

THE EFFECT OF 5-HYDROXYTRYPTAMINE ON THE UTERUS OF CONSCIOUS AND OF ANAESTHETIZED DOGS

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The following observations were made on the response of the uterus of the dog to 5-hydroxytryptamine (5-HT) in order that it might be possible to compare the minimum dose to which this organ reacts with the minimum effective dose for the ureter, the kidney, and the systemic blood pressure, in the same species.

METHODS

Observations were made on conscious and anaesthetized bitches. The former were ovariectomized and provided with a fistula of one uterine horn; the spontaneous and induced movements of the uterus were recorded by means of a balloon inserted into the lumen. The method has previously been described (Abrahams and Pickford, 1954). Four dogs were observed under anaesthesia which was induced by the intravenous administration of 0.1 g./kg. chloralose in 0.9% NaCl solution. For 7 to 10 days before observation the dogs received 0.25 to 0.5 mg. stilboestrol dipropionate in oil (British Drug Houses preparation) given subcutaneously on alternate days. Two of the 4 animals were subjected to a preliminary operation 2 days before the experiment. One uterine horn was exteriorized so that its movements could be recorded by means of a balloon, as in the conscious dogs. In the other 2 dogs the preliminary operation was omitted, and, instead, uterine contractions were recorded by tying a thread to the upper end of one uterine horn and passing it over pulleys to a lever writing on a kymograph. The lower end of the uterus was fixed by gripping the cervix in volsellum forceps passed up the vagina, the forceps then being clamped to a stand. The abdominal incision was closed round a wide glass tube filled with warm paraffin which guarded the uterine horn and its attached thread. Unless otherwise stated all injections were made into the malleolar vein. 5-HT was administered in the form of the creatinine sulphate dissolved in 0.9% NaCl solution. All doses are calculated and given as μ g. base/kg. body weight.

RESULTS

Conscious Dogs.—Observations were made on 3 dogs, whose uteri all showed regular spontaneous contractions. In all 3 the uterus gave the same

type of response to an intravenous injection of 5-HT, namely, a contraction which was usually larger than the spontaneous ones, followed by a period of quiescence during which spontaneous contractions were suppressed and tone sometimes diminished (Fig. 1). The minimum effective dose was less than 1 μ g./kg.; 17 μ g./kg. was a supra-maximal dose, since the contraction induced was no larger, nor the inhibition longer in duration, than after the injection of 10 μ g./kg. The longest observed period of inhibition was 7 min.

Anaesthetized Dogs.—In all 4 animals, regardless of the recording system used, the response to

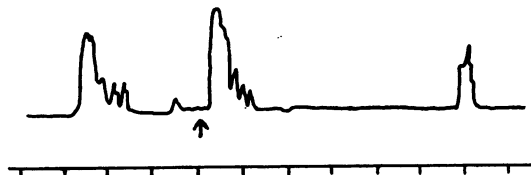


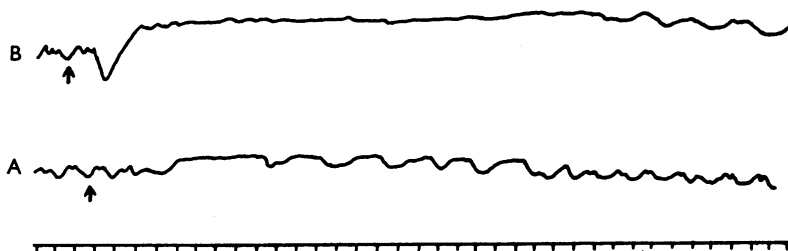
FIG. 1.—Tracing from record of uterine contractions in conscious dog. Effect of 1.4 μ g./kg. 5-HT intravenously at arrow. Upward movement indicates contraction. Upper line, uterine contractions. Lower line, time in 50 sec.

the intravenous injection of 5-HT was the same as that of the conscious dog, with the addition that a loss of tone was apparent (Fig. 2). The minimum effective dose in 3 dogs was less than 1 μ g./kg., and in one was 0.45 μ g./kg. The effect of intravenous and intracarotid injections was compared. An intravenous dose of 3 μ g./kg. caused a contraction, followed by an inhibition lasting 5.5 min. The same dose given into the carotid artery caused a contraction followed by an inhibition lasting 2 min.

DISCUSSION

These experiments show that the uterus of the dog, when *in situ*, is highly sensitive to 5-HT and responds to the intravenous injection of 1 μ g./kg., or even less, by a contraction, followed by some minutes' inhibition. No tachyphylaxis was shown

FIG. 2.—Tracing from record of uterine contractions in anaesthetized dog. Effect of intravenous administration of 5-HT. Downward movement indicates contraction. Upper two lines, uterine contractions. Lowest line, time in 10 sec. In A, 0.45 μ g./kg. 5-HT at arrow; in B, 2.5 μ g./kg. 5-HT at arrow.



to injections given repeatedly at 10 to 15 min. intervals. The action of 5-HT appears to be wholly peripheral, since intravenous injections were more effective than intracarotid ones, and the results were the same whether or not the dog was anaesthetized. The response of the uterus differs from that of the ureter, since, in the latter, there was no sign of any inhibitory phase following the contraction of the muscle (Abrahams and Pickford, 1956a). It is clear that the uterus of the dog is more sensitive to intravenous injections of 5-HT than is the ureter, kidney or general blood pressure (Abrahams and Pickford, 1956a and b).

SUMMARY

1. The effect of 5-HT on the uterus of dogs was observed, both in conscious animals and in those anaesthetized with chloralose.

2. In response to an intravenous injection of 5-HT the uterus gave a contraction which was often greater than those occurring spontaneously. This was followed by a period of inhibition which might last for as long as 7 min.

3. In all dogs tested the minimum effective intravenous dose was less than 1 μ g./kg. In one dog it was 0.45 μ g./kg.

We wish to record our gratitude to the Upjohn Company for a gift of 5-HT.

REFERENCES

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