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Cardiac Catecholamines in Rabbits: Seasonal Changes and Norepinephrine Effect

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ABSTRACT

In an attempt to determine whether myocardial catecholamines vary from season to season, their concentration in rabbits was measured throughout the whole year by the spectrophotofluorometric method. The highest concentration of cardiac catecholamine was observed in summer.

Measurement of the atrial response to norepinephrine revealed no significant alteration during the entire period of the experiment.

INTRODUCTION

It is well established that catecholamines are normally stored within the cells of the sympathetic nervous tissues in the myocardium and that the store of catecholamines in this tissue is involved in maintaining normal cardiac function (Axelrod et al. 1959; Lee and Shideman, 1959). Furthermore, extensive studies have shown that the catecholamine content of normal hearts or of the adrenal medulla is consistently affected by various factors such as species, age, sex, body weight and environmental temperature (Hökfelt, 1951; Euler et al. 1954 a; Kärki, 1956; Taylor, 1960; Oliver, 1963). Recently, in this laboratory an interesting finding was presented by Lee et al. (1969) who having determined the myocardial catecholamines spectrophotofluorometrically in animals of various species and ages, found that, as the animals progress phylogenetically, larger amounts of catecholamines were present in their hearts, and greater ratio of norepinephrine to epinephrine was also present. As a result of these experiments, the present study was designed to examine the normal level of cardiac catecholamines in rabbits and cardiac sensitivity to norepinephrine as related to change in season.

METHODS

Normal male albino rabbits weighing approximately 2.0 Kg were used in this experiment.

Determination of Catecholamines

The concentration of cardiac catecholamines was determined by the spectrophotofluorometric procedure described by Shore and Olin (1958). The left ventricle was weighed and homogenized in 2 volumes of 0.01 N HCl. A 2 ml sample of the homogenate was transferred to a 35 ml glass-stoppered reaction vessel containing 2 gm of sodium chloride and 20 ml of butanol. The remainder of the procedure did not differ significantly from that described by the above authors.

Preparation of atria

Under ether anesthesia the heart was rapidly removed from the rabbits. Ventricular muscle, connective tissue, fat and blood vessels were excised from the atria which were then suspended in muscle chambers containing 100 ml of modified Tyrode's solution, pH 7.4 (Lee and Shideman, 1958), maintained at a constant temperature of 38°C. A mixture of 95 per cent oxygen and 5 per cent carbon dioxide was bubbled through a bathing fluid via a sintered glass plate at the bottom of the chamber. The solution also contained the disodium salt of ethylendiamine tetraacetic acid (EDTA) in a concentration of 10^{-5}M to exclude the effects of any heavy metal contaminants in the bathing fluid (Lee et al., 1965).

The atria were attached to a Grass force displacement transducer (FT .03C) and atrial beats and contractile amplitude were recorded on a Grass model 7 polygraph. A resting tension of 0.8~1.0 gm was placed on each preparation. The magnitude of changes in atrial beats and contractle amplitude were expressed as percent of the maximal response.

RESULTS

Myocardial catecholamines in rabbits at various months

The average concentration of the myocardial catecholamines in each month throughout the year was depicted in Figure 1.

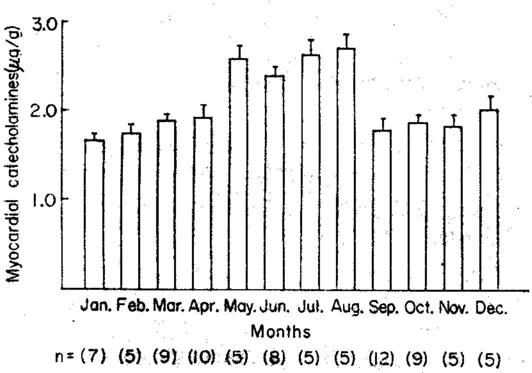

Fig. 1. Myocardial catecholamine content of normal rabbits. n indicates number of experimenths

The level of myocardial catecholamines examined during January averaged 1.60±0.107 µg/g, indicating the lowest monthly value. Subsequently, the concentration of the myocardial catecholamines increased to 1.85±0.140 µg/g in March, abruptly reached a high value ranging from 2.304 to 2.55 µg/g through May to August, and then markedly declined in September. Thereafter it remained relatively constant throughout the remainder of the year.

From these findings, it may be concluded that myocardial catecholamines increase during the summer season (from May to August) and maintain a fairly constant level in the other seasons of the year.

Response to norepinephrine of atria isolated from rabbits at various seasons:

In Figure 2, the positive inotropic and chronotropic responses of the atria to norepinephrine are compared with respect to changes in the seasons. All concentrations of norepinehrine, from 10^{-8}M to 10^{-5}M tested in this experiment, were associated with marked increase in both the heart rate and contractile amplitude. However, a comparison of the responses to norepinephrine revealed no significant monthly change during the whole period of study.

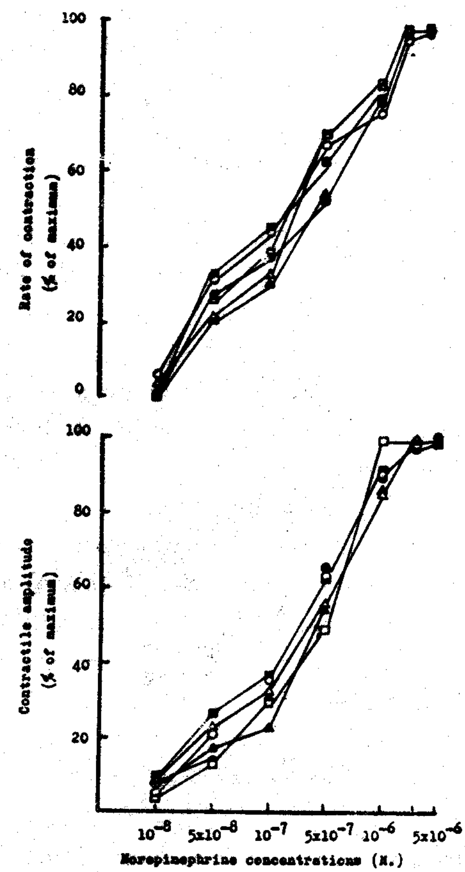

Fig. 2. The concentration-response curves obtained with norepinephrine on isolated atria from normal rabbits. Each point respresenths the mean response of atria obtained from rabbits, during January to February (▲—▲), March to April (○—○), May to June (△—△), July to August (●—●), September to October (■—■), November to December (□—□). Each curve is the mean of 3 to 4 dose-response curves.

DISCUSSION

In recent years, considerable information has become available concerning physiological variations in the excretion of catecholamines. In an extensive study on the urinary excretion of norepinephrine and epinephrine in different age human groups, Kärki (1956) showed that catecholamine excretion was related to the age and body weight of the subject. Subsequently, it was demonstrated that human beings exposed to cold showed an increase in epinephrine and norepinephrine excretion (Arnett and Watts, 1960; David et al. 1966) and that rats exposed to cold of 5°C for 3～5 weeks produced an increased epinephrine and norepinephrine content of adrenal gland (Moore, et al. 1961). In contrast, Herman and Vial (1949) observed a marked decrease in the epinephrine content of adrenal glands in rats placed in a cold room at 2°C for a period of fifteen minutes to two hours.

On the other hand, Raab(1941 a, b), using Shaw's colorimetric method of estimation, reported that the concentrations of adrenalinelike catechols in rat tissues were higher in winter than in summer. A subsequent study of Montagu(1959) demonstrated that the concentration of catecholamines in heart, brain, spleen, kidney, liver, diaphragm and leg muscles of rats were high in winter and summer.

The reports presented by Raab(1941 a, b) and Montagu are at variance with our finding that the concentration of total myocardial catecholamines was highest during the summer but lowest in the winter season. The discrepancy between our and above results may be attributed to the species differences.

Although the seasonal changes in the concentration of catecholamines in cardiac tissues might arise from intrinsic variations in any or all of the various internal factors followed by weathcr changes, the cause of the increase of catecholamines in summer is not adequatly explained. However, the variation of catecholamine content may explain some seasonal metabolic changes. Among these are changes of respiratory quotient (Cori and Cori, 1926), of heat production (Benedict & Macleod, 1929; Sherwood, 1936), of acid production by the gastric mucosa (Mizill, 1955), and of blood lactate (Swan, 1943).

The fact that the response of artia to norepinephrine was fairly constant at a time when the concentration of myocardial catecholamines was significantly changed in relation to seasonal changes, supports the concept that the sensitivity of an organ to norepinephrine is not a function of the amount of norepinephrine found in that organ (Trendelenburg, 1963).

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