

Diazepam Anesthesia and Myocardial Contractility

To the Editor:—In the paper by Jones and associates,¹ it was reported that diazepam caused a significant decrease in myocardial contractility in dogs when given in doses of 1 and 2.5 mg/kg; in smaller doses, this effect was not observed. The data were obtained in unanesthetized animals, which makes them especially valuable. However, the interpretation of these results by the authors, in my opinion, is unfounded. They compared the doses of diazepam that caused myocardial depression in experiments on *dogs* with doses used for induction of anesthesia in *man* and stated the following: "In the present study, a similar lack of effect of diazepam on the circulatory system was seen even in doses that exceed the usual induction dose five- to sevenfold." For correct interpretation of the authors' results, two pieces of information are needed that are not provided in the paper.

First, the authors do not provide data regarding the CNS effect of diazepam, although the drug was injected into conscious, chronically instrumented dogs. I examined the effect of diazepam on the conscious dog in a dose corresponding to the maximal doses used by the authors (2 mg/kg) and could not find any anesthetic effect (only profound relaxation of the hind legs). If the authors did not observe an anesthetic effect, the only possible conclusion is that in dogs, diazepam produces a significant decrease in myocardial contractility in doses that are not sufficient to cause anesthesia.

Second, Chai and Wang,² using an open-arch strain gauge in cats, convincingly demonstrated that diazepam, 0.1 mg/kg, causes a reduction of myocardial contractile force by 25 per cent ($P < 0.01$). Thus, two species, dogs and cats, seem to have quite different sensitivities to the cardiodepressant effect of diazepam. The decrease of contractility in cats occurs at a dose (mg/kg basis) even smaller than the doses used for induction of anesthesia in man. I doubt that it is justified to draw conclusions from such dose comparisons using a CNS effective dose of diazepam in man versus its cardiovascular effect in the dog (or in the cat).

The authors interpret their data as if diazepam has no cardiodepressant effect in anesthetic doses, in accordance with the common belief that in man this drug produces less circulatory depression than other anes-

thetics, thiopental in particular. Recently, a well-controlled study of relative potencies of various intravenous anesthetics in man was performed by Stella and associates,³ who used the patients' inability to open their eyes on command as a criterion of unconsciousness. According to their study, the doses necessary to produce unconsciousness in 95 per cent of patients were 0.5 mg/kg for diazepam and 2.6 mg/kg for thiopental (diazepam-to-thiopental ratio 1:5.2). Clinical data with regard to the cardiovascular effects of diazepam and thiopental have been obtained at significantly lower diazepam-to-thiopental ratios of 1:20–1:10. Despite this, some investigators^{4,5} could not find significant differences in the effects of thiopental and diazepam on blood pressure. It is possible that diazepam, due to its unique spectrum of CNS actions (especially the ability to cause anterograde amnesia), may be used to induce a very superficial level of anesthesia, which is not possible with thiopental. This might explain the discrepancy between the results in animal experiments and the present status of diazepam as an agent for induction of anesthesia without significant cardiovascular depression.

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