RESPIRATION IN GUINEA PIGS UNDER PENTOBARBITAL SODIUM ANESTHESIA

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MANY authors (1–7) have highlighted the depressant effect of barbiturates upon the adult respiratory center in humans and certain mammals. However, we were unable to find any reference to the action of these drugs on the adult guinea pig. It was pertinent that we obtain such information since we wished to study the influence which these drugs might have upon the offspring of heavily sedated, pregnant, female guinea pigs.

MATERIALS AND METHODS

Using adult female guinea pigs (600–800 Gm.) which were divided into two groups, measurements of respiratory rate, tidal and minute volume were obtained. In group A (table 1), xylocaine was used to place a special tracheal cannula so that control rate and volume measurements could be obtained prior to drug injection. Then, sodium pentobarbital (27 mg./kg.) was administered by heart puncture, and measurement continued at intervals throughout the sleeping and awakening periods. In group B (table 1), the sodium pentobarbital was injected first, tracheal cannulation followed, and measurements were made until a complete set of control values were obtained upon recovery.

To record respiratory rate, a kymograph lever was attached to the skin near the xyphoid process in order to pick up thoracic excursions during the waking state as well as abdominal breathing should respiration become considerably quiet after drug administration.

The special tracheal cannula used in measuring tidal and minute volumes is depicted in figure 1. Its two disc valves allowed for the intake of air at "B" and for its expulsion at "C." These valves, 0.32 centimeter apart, faced each other at the T-shaped junction in the cannula. The horizontal (and longer) arm of the T-tube (with valves removed) had an inside diameter of 1.143 cm. The inside diameter of the shorter, vertical arm was equal to the distance between the disc valves. The vertical arm connected at "D" with a very short length of PE 280 type of catheter for tracheal intubation. The total dead air-space in the system was no more than 0.194 cc., approximately the same dead air-space in the animal itself. The expired gas was collected at orifice "C" and was led by catheter under a 100-ml.

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TABLE 1

RATE AND MINUTE VOLUME IN CANNULATED, UNANESTHETIZED, FEMALE GUINEA PIGS

	Respiratory Rate		Minute Volume	
	Group A	Group B	Group A	Group B
	80	80	191	164
	58	60	284	171
	83	63	207	253
	126	45	418	220
	43	72	196	256
	65		166	
Mean	75.8	64.0	243.7	212.8
(S.E.)[2]	136.7	34.9	1,481.4	383.1
t	0.903		0.738	
P	> 0.30		> 0.40	
Combined mean	70.4		229.6	

graduated cylinder, filled and inverted over water. The amount of water displaced by gas after 20 expirations served in calculating tidal and minute volumes.

RESULTS

The normal respiratory rate, as predetermined in 40 unanesthetized animals, held fairly consistently between 120 and 125 per minute. This rate was always depressed by anesthesia. Figure 2 contrasts the normal respiratory pattern in an unanesthetized, non-cannulated animal with that in the same animal 15 minutes after the injection of sodium pentobarbital. The drop from a normal value of 120 per minute to one of approximately 50 per minute is clearly evident. No noticeable change in depth of respiration occurred in any of these animals, however.

The normal mean value for respiratory rate in 11 cannulated but unanesthetized animals was 70.4 per minute. This value was always

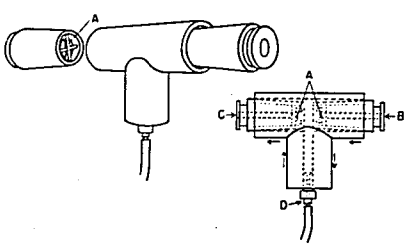

FIG. 1. Diagram of tracheal cannula showing disc valves (A); intake orifice (B); exhaust orifice (C) to be led by catheter under a 100 ml. graduated cylinder over water; and orifice (D) with catheter for tracheal intubation.

lower than that for noncannulated animals. Statistically, the population values for animals in groups A and B (table 1) were homogeneous as far as rate and volume determinations were concerned, and the data could be combined as one group. A subsequent drop in mean rate to 22.2 per minute for the combined groups A and B 30 minutes after anesthesia is shown in table 2. There was a gradual rise from this low level toward normal values over an 8 hour period. The table follows

TABLE 2

MEAN CHANGES IN RESPIRATORY RATE, MINUTE VOLUME AND TIDAL VOLUME WITH TIME AFTER INJECTION OF SODIUM PENTOBARBITAL

Data	Number of Animals	Normal (Unanesthetized) Value	Post Injection Time (minutes)			
			30	60	120	240
Rate	11	70.4	22.2	26.9	33.7	117.6
Minute volume (ml./minute)	11	229.6	70.0	97.1	117.3	171.9
Tidal volume	11	2.82	2.92	3.76	3.76	3.62

this rise for four hours only. Figure 3 shows examples from the record of one animal in the cannulated group indicating a change from an unanesthetized value of 83 breaths per minute to a rate of 48 per minute 15 minutes after drug injection. It should be noted once again that depth of respiration was not noticeably altered.

