peared to be altered or prevented by pretreatment with the ataraxic agents chlorpromazine, reserpine, and azacyclonol.

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## Similarity of Effect of "Adrenalin", Adrenaline and Nor-Adrenaline on the Cat Denervated Heart.* (22486)

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In view of the current interest in and conflict of evidence as to possible similarity or difference in action of adrenaline and noradrenaline, these have been tested as to their effect on the acutely surgically denervated heart of the cat. This report describes the chronotropic effect of extracted glandular adrenaline and of synthesized l-adrenaline and l-nor-adrenaline on this preparation.

*Methods.* Fasted cats, males and females, were anesthetized with Dial-Urethane (Ciba), 0.6 cc/kilo of body weight injected intraperitoneally. The heart was denervated by vagal section and removal of the stellate ganglia as first described by Levy(1); blood pressure and heart rate were recorded by mercury manometer from the left carotid artery; injec-

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TABLE I. Summary of Observations on All Animals Studied.

| Dose level (μg/kg/min.) | "Adrenalin" | | | | Adrenaline | | | | Nor-adrenaline | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | No. observations | Avg total change* | S.D.† | S.E.M.‡ | No. observations | Avg total change | S.D. | S.E.M. | No. observations | Avg total change | S.D. | S.E.M. |
| .25 | | | | | | | | | 10 | 51 | 30 | 9 |
| .5 | 29 | 111 | 52 | 10 | | | | | 7 | 117 | 43 | 16 |
| 1.0 | 30 | 193 | 63 | 11 | 17 | 266 | 120 | 29 | 10 | 177 | 81 | 26 |
| 1.5 | 31 | 279 | 74 | 13 | | | | | | | | |
| 2.0 | 30 | 338 | 100 | 18 | | | | | 9 | 289 | 141 | 47 |
| 2.5 | 29 | 361 | 87 | 16 | | | | | | | | |
| 3.0 | 28 | 390 | 131 | 25 | 16 | 430 | 140 | 37 | 8 | 396 | 216 | 76 |
| 6.0 | 31 | 573 | 106 | 19 | 20 | 569 | 154 | 34 | 6 | 481 | 249 | 102 |

* Avg total change in No. of heart beats for 10 min. test period. † Stand. dev. ‡ Stand. error of mean.

tion was by way of a cannula in the right saphenous vein. *Adrenaline* and *nor-adrenaline* were tested in the following preparations: (1) gland extract as commercial Adrenalin Chloride of Parke, Davis and Co. which will be referred to as "Adrenalin"; (2) synthesized l-adrenaline, the l-epinephrine d-bitartrate, control no. R-041-EK of Sterling-Winthrop Research Institute which will be referred to as adrenaline; and (3) l-nor-adrenaline, Levophed, l-arterenol d-bitartrate monohydrate of Winthrop-Stearns Inc. which will be called nor-adrenaline. Injections of freshly prepared solutions were given at a constant rate of 1 cc per minute for 5 minutes. A preinjection record was obtained just prior to each infusion with subsequent records taken of the last 10 seconds of each minute during the injection and of each of the 5 minutes immediately following injection. Not less than 25 minutes were allowed between each infusion. Doses were calculated as micrograms of base substance per kilo of body weight per cc injected per minute, the dilutions being made in isotonic saline solution. "Adrenalin" response was taken more or less as the general frame of reference for comparison and consequently was tested over a more complete dosage range than the other 2, as is shown in Table I which gives the doses used for each drug expressed as micrograms per kilo of body weight per cc injected.

*Results.* Table I also gives the total chronotropic change for the 10-minute period including the 5 minutes of injection and the subsequent 5 minutes recovery. It may be said that the effects during the 5-minute injection period only are, of course, of less magnitude but of exactly similar relative value. The response of the denervated heart of the cat to these 3 preparations is remarkably similar (Table I and Fig. 1). This is especially true within the physiological range between 0.25 and 3.00 μg per kilo per minute and at this latter dosage, presumably about the upper limit of the secretatory capacity of the adrenal medulla for sympathomimetic amines the similarity is complete (Fig. 2).

*Discussion.* When Goldenberg, *et al.*(2) studied the hemodynamic response to adren-

aline and nor-adrenaline in man, they claimed the 2 substances had opposite effects. Adrenaline acted as an over-all vasodilator and a powerful cardiac stimulant, increasing the rate and output while nor-adrenaline was an intense vasoconstrictor, slowing the heart and decreasing the cardiac output. This implies distinct qualitative differences not previously observed. There has been considerable reiteration of these findings by other investigators (3,4,5) and the suggestion is made that vagal inhibition is more readily responsive to nor-adrenaline since the bradycardia is abolished by atropine(2). Also, Lands and Howard say(6) nor-adrenaline is twice as effective as adrenaline in increasing the rate and amplitude of the perfused rabbit heart. On the other hand, Wakim and Essex(7) in a rather thorough comparison of adrenaline and nor-adrenaline effects in the dog maintain the cardiovascular responses to either agent are indistinguishable from one another. And a later study of isolated perfused hearts of rabbits, guinea pigs and dogs shows identical effects of adrenaline and nor-adrenaline on circulation through the heart with marked acceleration in all cases(8).

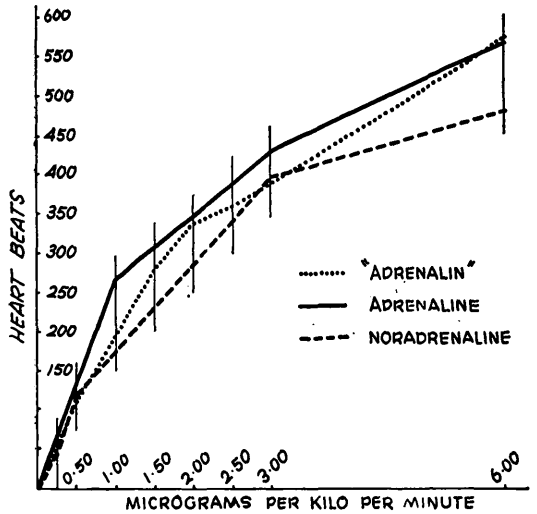


FIG. 1. Avg increase in heart beats over 10 min. period (5 min. injection and 5 min. recovery) at various dose levels of "adrenalin," adrenaline and nor-adrenaline.

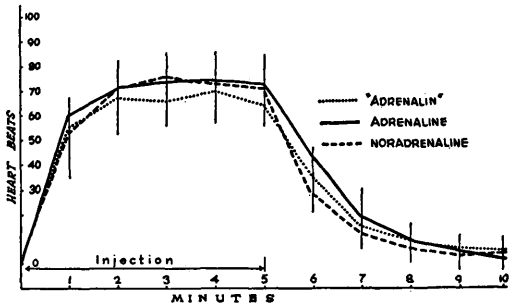


FIG. 2. Avg change in heart rate for each min. over 10 min. period at dose level of 3.00 μg per kilo per min. for 5 min. for "adrenalin," adrenaline and nor-adrenaline.

The results obtained here are in agreement with the above and with the views of others (9) who find that adrenaline and nor-adrenaline affect the excitability of the heart in a quantitatively and qualitatively similar manner.

*Summary.* No difference can be seen in the quantitative responses of the acutely surgically denervated heart of the cat to "Adrenalin," adrenaline or nor-adrenaline.

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