

Legend. Here and in Table 2 confidence interval calculated by method at P = 0.95 level.

TABLE 2. Spontaneous Embryonic Mortality in Swiss Mice from CENIC Nursery

Crossing version	Number of females studied	Number of females studied			Number of living embryos			Number of implantation sites			Number of corpora lutae	
		absolute	%	confidence interval, percent	absolute	%	confidence interval, percent	absolute	%	confidence interval, percent	total	at 10+
Rotating	100	612	70,02	59,3—79,7	262	29,38	20,3—40,6	874	85,60	78,2—91,6	1021	10,2±0,16
Inbred	50	284	62,83	41,3—82,0	168	37,17	18,1—58,7	452	84,01	68,7—94,8	538	10,7±0,19

sive lethal genes in the genetic pool can give some idea of the processes taking place in the population over a period of several years, these parameters were studied in females during the first pregnancy for animals of both species. The results for mice were compared with the corresponding results of an experiment in 1977 [3].

EXPERIMENTAL RESULTS

Analysis of the results of autopsy on female rats on the 15th-17th days of pregnancy (Table 1) showed a difference between the number of corpora lutea in the ovaries, which must correspond to the number of ovulated oocytes [6], and the number of implantation sites in the autobred and inbred crossing groups. This difference gives the proportion of oocytes giving rise to preimplantation losses. Its value for the autobred crossing group was 14.45%, and for the inbred group 14.29%. Clearly the contribution of preimplantation losses was considerable in both crossing versions. The difference between the groups with respect to embryonic mortality at this stage was minimal.

In noninbred Swiss mice (Table 2) preimplantation losses in the rotating cross group amounted to 14.4% and in the inbred group 16%. The difference between the contributions of preimplantation losses between the groups likewise was not statistically significant.

According to the experimental data, in rats of the autobred cross group the spontaneous embryonic mortality after implantation was 8.15%. This was much higher than the mean value of this parameter for noninbred rats [2]. In females of the inbred cross group, its value was much higher, namely 13.33%. The difference between the inbred and autobred crossing groups with respect to the level of embryonic mortality at this stage of development is statistically significant ($P < 0.01$).

The postimplantation embryonic mortality in mice was 30% in the autobred cross group and 37.2% in the inbred cross group; the difference between the groups is highly significant ($P < 0.001$).

Differences between the groups with respect to spontaneous embryonic mortality as a whole, i.e., the contribution of recessive lethal genes, converted into the homozygous state, to this process amounted to about 5.2% in rats and 7% in mice. It must be pointed out that recessive lethal genes were manifested in both species of animals mainly in the postimplantation period of development. The connection here is evidently such that death of the embryo in the postimplantation stage is caused by more severe genomal and chromosomal disturbances [1-4, 5, 7] than after implantation. In other words, the main mass of recessive lethal genes in the homozygous state cannot interrupt development of the embryo at the preimplantation stage.

Mortality among progenies from sib crosses (brothers and sisters) in rats was thus 5.2% higher, and in mice 7% higher than among progenies from unrelated males and females (autobred crossing). We

know that in progenies from sibs 1/4 of the genes, normally heterozygous, are converted into the homozygous state. Since conversion of 1/4 of genes into the homozygous state led to an increase in embryonic mortality of 5.2% in rats and 7% in mice, if all genes were in the homozygous state, the mortality ought to have been increased fourfold. This means that the increase in mortality would have been 20.8% (5.2 × 4 = 20.8) in rats and 28% (7 × 4 = 28) in mice. Hence it must be concluded that the frequency of recessive lethal genes in the genetic pool of the rat colony of the CENIC Nursery was 20.8% and in the Swiss mouse colony 28%.

Naturally this is a somewhat simplified method of determining the frequency of recessive lethal genes, which may be valid if one essential assumption is made: The action of genes on viability is independent or, as it is usually said, synergism is absent in the action of genes.

It will evidently be more accurate if we speak of the "lethal equivalent" and not of the lethal effect of a single gene. A "lethal equivalent" may be a single lethal gene or a group of partially lethal mutant genes. This means that if partially lethal genes together equal to one "lethal equivalent" are converted into the homozygous state, their action will be reduced on average to the death of one individual. The frequency of heterozygotes carrying recessive factors which, on conversion into the homozygous state, cause death of the embryos, was thus 28% in the colony of Swiss mice and 20.8% in the rats.

Analysis of the results obtained previously [2] and those of the present investigation showed that in the course of four years (1977-1981) no significant changes were found in the parameters of normal ovulation in the Swiss mice. However, during the period under study there was a sharp increase in mortality both before and after implantation, which may have been due to genetic differences taking place among the animals and to the effect of ecologic factors.

LITERATURE CITED

1. A. P. Dyban and V. S. Baranov, in: Cytogenetics of Mammalian Development [in Russian], Moscow (1978), p. 154.
2. V. P. Kryshkina and A. M. Malashenko, in: Laboratory Animals in Medical Research [in Russian], Moscow (1974), p. 16.
3. V. P. Kryshkina, M. Tolon, C. Cordoves, et al., Genetika, No. 2, 318 (1980).
4. Kh. Kh. Semenov and A. M. Malashenko, Byull. Éksp. Biol. Med., No. 10, 107 (1975).
5. Kh. Kh. Semenov and A. M. Malashenko, Byull. Éksp. Biol. Med., No. 9, 353 (1979).
6. A. W. H. Braden, Genetics, 55, 476 (1957).
7. B. E. Matter and J. Jager, Mutat. Res., 33, 251 (1975).