

Pharmacological Action of Morphine on the Red Fox, *Vulpes fulva*

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Since the isolation of morphine from opium by Sertürner (1) its effects on various animals and on isolated organs have been studied by many. Probably no other drug has been so widely investigated. Even Claude Bernard (2) investigated its effects on the cat, rabbit, rat, guinea pig, dog, pigeon, and frog. He came to the conclusion that its action was similar on all of these species with "due allowance being made for the sensibility of the animals operated upon." Thus he failed to notice its excitatory effect on cats and its diphasic action on animals in general. The only animals showing no pharmacological reactions to morphine are the invertebrates. The excellent comprehensive summary of the works on the opium alkaloids by Krueger, Eddy, and Sumwalt (3, 4) give no reference to the effects of morphine on the fox. At least fifteen species of mammals other than man have been used. Foxes in some behavior characteristics resemble both dog and cat and because morphine affects those species in essentially opposite ways we thought it interesting to determine the pharmacological response of the fox to morphine.

Morphine exhibits a diphasic action being depressant as well as stimulant. The degree of depression is presumably proportional to the degree of cerebral organization and therefore man shows the highest degree of depression while animals lower than the primates, monkeys, and dog exhibit primarily excitatory effects. In general it depresses the cerebral cortex and stimulates the cord. The Straub mouse-tail reaction (5) is typically characteristic of the stimulant action of morphine.

Dogs show an initial depression followed by increased reflex excitability of the cord. The usual dosage for dogs is 10 mg. per kilo which produces light sleep and muscular relaxation and facilitates inhalation anesthesia.

Cats show excitement to morphine becoming convulsive when frightened. No depression is apparent although Guinard (6) has stated that morphinized cats are more susceptible to chloroform narcosis than are non-morphinized ones.

A summary of the species effects of morphine on various animals can be made as follows:

A. Those showing primarily depression: man, chimpanzee, monkeys, dog.

B. Those showing primarily stimulation: frog, mouse, rat, guinea-pig, rabbit, horse, ass, sheep, goat, pig, cat, lion, tiger, panther, bear, marmot, hedgehog.

Birds (chicken, duck, sparrow, and pigeon) are relatively insensitive to it. With small doses they are depressed, with larger doses excited. It

should be pointed out that the above classification is questionable because of the possibility of the existence of two doses, one causing primarily stimulation and the other depression. This has been aptly demonstrated by Tatum, Seevers, and Collins (7) for the monkey, *Macacus rhesus*, for which there are two lethal doses, one causing death by depression, the other by convulsion.

Experimental: Two adult red foxes, *Vulpes fulva*, one of which had been ovariectomized some months previously, were each injected with 32 mgm. of morphine sulphate intramuscularly. Both of these animals had become quite wild and were handled with a snare at the end of a long brass tube. The morphine effects became apparent in about 10 minutes and are shown in the following protocol:

10-15 minutes: loss of hind leg coordination, ataxia, excessive salivation, tongue extended beyond front teeth even while mouth was kept closed in jaw spasm, muscular tone increased, no evidence of atonia of legs or abdomen.

15-30 minutes: head sagged as foxes lay in crouching position, poor coordination in balancing on board 4 inches wide above ground, easily handled with no attempt to bite or struggle.

60 minutes: tongue excessively dry, evidence of beginning recovery, some ambulatory activity.

360 minutes: hyperirritable but still psychically depressed, good auditory acuity, hyperesthetic to sounds such as snapping of the fingers.

Thus the fox shows both psychic depression and hypertonicity. Early ptialism is followed by antisialogogic action. Muscle tonus is exaggerated simultaneously with a tendency toward narcolepsy. Morphine causes less depression in the fox than in the dog for equal doses per unit of weight or in other words the fox falls lower in the scale than the dog to morphine but not as low as the cat.

Conclusions

Morphine causes psychic depression and spinal hypertonicity in the red fox, *Vulpes fulva*. Depression is less in the fox than in the dog where spinal excitability is greater putting the fox lower than the dog but higher than the cat in the morphine series.

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