INTRODUCTION: Halothane (V), and isoflurane (I) have been shown by Knill and colleagues [1,2] to depress hypoxic ventilatory response at 0.1 MAC but have no effect on the CO$_2$ response. In humans, the sedative effects of volatile anesthetics on central respiratory drive as measured by P 0.1, phrenic nerve output, diaphragmatic ENG, or effects on the medullary chemoreceptor have not been investigated. There has been little or no investigation in these areas with other drugs which effect respiratory control in man. This is due in large part to the lack of an animal model where invasive procedures can be performed to analyze drug actions in sedated but not anesthetized animals. Smith and colleagues [3,4] have used awake goats to investigate central-peripheral chemoreceptor interactions and exercise effects on ventilation. To be a satisfactory animal model, the goat must have respiratory responses similar to those documented in man at comparable anesthetic concentrations. This study was designed to evaluate the goat as an animal model which could be a substitute for man in respiratory control research.

METHODS: Seven female goats were used. Each had a carotid artery loop placed and were trained to wear a respiratory mask for prolonged periods. All arterial blood gases (ABG) were analyzed using a Corning 178 blood gas machine. Inspired, expired, mixed, and end tidal CO$_2$, O$_2$, and I were continuously analyzed using a mas spectrometer (Perkin Elmer NGA1100). Ventilation was measured using a pneumotachograph and recorded on both polygraph and magnetic tape. Inspired time (T$_i$), expired time (T$_e$), and total breath volume (Vt) were measured directly. Total breath time (Ttot) inspired minute ventilation (Ve), mean inspiratory flow (VT/T$_i$) and T/Ttot were calculated for each breath using a PDP 11/34 computer (DEC). On an experimental day the goat had a control study followed by either 0.23% I or 0.2% V. Identical protocols were used for control and the agent. After placing the mask, the goat was allowed to acclimate to the experimental set-up for 20 min. Goats inspired the anesthetic for 30 min prior to data collection. During the room air control or agent control, breathing was recorded and immediately analyzed for 20 min and 6 ABG performed. During hypocapnic and hypoxic periods, the animal was equilibrated with the inspired gas for 5 min prior to data collection. Four ABG were performed during the 5 min data collection period. The goats were exposed to 5% then 7% inspired CO$_2$ and after a 15 min rest, they were exposed to 12% O$_2$. After a 20 min interval, the CB was stimulated by injecting 1.0 mg NaCN intravenously on 5 separate occasions 5 min apart. The response to NaCN was the mean of the 3 maximum breaths (Ve and Vt) which occurred within 30 to 60 sec after the NaCN injection. Due to variation in size of the goats, the data were expressed as fraction of control values. One way ANOVA and Wilcoxon rank sign test (WRST) was used for statistical analysis and 0.05 considered significant.

RESULTS: There were no significant differences in CO$_2$ slopes between H, RA control or I and RA control using a 1 way ANOVA (Fig. 1). However, all goats increased the CO$_2$ slope with I exposure and decreased the CO$_2$ slope with H exposure (sign wrst). There was no significant change in response to hypoxia or NaCN from the control response either for H or I. Exposure to H or I caused no significant change in Ve/T,$i$, Ve/T,$e$, and Ti/Ttot from their control values. Both hypoxia and hypercarbia caused characteristic changes in Ve/T,$i$, Ve/T,$e$, and Ti/Ttot. During I all 7 goats increased Ve/T,$i$, Ve, Vt, and decreased their f when compared to control values (sign wrst). However, during H sedation all 7 goats decreased Ve/T,$i$, Ti/Ttot, Ve, and Vt while f increased when compared to control (sign wrst).

DISCUSSION: The effect of sedative levels of I and H on the CO$_2$ response of mixed breed goats is similar to that of humans. They did not have significant depression in the CB hypoxic response when tested with P102 of 0.12 or NaCN. Greater inspired I and H concentration may produce more depression. The goat does not appear to have the exquisite sensitivity of man and so may not make a good animal model. However these data found characteristic respiratory drive and volume changes which have not been studied in man at sedative drug concentrations. The goat may make a good animal model for other drugs or higher anesthetic concentrations. More extensive investigation will be necessary to rule out the goat as an awake experimental model for respiratory research.

REFERENCES: