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# *Halothane Requirement during Pregnancy and Lactation in Rats*

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Near-term pregnancy is associated with a decrease in the minimum alveolar concentration (MAC) for halothane in ewes. Although increased progesterone levels might account for this change, a correlation between MAC and the known variations of progesterone levels which occur throughout gestation and the postpartum period has not been performed. Therefore, MAC for halothane was determined in nonpregnant, 10 days pregnant, term, and postpartum lactating rats. MAC values were significantly decreased by 19 per cent on the tenth day of pregnancy, and by 16 per cent at term, but they returned to control values 5 days postpartum. These changes did not correlate with the known changes in progesterone levels during pregnancy and lactation, and the authors conclude that progesterone is not responsible for the reduction in halothane MAC. (Key words: Anesthesia: obstetric. Anesthetics, volatile: halothane. Potency, anesthetic: MAC. Pregnancy.)

MINIMUM ALVEOLAR CONCENTRATION (MAC) is recognized as a standard of anesthetic potency.<sup>1,2</sup> Palahniuk *et al.* found that the MAC values for halothane, methoxyflurane, and isoflurane were decreased by 25, 32, and 40 per cent, respectively, in pregnant ewes within three weeks of terms.<sup>3</sup> Because of the known anesthetic properties of progesterone<sup>4</sup> and other steroids,<sup>5</sup> they postulated that hormonal changes and, in particular, the increased progesterone levels which occur during pregnancy could account for this phenomenon. Since they determined MAC at one stage of pregnancy only, they could not correlate the changes in MAC with the known variations in progesterone levels during pregnancy.<sup>6</sup> In addition, MAC was not studied in the postpartum period. Therefore, we have determined the MAC of halothane at two stages

of pregnancy and during lactation in rats, and compared these anesthetic requirements to control values in nonpregnant animals.

### Methods

Halothane MAC was determined in young adult (7-12 wk), female Sprague-Dawley rats obtained pre-bred and dated from Charles River Breeders, Wilmington, Massachusetts. Four groups of animals were studied. Seven were nonpregnant, virgin controls ( $205 \pm 12$  g; mean  $\pm$  SE), six were at 10 days of pregnancy ( $246 \pm 7$  g), eight were at term ( $312 \pm 8$  g), and six were postpartum lactating rats ( $269 \pm 10$  g). Pregnancy was confirmed by examination of the uteri at the conclusion of the experiment or by palpation of the fetuses in the term rats. All the rats were anesthetized with halothane between 8 A.M. and 11 A.M. to permit tracheostomy. MAC was then determined by the method described by White *et al.*<sup>7</sup> except, that a  $25 \times 31 \times 12$  cm plastic container with a glass top served as the anesthetizing chamber so that up to five rats could be anesthetized at one time. Halothane was delivered via a Drager<sup>®</sup> vaporizer in 4 l of oxygen/min. Colonic temperatures, as measured by Yellow Springs<sup>®</sup> thermistor probes, were maintained at  $36-38^{\circ}\text{C}$  by a heat lamp. After a minimum of 25 min equilibration time at each halothane concentration, a tail clamp was applied for at least 1 min and end-expiratory gas samples were obtained and analyzed for halothane concentrations with a Gow-Mac gas chromatograph. The mean end-expiratory  $P_{\text{CO}_2}$  for all groups combined was  $52 \pm 2$  torr as measured by a Radiometer<sup>®</sup> BMS MK-2 Blood Micro System analyzer. Statistical analysis was accomplished using analysis of variance ( $F = 24.3$ ,  $P < 0.001$ ) followed by Student's unpaired  $t$  test.

### Results

The mean MAC value in the nonpregnant control group was 1.13 per cent (table 1) which compared well with the value of 1.11 per cent previously reported for young (3.5-month-old) adult rats.<sup>7</sup> MAC was decreased significantly (16-19 per cent) in the two

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TABLE 1. Halothane MAC in Rats Before, During and After Pregnancy

Conditions	n	Halothane MAC* (Per Cent)	P vs. Control	P vs. Postpartum
Nonpregnant (Control)	7	1.13 ± 0.03	—	>0.10
10 Days gestation	6	0.91 ± 0.03	<0.001	<0.001
21–23 Days gestation	8	0.95 ± 0.02	<0.001	<0.001
5 Days postpartum	6	1.09 ± 0.02	>0.10	—

\* Values are means ± SE.

pregnant groups and returned to control levels in the postpartum lactating group. There was no significant difference in MAC between the two pregnant groups ( $P > 0.10$ ), but the difference between each of the pregnant groups and the lactating group was significant.

### Discussion

Our finding of a reduction in halothane MAC in pregnant rats lends support to the decrease in pregnant ewes reported by Palahniuk *et al.*<sup>3</sup>. However, these data do not suggest that changes in progesterone level cause the decrease in MAC. Grota and Eik-Nes<sup>8</sup> have reported a progressive decrease in plasma progesterone concentrations in rats from about 260 ng/ml on day 10 of pregnancy to 10 ng/ml on day 22. By day 4 of lactation, plasma progesterone levels had risen to 123 ng/ml and plateaued there until at least eight days postpartum. If increased progesterone levels are responsible for decreased MAC, we would expect to see a reduction in MAC at day 10 of gestation followed by a

return toward control at term. Also, MAC during lactation should be reduced.

We therefore conclude that MAC is decreased during pregnancy and returns to normal levels during lactation. Our findings indicate that progesterone is not responsible for these changes. The physiologic alterations occurring during pregnancy are complex, and the mechanism responsible for the reduction in halothane MAC remains to be determined.

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### References

1. Eger EI, Saidman LJ, Brandstater B: Minimum alveolar anesthetic concentration: A standard anesthetic potency. *ANESTHESIOLOGY* 26:756–763, 1965
2. deJong RH, Eger EI: MAC expanded:  $AD_{50}$  and  $AD_{95}$  values of common inhalation anesthetics in man. *ANESTHESIOLOGY* 42:384–389, 1975
3. Palahniuk RJ, Shnider SM, Eger EI: Pregnancy decreases the requirement for inhaled anesthetic agents. *ANESTHESIOLOGY* 41:82–83, 1974
4. Merryman W, Boiman R, Barnes L, et al: Progesterone “anesthesia” in human subjects. *J Clin Endocrinol Metab* 14: 1567–1569, 1954
5. Selye H: Studies concerning the anesthetic action of steroid hormones. *J Pharmacol Exp Ther* 73:127–141, 1941
6. Stabenfeldt GH, Drost M, Franti CE: Peripheral plasma progesterone levels in the ewe during pregnancy and parturition. *Endocrinology* 90:144–150, 1972
7. White PF, Johnston RR, Eger EI: Determinations of anesthetic requirement in rats. *ANESTHESIOLOGY* 40:52–57, 1974
8. Grota LJ, Eik-Nes KB: Plasma progesterone concentrations during pregnancy and lactation in the rat. *J Reprod Fertil* 13:83–91, 1967