

Title : HALOTHANE MAC AND PREGNANCY: ENDORPHINS, PROGESTERONE, OR ?  
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**INTRODUCTION.** Near-term pregnancy has been associated with a decrease in halothane MAC in ewes<sup>1</sup> as well as in rats.<sup>2</sup> The reason for this decrease in anesthetic requirements remains unclear. Palahniuk et al.<sup>3</sup> suggested that increased progesterone levels may account for the change but Strout and Nahrwold<sup>4</sup> presented contradictory evidence against this hypothesis. They were unable to correlate changes in MAC with known changes in progesterone levels in pregnant rats. However, they did not measure progesterone levels and were therefore unable to confirm the plasma progesterone concentration profile in their test animals. A progressive rise in pain thresholds during pregnancy has also been shown in rats.<sup>5</sup> This was abolished by the narcotic antagonist naltrexone and has been assumed to be endorphin mediated. We, therefore, undertook these experiments to determine if the decrease in MAC seen in pregnancy is (1) endorphin mediated or (2) due to increased levels of progesterone.

**METHOD.** Halothane MAC was determined using either virgin female Sprague-Dawley rats or dated pregnant rats of the same species. In the first series of experiments 4 groups of animals were studied. Groups I and II were non-pregnant. Group I were injected with 10 mg/kg naloxone intramuscularly; Group II were injected with an equivalent volume of saline. Groups III and IV were injected as above but were all 17-20 days pregnant at the time of MAC determination. In the second series of experiments two groups of non-pregnant rats were injected with either (1) 0.2 ml of a mixture of 125 µg progesterone in 5 ml propylene glycol or (2) 0.2 ml propylene glycol alone. Immediately after determination of MAC blood was drawn from the heart and progesterone levels were measured by a radioimmunoassay method. All rats were tracheostomized and MAC was determined by the method described by White et al.<sup>6</sup> The determination of MAC was made between 45-75 min after intramuscular injections of drugs were made. Colonic temperatures were maintained at 37°C by a heat lamp controlled by a temperature controller (Yellow Springs Instruments, model 73ATP). After an equilibration period of 30 min, 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 gas chromatograph. Statistical analysis was accomplished using Student's unpaired t test.

#### RESULTS.

(1) There was a significant diminution in MAC in the pregnant rats compared to the non-pregnant rats.

(2) There was no increase in MAC in the control groups compared to the pregnant or non-pregnant rats that received naloxone.

(3) There was no decrease in MAC following injection of progesterone in non-pregnant rats.

(4) Progesterone levels in the control and progesterone treated animals were  $22.2 \pm 5.4$  ng/ml and  $196 \pm 34$  ng/ml respectively.

(5) Determination of MAC done in animals 24 hrs following parturition yielded results in the non-pregnant range.

	Pregnant Vs Non-pregnant	Pregnant Rats Naloxone Vs Control	Progesterone Vs Control
Change in MAC	$-0.181 \pm .05^*$	$0.000 \pm .003$	$+ .02 \pm .02$
N	19	16	12

\*  $p < .005$

**DISCUSSION.** Our data suggest that the decrease in MAC observed in near-term pregnancy is not endorphin mediated nor is it due to increased progesterone levels alone. This decrease in MAC may well be due to more than one of the many and complex physiologic changes that occur in pregnancy.

#### REFERENCES.

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