

Results. There was an average fall of 35% in the circulating eosinophils 4 hours after the administration of 0.2 mg epinephrine. In 50% of the observations the fall in eosinophils was greater than 30%. On the whole, a consistent fall in the number of eosinophils was not noted following the administration of 0.2 mg of nor-epinephrine with the exception of two subjects who showed drops of 36% and 31%. (Fig. 1). An average fall of 48.6% in the circulating eosinophils was found after the administration of 0.3 mg of epinephrine. One subject with schistosomiasis and a high initial eosinophil count (418 cells per cu mm) showed no significant change. Following the injection of 0.3 mg nor-epinephrine no significant change in the eosinophile count was found. One patient responded with a drop of 23%. (Fig. 2).

Many of the subjects receiving 0.3 mg of

epinephrine complained of mild palpitation, tremor and tingling. The majority of the patients receiving nor-epinephrine complained of mild pressure headaches and demonstrated a moderate bradycardia.

It was our impression that the 3 patients who, following the administration of nor-epinephrine, responded with a drop in the circulating eosinophils, were all tense, anxious, and emotionally disturbed by the experimental procedure. No other obvious factors were in operation.

Conclusion. (1) Nor-epinephrine (levo) in dosage given (0.2-0.3 mg) produces no consistent change in the number of circulating eosinophils of man.

(2) Nor-epinephrine is probably not a physiologic excitator of the pituitary adrenal system.

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Sex Difference in the Response of Rats to Sodium Pentobarbital.* (17896)

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Considerable difference of opinion has been expressed in the literature concerning the part played by sex in the response of the rat to anesthetic doses of sodium pentobarbital (Nembutal). Thus Barron(1) and Carmichael(2) found this anesthetic equally effective in both sexes, while Holck and Kanan(3) found that males were more resistant to its action. This resistance was confirmed by Moir(4) and Homburger *et al.*(5)

in adult males, but the difference between the sexes disappeared or was actually reversed in immature animals. These reports are based upon "sleeping time" following single doses of sodium pentobarbital given once or repeated upon successive days. In the course of a series of experiments on neuromuscular function, the opportunity arose of examining this problem from a different point of view. The necessity for maintaining deep surgical anesthesia over periods of several hours served to sharpen the contrasting response of the two sexes to the narcotic. The size of the series was sufficient to allow statistical analysis.

The rats used were adults of the Sherman and Whelan strains weighing from 160 to 420 g. They were fed on a diet of Purina

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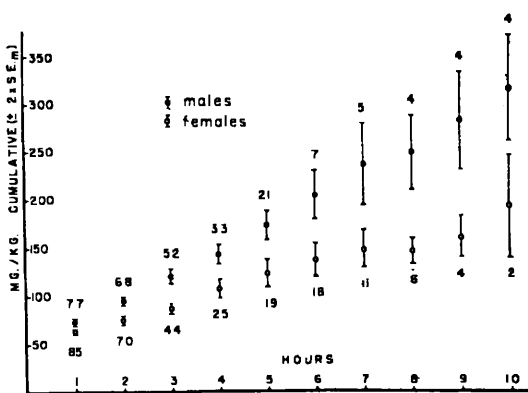


FIG. 1.

pellets with unlimited water intake. Each received an initial intraperitoneal injection of sodium pentobarbital, 50 mg/kg freshly prepared in 2.5% solution in distilled water. Tracheotomy was performed and, in most instances, one hind leg was prepared for the recording of muscle twitches or action potentials. Since skin incisions and nerve sections were required, a deep stage of surgical anesthesia was maintained. Depth of narcosis was gauged at frequent intervals by pinching the animal's tail with forceps. If there occurred a sharp expiratory movement, consisting of explosive contraction of both abdominal and chest walls, a supplementary intraperitoneal injection of 2.5 to 7.5 mg was given. With this schedule it was possible to maintain relatively even anesthesia over prolonged periods.

It soon became evident that males required noticeably larger total doses, *i.e.* more frequent injections, if the desired depth was to be smoothly maintained. The results are presented graphically in the figure. Each point represents the average of cumulative doses at the end of the hour indicated by the abscissa, zero being the time of the original injection of anesthetic. The vertical bars represent twice the standard error of the mean. The figures above and below these symbols are the numbers of animals of each sex in each hourly group. The series decreases in size with time because of the termination of the neuromuscular experiments from which the anesthesia figures were derived. Despite the small numbers available

in the later hours, the difference between the two sexes continues to show high statistical significance. An attempt was also made to rule out unconscious weighting of the curves. Three male and 3 female animals were dressed in cloth bags in a manner effectively concealing their sex from the experimenter. Observations were then made simultaneously on the group. The difference between the sexes noted in the larger series was again apparent. It is also noteworthy that over half of the total series was accumulated before attention was directed to the observation here reported. Since the average adult male rat is considerably heavier than the female of comparable age, the results were also analyzed according to weight. Spot diagrams showed no correlation between weight and utilization of the drug.

No attempt has been made to explain this difference in anesthetic response of the 2 sexes. The studies of others have demonstrated that castrated males tend toward the female sensitivity to sodium pentobarbital, and that this effect may be at least partially reversed with androgens(6,7). It has also been noted that sex difference is demonstrable only with certain barbiturates, and that these are all short-acting drugs detoxified in the liver(7). Since the curves presented herewith are very nearly straight lines with a common origin at 50 mg/kg, it appears likely that the initial anesthetic process is similar for all adult rats, but that detoxification of the narcotic proceeds at a constant but different rate in each sex.

Conclusions. Adult male rats require significantly larger amounts of sodium pentobarbital than do females for the maintenance of deep surgical anesthesia.

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