Table 2 also gives the changes in values for minute and tidal volumes in this group of cannulated animals over a 4 hour period after drug injection. Lowest mean values for minute volume were reached 30

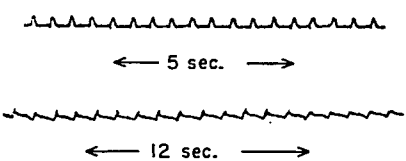

FIG. 2. Kymograph record of respiratory rate before (top) and 15 minutes after (bottom) injection of sodium pentobarbital in the intact, noncannulated, female guinea pig.

minutes after injection in 10 of the 11 animals. In the odd animal it was delayed until 120 minutes. Thereafter, as in the case of respiratory rate, there was a gradual return to normal levels at the end of 6 to 8 hours.

Like depth of respiration, tidal volume values remained relatively static showing no significant change throughout the sleeping and awakening periods of observation.

Discussion

Using rate and minute volume as criteria we are inclined to agree with those authors (1, 6, 7) who maintain that the one consistent action of the barbiturates is the depression of the respiratory center. We have shown a marked decrease in both rate and minute volume with time when 27 mg./kg. of sodium pentobarbital is administered (table 2). Dripps and Dumke (1) indicate that in dogs and cats this depression is greater, the greater the dosage of drug. Patrick and Faulconer (7) confirm this for rate effects in man; they made no volume determinations.

Whether or not a hypoxia develops and whether, in the last analysis, respiratory control is governed by the respiratory center or by chemoreceptor mechanisms under barbiturate narcosis seems to be an unsettled matter. Some investigators (1, 6) contend that indeed, a state of hypoxia and hypercarbia exists, and that breathing under

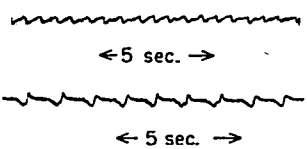

Fig. 3. Kymograph record of respiratory rate before (top) and 15 minutes after (bottom) injection of sodium pentobarbital in the cannulated, female guinea pig.

these conditions is regulated by reflex chemoreceptor mechanisms. Contrary to Moyer and Beecher (6) who did not often find volume changes, Dripps and Dumke (1) maintain that in every shift to chemoreceptor control in deep barbiturate anesthesia there was a decrease in minute volume.

The more recent work of Patrick and Faulconer (7) on human subjects would argue for the integrity of the respiratory center even under fairly deep barbiturate narcosis. They found that oxygen concentration of the arterial blood remained high tending to rule out a condition of hypoxia. Except in very deep anesthesia, Patrick and Faulconer also throw doubt upon the status of hypercarbia. Determinations on CO_2 tension fall within normal range in the human or are only slightly elevated above normal.

Lehman (5) supports the idea of central control of respiration under barbital anesthesia by testing the effect of the drug upon the rhythmic activity of an isolated leaf of diaphragmatic muscle when one phrenic nerve is left intact. By means of such a test, if diaphragmatic activity remains unimpaired after drug injection, it is assumed that the respiratory paralysis is not central in action. Barbi-

tal did reduce the rate and amplitude of the muscle strips indicating central depression.

Our own findings (table 2) indicate that tidal volume was in no way affected by sodium pentobarbital anesthesia. This finding is contrary to what Goodman and Gilman (2) have suggested might be the case. Some of the differences we point out here may very well represent species variation.

Summary

In 40 unanesthetized female guinea pigs (600-800 Gm.) the administration of 27 mg./kg. of sodium pentobarbital by cardiac puncture reduced respiratory rates from a normal mean value of 122 per minute to a mean value of 50 per minute within 15 minutes.

In 11 animals with a special tracheal cannula inserted for the purpose of making minute and tidal volume determinations, respiratory rate under the influence of sodium pentobarbital fell from a normal mean value of 70 per minute to its lowest mean level of 22 per minute within one-half hour of drug administration.

Minute volume likewise decreased drastically over this 30 minute period in cannulated animals while tidal volume remained unchanged.

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