TRANSIENT HYPOTENSION IN THE CAT INDUCED BY GALLAMINE*

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While investigating certain aspects of the neuromuscular blocking properties of gallamine in cats it was observed that in some animals the intravenous injection of small quantities of the drug was followed by a transient hypotension. As any activity displayed by a drug in the experimental animal may also reveal itself in clinical practice (Paton, 1959) it seemed desirable to examine this phenomenon more closely.

In a series of twenty cats hypotension occurred on four occasions. Characteristically the fall in blood pressure was constant for each animal (fig. 1) although the effect varied from cat to cat. The smallest change was a fall of 20 mm Hg, while the largest was over 100 mm. The remaining two dropped by 30 and 50 mm Hg respectively.

In one cat anaesthetized with chloralose it was possible to investigate the hypotensive response in some detail (fig. 1). In this animal a dose of gallamine (0.25 mg/kg) too small to produce any neuromuscular blocking effects was sufficient to lower the blood pressure by 50 mm Hg. On analyzing this response it was found that the HYPOTENSIVE EFFECT OF GALLAMINE

![Hypotensive Effect of Gallamine](image)

Cat, male, 3.4 kg, chloralose. Ant. tibialis contractions in response to indirect stimulation. Blood pressure. Hypotensive effect of gallamine uninfluenced by bilateral vagal section but antagonized by atropine. No effect on neuromuscular blocking action.

*Work done in the Department of Pharmacology, Royal College of Surgeons of England.
blood pressure began to fall within 4 seconds of the injection of gallamine into the external jugular vein and the limit of the response was reached in a further 8 seconds. Recovery began 15 seconds later and was usually complete within 45 seconds of the time of the injection.

Doubling the dose and increasing it tenfold did not enhance the fall in blood pressure. Repeated doses (6) at 2-minute intervals did not modify the response nor did the provision of an interval of 60 minutes between injections. The division of both vagus nerves had little effect on the extent of the blood pressure fall although from figure 1 it is obvious that the recovery time has been prolonged. But when the injection of gallamine was preceded by the administration of intravenous atropine (4 mg) 1 minute beforehand, the hypotensive response was abolished. That this was a true atropine antagonism was shown by the fact that after sufficient time had been allowed for the effects of atropine to wear off gallamine again produced hypotension.

It is perhaps worth noting that despite the marked fall in blood pressure, the pulse rate was relatively slightly altered from 130 beats per minute to 145.

DISCUSSION
When hypotension follows the intravenous injection of a drug several possibilities need to be considered. A central action is not uncommon with many drugs and the possibility of vagal effects should not be ignored. Ganglionic block may be a side effect of certain relaxant drugs and histamine release is common to all of them. Finally, in this group the possibility of an anticholinesterase activity should be examined.

Except under markedly artificial conditions, the possibility of a central action by gallamine is too remote to be considered. The drug is a highly ionized compound containing three quaternary ammonium groups; such substances do not cross the blood-brain barrier and cannot act centrally when given intravenously.

The vagolytic action of gallamine demonstrated by Riker and Wescoe (1951) makes it unlikely that the fall in blood pressure is due to vagal stimulation, and the occurrence of hypotension when gallamine was injected after the division of both vagus nerves confirms this conclusion.

Riker and Wescoe further investigated the action of gallamine on ganglionic transmission and showed that even with doses as high as 10 mg/kg injected intra-arterially into cats there was no depression of transmission across ganglia. They concluded that gallamine cannot be regarded as a ganglionic blocking drug.

While histamine release must always be remembered when considering relaxant drugs, the absence of the typical response to histamine as described by Paton (1959) seems to exclude this possibility in the experiments under discussion.

According to Foldes (1957) all relaxant drugs show some anticholinesterase activity and the fact that the hypotension in this case was antagonized by atropine supports this view. Moreover, the pattern of response is closely similar to that obtained when acetylcholine is injected intravenously into cats in large doses (Payne—unpublished observations).

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REFERENCES
