Editorial

Catecholamine and Heart Disease

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The sympathoadrenal system is an important mechanism for homeostasis of the internal milieu of the body. The quantitative measurement of catecholamine has presented a new investigative problem concerned in endocrinological research. Recent increasing reports on catecholamine problem have been confirmatory for its significance.

The crude extract obtained by the method of absorption\(^1\) or dialysis using urine, plasma or tissue emulsion would be purified further by means of the chromatography\(^2\)-\(^6\) of the various types. The fluorescence method\(^7\)-\(^9\) is available for determining catecholamine contained in the purified extract because of its sensitivity, its specificity and stability. The precursors and metabolites, besides the active catechols, adrenaline and noradrenaline, have been determined for the diagnostic purposes; DOPA and dopamine\(^10\) as the precursors and metanephrine, normetanephrine\(^11\), VMA\(^12\), DOMA\(^11\) and HVA as the metabolites.

The values of catecholamine in the urine, blood and tissue emulsion have been found as follow, taking into consideration of differences in the figures by the authors. Adrenaline 0.1 µg. and noradrenaline 0.5 µg.\(^14\) are found in the plasma of 1 L. of normal subject. The daily urinary figures in rest are identical with 5 µg. of adrenaline and 20 µg. of noradrenaline.\(^15\) Besides the adrenal glands, the cardiac muscle contains the greatest amount of 1.5 µg./Gm., followed by the aortic wall which has 0.85 µg./Gm. Then, the catecholamine content is reduced in the order of the spleen, cerebral stem, small intestine, liver, kidney and lung.\(^16\) The tissue content of catecholamines are presumably related to the distribution of the sympathetic nerve and uptake of the pressor hormones by the tissue. Myocardial content of catecholamine shows the specie variation. Catecholamine is found to be richer in the auricle than in the ventricle, but no significant high level is found in the sinoauricular node; there was no great difference between the right and left sides of the cardiac chamber.

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Synthesis of catecholamine has been known and its metabolic pathway has been studied. Besides monoaminoxidase (MAO), an attention has recently been called for catechol-o-methyltransferase (COMT). The concept of alpha and beta receptors proposed by Aliquist has promoted a better understanding of physiological action of catecholamine. It has been proved that antiadrenergic drug compete catecholamine with the receptor. Antagonistic effect on sympathetic activity of reserpine, guanethidine, bretylium, MAO and COMT as well as catecholamine release action of tyramine, phenylethylamine, ephedrine, amphetamine and metaraminol have brought various important informations about production, storage, uptake, release, binding with the receptor and degradation. It is reasonably assumed that there are 2 types of catecholamine, namely, available and bound or otherwise, it is possible to suppose the existence of the mobile and storage pool. It is not the bound but the available catecholamine that is released with guanethidine or tyramine and the sympathetic nerve stimulation can release the bound part. The catecholamine released in such a manner shifts toward the receptor sites to combine with them, being hardly affected by the inactivation mechanism. The catecholamine set free from the receptor sites, though a part of it may be taken up to the mobile pool is metabolized or released into the circulating blood. Brodie has postulated that catecholamine is stored by the mechanism of “pump and leak” because catecholamine in the absence of the sympathetic nerve stimulation may passively diffuse from the pool into the cytoplasm where a part of it is affected with MAO and the rest returns to the pools. It is justifiable to think of operation of an active transport mechanism.

Catecholamine has inotropic, chronotropic and calorigenic actions but because of the facts that lowering of myocardial efficiency, causing the vascular changes and eliciting the ischemic electrocardiogram in normal subjects, some authors believe that those with an increased sympathoadrenal activity would often be victims of the ischemic heart disease even without a demonstrable changes of the coronary arteries. Since catecholamine is one of the important factors participating in the homeostatic regulation of hemodynamic, even though Cannon and his coworkers succeeded in survival of the normal animals subjected to sympathoadrenalectomy, in the pathological condition sympathoadrenal activity should bound to participate due to its inotropic effect. In the cardiac failure, anginal seizure and acute myocardial infarction, catecholamine is found to be increased in urine, circulating blood and probably myocardium. Reserpinization, however, induces the reduced cardiac contractility and may cause cardiac failure. The reserpinization may result in lowered tolerance of the animal in the experi-
mental coronary occlusion.\(^{35,39-40}\) It is also suggested that there seemed to be some relation with reference to the efficacy between the cardiac glycoside and myocardial catecholamine.\(^{39,40}\) Considering all these points, positive inotropic action of catecholamine offers a challenging problem. It has been proved that catecholamine promotes formation of a cyclic nucleotide, adenosine-3',5'-phosphate\(^{41,42}\) which stimulates the accumulation of active phosphorylase by converting from inactive type.\(^{43}\) Some authors stated that increased phosphorylase activity in myocardium induced by catecholamine is closely related to its positive inotropic action. Enzymatic activity of the inotropic mechanism of catecholamine has been introduced recently, however, a number of objections\(^{44-46}\) have been presented because of lack of a significant quantitative relation between phosphorylase activity and catecholamine content. This does not necessarily mean that phosphorylase activity should be disregarded in connection with the positive inotropic effect of catecholamine.

**References**