

Title: EFFECT OF AGE AND HALOTHANE CONCENTRATION ON APNEIC THRESHOLD IN LAMBS

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**Introduction.** Young preterm infants frequently have periods of apnea during recovery from inhalational anesthesia, while older preterm and full-term infants rarely do.<sup>1</sup> The immature central respiratory controller (CRC) of preterm infants is thought to play a role in postanesthetic apnea. In young mammals, stimulation of the superior laryngeal nerve (SLN) causes apnea by inhibiting the CRC.<sup>2, 3</sup> To test the effect of age on CRC sensitivity to inhalational anesthetics, we measured apneic thresholds to CO<sub>2</sub> and SLN stimulation in newborn and older lambs anesthetized with different concentrations of halothane.

**Materials and Methods.** We studied 3 newborn (4-6 days) and 4 older (27-56 days) lambs. After anesthesia with 1-2% halothane/O<sub>2</sub>, the trachea and femoral vessel were cannulated. We determined minimal alveolar concentration (MAC) for halothane. Wound margins were infiltrated with marcaine 0.25% (2 mg/kg). To not activate other reflexes that might affect the CRC during apnea, we cut the vagi and paralyzed (pavulon 0.1 mg/kg) and mechanically ventilated (100% O<sub>2</sub>) the lambs. Breathing was assessed by measuring phrenic nerve (PN) output. The right C5 root of the PN and right SLN were cut and desheathed; the central ends were bathed in mineral oil and placed on bipolar platinum electrodes. PN signal was amplified, filtered, and recorded as an integrated neurogram. We recorded PN activity at four concentrations of halothane (Servo Gas Analyzer) selected in random order. After obtaining a constant end-tidal concentration for 15 min with the lambs ventilated so the PN was inactive, we gradually added CO<sub>2</sub> to the inspired gas. The PaCO<sub>2</sub> at which the PN was activated was considered the CO<sub>2</sub> apneic threshold. When the PN signal became rhythmic, the SLN was stimulated for 5 s (15 Hz, 0.5 msec) via an isolation unit (Grass PSIU6) that delivered a known current; the current required to suppress PN activity for the 5-s stimulus period was considered the SLN apneic threshold. Values are means  $\pm$  SEM.

**Results.** The CO<sub>2</sub> apneic threshold was linearly related to the end-tidal concentration of halothane for newborn ( $r = 0.88$ ,  $p < 0.01$ ) and older ( $r = 0.69$ ,  $p < 0.01$ ) lambs (fig. 1). However, the CO<sub>2</sub> apneic thresholds between 0.1% and 0.7% halothane for newborns were significantly greater than for older lambs (ANOVA,  $p < 0.05$ ). Although the difference at 0.1% was slight ( $49.1 \pm 1.5$  vs.  $42.9 \pm 3.9$  mmHg,  $p < 0.05$ ), the difference at 0.7% was greater ( $83.7 \pm 7.6$  vs.  $65 \pm 6.9$  mmHg,  $p < 0.05$ ). For newborn and older lambs, the SLN apneic threshold varied inversely with end-tidal concentration of halothane (table 1). Relatively higher currents had to be applied to the SLN to suppress PN activity at 0.1% than at 0.7% halothane. At the 4 halothane concentrations, in all newborn lambs, only a low current was required to induce SLN apnea and, in older lambs, low to very high current. MAC, hematocrit, and mean arterial blood pressure did not differ significantly between newborn and older lambs.

**Discussion.** The data suggest that the CRC of newborn lambs is more sensitive to halothane than the CRC of older lambs. Apnea could be induced in newborn lambs with minimal stimulation of the SLN at very low concentrations of halothane. Since aspiration of water droplets into the larynx causes apnea from SLN stimulation, some instances of postanesthetic apnea may arise by this mechanism.<sup>3</sup>

#### References

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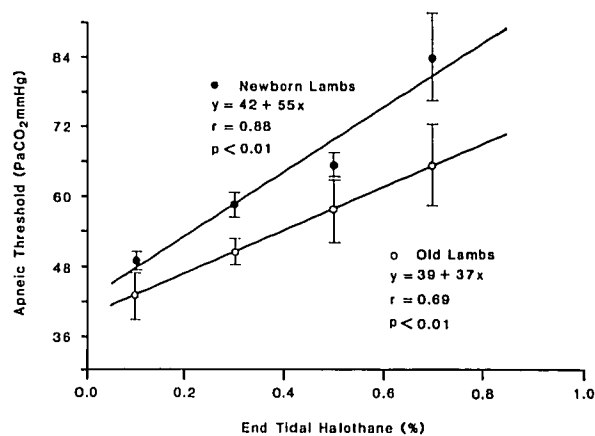


FIG. 1. CO<sub>2</sub> apneic thresholds (PaCO<sub>2</sub> at which the phrenic nerve was activated) at different concentrations of halothane in lambs (old lambs were 27-56 days).

TABLE 1. Superior Laryngeal Nerve (SLN) Apneic Thresholds

Lamb	Lamb Age (days)	Apneic Thresholds ( $\mu$ amps) at Different End-Tidal Halothane Concentrations			
		0.1%	0.3%	0.5%	0.7%
1	6	8*	18	15	7
2	6	150	120	20	10
3	27	12	10	5	5
4	45	200	200	60	50
5	49	>8,000†	>8,000†	>8,000†	3,000
6	56	4,500	2,000	1,000	1,500

\*Current applied to the SLN to inhibit phrenic nerve activity for 5 s.  
†Apnea did not occur at currents > 8,000  $\mu$ amps.