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Pressor and Other Effects of Antipyretics on Digitalis Action.

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The present investigation is concerned with the influence of antipyretics on digitalis. The antipyretics investigated were: the salicylates, acetanilid, phenacetin, aminopyrine, aspirin and antipyrine.

Dogs are quite sensitive and uniform in their reaction to digitalis. The average fatal dose of the tincture of digitalis, injected intravenously at the rate of 0.1 cc. per kilo body weight every 5 minutes, is 1.2 cc. per kilo, when dogs are anesthetized with 35 mg. of pentobarbital per kilo intraperitoneally. In previous work it was shown that high body temperature does not prevent the action of digitalis nor influence its toxicity. The variation from this fatal dose is surprisingly small. Therefore, the effect of the various antipyretics in changing the fatal dose of digitalis was tested.

In this report the point to which we wish to draw attention is the astounding effect on blood pressure which is effected by digitalis after all antipyretics. We select in this case antipyrine as the type.

I. Dog—23.2 kg., female; normal blood pressure 150 mm. Ten equal doses of 10% antipyrine were injected intravenously, making a total dose of 100 mg. per kg. The blood pressure after the antipyrine had been given was 130. At this point, digitalis was started in doses of 0.1 cc. per kg. The pressure rose gradually to 170 after 6 injections of digitalis. At this point the pressure rose sharply to 210, and, after another injection, it went to 300. The pressure was actually higher than this, as our manometer was incapable of recording a higher figure. After one more injection the dog died. The total dose of digitalis was 0.8 cc. per kg., as compared to a normal lethal dose of 1.2 cc. per kg.

This rise in pressure with a decrease in the fatal dose of digitalis was typical of all the antipyretics we have tried so far, when the antipyretic was followed by the digitalis. In cases where the 2 drugs are given simultaneously, the increase in pressure is usually not so marked, though it does occur. Thus, in 2 experiments in which the 2 drugs were given simultaneously (0.1 cc. per kg. of each at each injection), a rise of only 20 mm. was noted. However, the lethal dose in each case was only 7 injections, as compared to

9 in the first case. The amount of antipyrine used was thus less. Only 70 mg. per kg. were injected, as compared to 100 mg. per kg. in the first case.

It may be seen from these data that antipyrine markedly decreases the lethal dose of digitalis. More remarkable, however, is the extreme rise in blood pressure, which we have noted with other antipyretics also. Neither of these drugs alone produces a notable rise.

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Carotid Sinus Pressor Reflexes in Anoxia.*

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Whereas the rôle of the chemoreceptors in the carotid body and aorta for the blood pressure response to oxygen deficient gas mixtures was discussed in the preceding paper[1] the influence of the inhalation of low oxygen on the pressor reflexes will be presented in this paper. Gellhorn[2] reported that in the erect posture the blood pressure, after an initial rise, fell rapidly when the experimental subject inhaled 8% oxygen. Such a fall in blood pressure which readily leads to collapse was not seen when the subject inhaled the same gas mixture while in the recumbent position. These findings were explained by assuming a weakening of the pressor reflexes in anoxia. The following experiments were devised to test the validity of this hypothesis.

1. The influence of a change in posture on the blood pressure in the carotid artery was studied in narcotized dogs which were tilted from the horizontal to the vertical (feet down) position for 20 seconds. In a typical experiment the blood pressure fell about 40 mm. Hg. Hereafter 7% oxygen was inhaled and the same test was repeated. The fall of blood pressure increased to 70 mm. Hg.

* The experiments will be published *in extenso* in a monograph published by the University of Illinois Press.

† Aided by a grant from the Graduate School of the University of Illinois to E. Gellhorn.

1 Lambert, E., and Gellhorn, E., PROC. SOC. EXP. BIOL. AND MED., 1938, **38**, 427.

2 Gellhorn, E., *Arch. Int. Med.*, 1937, **10**, 1267.