classes + and Sb ($r = -0.019$; $t = 0.63$; $P > 0.05$) nor between classes Cy and Sb ($r = 0.14$; $t = 0.53$; $P > 0.05$). Consequently, inbreeding depression is similar in the + and Cy classes but independent of that in the Sb class. As a result of our experimental scheme, all wild type individuals descending from the brother-sister matings were homozygous Is^-/Is^-. So, the difference between the +, Cy and Sb classes seems associated with the homozygous Is^-/Is^- constitution of the flies of the + and Cy class as compared with the Is^-/Is^+ heterozygous state of the flies of the Sb class. This observation suggests that the proportion of wild type flies, therefore the mortality rate during development, depends on the genomic constitution of the parents. The extent of inbreeding depression appears to characterize the parental couple, thus suggesting regulation by cytoplasmic factors, as previously inferred (Biémont 1978).

Such a parental effect has to be taken into account when inbreeding effects with different mating systems, or various natural populations, are compared. Indeed, whatever the nature of the implied gene, variation of its frequency in populations may influence the extent of viability depression after inbreeding and thus estimate of genetic load.

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References: Lewontin, R.C. 1974, The Genetic Basis of Evolutionary Change, Columbia University Press, New York, London; Biémont, C. 1978, Mech. Ageing Develop. 8:21-42, ____ 1979, Experientia (in press).

Bishop, C.P. and A.F. Sherald*. University of Virginia, Charlottesville, Virginia; *George Mason University, Fairfax, Virginia. Isolation of two third chromosome mutants conferring resistance to α-methyl dopa.

α-methyl dopa (α-MD) is an in vitro inhibitor of dopa decarboxylase (DDC) and it was originally thought that α-MD might be used to screen for mutants with altered levels of the DDC enzyme. Although the original screen for resistance to α-MD produced two strains with elevated levels of DDC (Sherald and Wright 1974), screens for sensitivity to the inhibitor produced mutants with no effect on the enzyme (Sparrow and Wright 1974). Furthermore, it has been subsequently shown that the greater the number of DDC gene copies, the greater the sensitivity to α-MD (Wright, unpublished). Sensitivity to α-MD, it was discovered, was due to a locus, 1(2)amd, other than the structural locus for DDC (Wright et al. 1976a, 1976b). Since the 1(2)amd locus maps very close to the structural gene for DDC, the mutants with both elevated resistance and enzyme activity may be control mutants (Marsh and Wright 1979).

The two α-MD resistant mutants we report here were isolated from a total screen of 1,715 EMS mutagenized (Lewis and Bacher 1968) progeny from a lethal free third chromosome bw; st stock. They were isolated by survival on 0.8 mM DL α-MD, well above the concentration that is lethal to wild type flies (less than 0.4 mM). A total of 80 putative resistant mutants were recovered, 18 of which showed resistance upon retesting and two (PR40 and PR45) of these were selected for further study.

Table 1 shows that the locus responsible for resistance clearly segregates with the mutagenized third chromosome. Preliminary mapping of one of the mutants, PR45, places the locus between hairy (3-26.5) and thread (3-43.2) (Lindsley and Grell 1968). Using the L form of α-MD, which is roughly twice as lethal as the DL form, the LD_{50} for the two mutants has been established at 0.325 mM L α-MD for PR40 (bw; Tm3 Ser Sb/st*40) and 0.35 mM L α-MD for PR45 (bw; Tm3 Ser Sb/st*45). The LD_{50} for control stocks was below 0.1 mM L α-MD.

In addition to showing dominant resistance to α-MD, these mutagenized third chromosomes are recessive lethal. During preliminary mapping of PR45, replacement of large portions of the third chromosome did not permit construction of a homozygous resistant stock. Crosses between the two resistant mutants produced very few flies (roughly 5% of expected) carrying both resistant chromosomes, indicating that the two chromosomes fail to complement. The fact that the two independently isolated mutants are lethal in trans configuration and that a homozygous resistant stock could not be established even after replacement of significant portions of the third chromosome suggests that dominant resistance and recessive lethality may be due to hits in a single locus.

It is not surprising that more than one locus can affect resistance to a lethal substance. The function of the 1(2)amd locus and the locus reported here are unknown. The sites of possible action could include uptake or detoxification of the compound or alterations in the target protein. The genetic relationship between 1(2)amd locus and the third chromosome

locus is being explored as is the relationship of the other 16 putative resistant mutants.

Table 1. Segregation of resistance to α-MD with the mutagenized third chromosome.[1]

PR45 (bw; Tm3 Ser Sb/st*^{45}) X Con B (bw; Tm3 Ser/st^{B})[2]

Conc. L α-MD	#eggs hatched	bw; Tm3 Ser/st*^{45}	bw; st*^{45}/st^{B}	bw; Tm3 Ser Sb/st^{B}
0 mM	271	50	63	63
.1mM	257	71	58	26
.2mM	241	60	61	7
.3mM	265	50	43	0
.4mM	178	11	12	0

PR40 (bw; Tm3 Ser/st*^{40}) X Con #1 (bw; Tm3 Ser Sb/st*$^{\#1}$)[3]

Conc. L α-MD	#eggs hatched	bw; Tm3 Ser/st*$^{\#1}$	bw; st*^{40}/st*$^{\#1}$	bw; Tm3 Ser Sb/st*^{40}
0 mM	249	62	53	63
.1mM	276	2	61	78
.2mM	286	0	37	56
.3mM	287	0	12	41
.4mM	121	0	0	8

1) Data from reciprocal crosses were pooled since no maternal effect was found.
2) Con B was a control stock which had been through the same crosses as PR40, except that it was not mutagenized.
3) Con #1 was a mutagenized control stock isolated from the screen and carried through the same crosses as PR45.

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References: Lewis, E.B. and F. Bacher 1968, DIS 43:193; Lindsley, D.L. and E.H. Grell 1968, Carnegie Inst. of Wash. Publ. No. 627; Marsh, J.L. and T.R.F. Wright 1979, UCLA Symp. M. and Cell Biol. 14:183; Sherald, A.F. and T.R.F. Wright 1974, Molec. gen. Genet. 133:25; Sparrow, J.C. and T.R.F. Wright 1974, Molec. gen. Genet. 130:127; Wright, T.R.F., R.B. Hodgetts and A.F. Sherald 1976, Genetics 84:267; Wright, T.R.F., G.C. Bewley and A.F. Sherald 1976, Genetics 84:287.