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 Title : POTENCIES OF ENFLURANE, ISOFLURANE, CYCLOPROPANE, AND ETHANOL IN MICE SELECTIVELY BRED FOR RESISTANCE AND SUSCEPTIBILITY TO NITROUS OXIDE ANESTHESIA
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Introduction. Mice from a normal population can be sorted into two groups, one group having a reproducibly high, and one a reproducibly low, nitrous oxide requirement ("HI" and "LO" mice, respectively). By breeding HI mice with HI mice and LO with LO, these differences in N₂O potency can be perpetuated in the offspring.¹ We continued this selective breeding through eight generations, and have now determined anesthetic potency for agents other than N₂O in HI and LO mice.

Methods. ED₅₀s were determined for nitrous oxide, enflurane, and cyclopropane by measuring the partial pressure of the agent required to abolish the righting reflex in half of the mice. In addition, potencies of isoflurane, enflurane, and cyclopropane were determined by measuring the concentrations required to abolish movement in response to a clamp applied to the tail. Ethanol-induced sleep times (time period over which the mouse could not right itself) were measured following an intraperitoneal injection of ethanol, 4.0 g/kg. Blood alcohol present on awakening was determined by an enzymatic procedure. Rectal temperatures were maintained between 36.5 and 38.0 C. In all experiments, the observer was unaware of the identity (HI or LO) of the animals. We used HI and LO mice from the fifth through eighth generations.

Results. HI and LO mice of the eighth generation had a difference of approximately 0.7 atm in N₂O requirement (table 1). Similarly, anesthetic requirements of isoflurane, enflurane, and cyclopropane were significantly (P < 0.005) greater in the HI than in the LO mice, as measured by both the righting reflex (RR) and tail-clamp (TC) tests (table 1). HI mice (n = 25) given an intraperitoneal injection of alcohol had a sleep time (mean ± SE) of 57 ± 3 min and a blood alcohol level upon awakening of 0.416 ± 0.006%, whereas LO mice (n = 32) had a sleep time of 100 ± 6 min and a blood alcohol level of 0.371 ± 0.006%.

Discussion. Mice selectively bred for their resistance and susceptibility to N₂O anesthesia are also more resistant and susceptible to other anesthetics. The ratio of the high to low value does not appear to be constant for all anesthetics, but decreases as lipid solubility (oil/gas partition coefficient) increases (table 1). For example, the highest ratio for the righting reflex is that for nitrous oxide (1.60); cyclopropane has an intermediate value (1.49); and enflurane has the lowest value (1.19). A biochemical or biophysical basis for these differences in anesthetic requirement remains to be determined.

Reference

1. Koblin DD, Dong DE, Deady JE, et al: The breeding of mice resistant to and susceptible to nitrous oxide anesthesia. *Anesthesiology* 51(3S):S17, 1979 (abstract)

Table 1. ED₅₀s (Mean ± SE) of Nitrous Oxide (N₂O), Cyclopropane (C₃H₆), Isoflurane (Iso), and Enflurane (Enfl) in HI and LO Mice

Anesthetic and Testing Method	HI - ED ₅₀ (% atm)	HI (n)	LO - ED ₅₀ (% atm)	LO (n)
N ₂ O (RR)	193 ± 2	61	121 ± 2	88
C ₃ H ₆ (RR)	16.8 ± 0.4	30	11.3 ± 0.2	57
C ₃ H ₆ (TC)	26.6 ± 0.5	27	20.8 ± 0.5	51
Iso (TC)	1.63 ± 0.04	35	1.45 ± 0.04	54
Enfl (RR)	1.40 ± 0.04	33	1.18 ± 0.04	23
Enfl (TC)	2.52 ± 0.06	24	2.17 ± 0.08	18