Study on Myocardial Content of Catecholamine, with Special Reference to Heart Disease

TATSUYA TOMOMATSU

DETERMINATION of the urinary excretion of catecholamine has been employed as an index of sympathetic activity, catecholamine content of organs including heart, however, has not been accepted for the clinical use yet, partially because of the hazard. It is really hard to measure the myocardial content of catecholamine, so it is only natural hardly to know the physiological as well as the pathophysiological significance.

Author and his colleagues have challenged measuring the myocardial catecholamine in animals and patients for the purpose of grasping a clue to the solution of the question.

The method used for determining catecholamine in organs was followed by *Crout's* one.¹ The rabbits, rats and dogs were used for determining the normal level of catecholamine in various organs. Twenty-four hour observation on the postmortem changes was made in myocardial catecholamine in rabbits. The rabbits were also used for measurement of myocardial catecholamine for 14 days after ligation of anterior descending branch of the coronary artery. The measurements were applied to other organs like adrenal gland, spleen, lung and kidney. Concerning myocardial catecholamine in man, autopsy was attempted in six cases within three hours after

death and myocardial biopsy was carried out in 21 cases with acquired valvular disease and in 80 cases with congenital heart disease at surgical intervention.

Catecholamine content in various organs such as brain, heart, aorta, lung, liver, kidney, spleen and adrenal gland was presented in Table I. The results obtained were found to be no significant differences among other authors.²⁻⁴ It was the common finding that the content of catecholamine in the heart was the greatest among the varieties of organs but the adrenal gland; namely about 1.50mcg/gm. It is suggestive of importance of the pressor hormone in the myocardium in the physiological sense.

Speaking of distribution of catecholamine in the myocardium catecholamine content was greater in the auricle than in the ventricle. Catecholamine was occasionally found more in the right auricle than in the left, but it was not necessarily consensus of opinion. There was no significant difference between the right and left ventricle. (Table II)

Using the specimens taken at the cardiac surgery, myocardial catecholamine has already been presented.⁴ It is quite difficult, however, to carry out the biopsy to determine catecholamine in the myocardium, and particularly in a healthy person. Attempts have been made to measure the myocardial catecholamine in the patients who were autopsied within three hours after death. As shown in Table III catecholamine was found to be 0.52–1.51 mcg/gm in the au-

Key Words:

Catecholamine
Heart disease
Coronary occlusion

Department of Internal Medicine, Division-1, Kobe University School of Medicine.

* Present on the Symposium 'Catecholamine and Heart Failure' of the 34th Annual Meeting of the Japanese Circulation Society in Kobe, 29 March, 1970

TABLE I

	Rabbit		Rat		Dog	
	by SHORE		by ANTON		by ANTON	
Brain	0.51	0.50		0.15		0.1
Heart	1.50	2.00	1.66	0.3	1.46	1.0
Aorta	0.61	0.85				
Lung	0.18	0.08	0.20	0.02	0.20	
Liver	0.11	0.11	0.13	0.02	0.50	0.3
Kidney	0.24	0.17	0.37	0.1		0.3
Spleen	0.74	0.69		0.5	2.15	1.3
Adrenal G.*	466		717	600		290

* Adrenaline Others; Noradrenaline ($\mu\text{g/g}$)

TABLE II

		Rabbit		Dog	
		by MUSCHÖLL		by ANTON	
Atrium	R	2.14	3.03	3.32	2.7
	L		1.51		2.3
	Septum		1.62		
Ventricle	R	1.25	1.98	1.46	1.4
	L	1.55	1.52		1.3
	Septum		1.59		1.6
	Apex		1.82		1.3

($\mu\text{g/g}$)

TABLE III

Cases	Clinical Diagnosis	Atrium		Ventricle		Papillary Muscle
		R	L	R	L	
1	Mitral Stenoin sufficiency	0.08	0.14	0.51	0.63	0.30
2	Myocardial Infarction				1.80 (0.76)*	
3	Cor Pulmonale	0.12	0.24	0.19	0.35	0.16
4	Pancreas Cancer	0.52	0.76	1.96	1.28	0.80
5	Lung Cancer	1.51	0.78	2.02	1.11	2.00
6	Brain Tumor				1.20	

* Non-infarcted Area

($\mu\text{g/g}$)

ricle, 1.11–2.02 mcg/gm in the papillary muscle in three cases of malignancy. No great differences were demonstrable between the right and left heart, catecholamine content was rather greater in the ventricle than in the auricle. It would be attributable to the postmortem events, the racial difference or the malignant tumor. In one case of myocardial infarction it is worthy of note that catecholamine was reduced but its value was greater in the infarcted area than in the noninfarcted. In the rest of the two cardiacs myocardial catecholamine was reduced in any parts of the heart. In order to follow the postmortem variations of myocardial catecholamine, measurements have been made on the rabbit hearts which were kept in room temperature (about 20°C) for 3, 6, 9, 12, and 24 hours after the

animals were killed. Each groups consisted of three. Catecholamine was seen gradual decrease as shown in Fig. 1 from 1.6 mcg/gm to 1.2 mcg/gm in the left ventricular myocardium in the course of 24 hour observation, but remarkable reduction was found in the atrium between 3 and 9 hours after death, namely, from 2.0 mcg/gm to 1.0 mcg/gm. The change in early 3 hours was least. It is justifiable to consider that there is no great reduction in myocardial catecholamine if the measurement is made within 3 hours after death.

Determination of catecholamine in the specimen taken from the right atrium at cardiac surgery has been made in the acquired and congenital heart disease, demonstrating a significant difference between the two. Catecholamine content was more than 2.0 mcg/gm

Fig. 1. The postmortem decline of catecholamine contents in heart (20°C).

in 61 cases of 80 with congenital heart disease including atrial septal defect, ventricular septal defect, pulmonary stenosis and Tetralogy of Fallot, showing a marked increase particularly in the former two. On the other hand, it was less than 1.0 mcg/gm in 14 cases of 21 with the valvular disease, indicating a considerable decrease. It is interesting to note that the remarkable difference of catecholamine content can be seen in the right atrial muscle between the two groups of the heart disease, although there are no great difference of urinary output of catecholamine. The demonstrable difference may be explicable by the fact that the right auricle is liable to be exposed to the overload in the congenital heart disease in spite of the left auricle subjected to the excess load in the valvular disease.

Catecholamine in myocardial infarction is one of the challenging problem. Although no demonstrable change in the urinary output of

the pressor hormone was seen in the old myocardial infarction without anginal pain it was found to be remarkably increased immediately after acute myocardial infarction; namely, occasional increase of more than 150 mcg/day in noradrenaline and about 40 mcg/day in adrenaline. The urinary output was usually restored to the normal range in one week or two. It took rarely three weeks.

Attention has to be aroused to the postmortem determination of the myocardial catecholamine in one autopsy case of myocardial infarction described previously. In order to know variations in myocardial catecholamine in myocardial infarction catecholamine content has been measured not only in the infarcted area but also in the non-infarcted. The rabbit hearts were used to make measurements on 3, 7, and 14 days after ligating the anterior descending branch of the coronary artery. The myocardial catecholamine was found, as shown in

Fig. 2. Changes of myocardial contents of catecholamine in rabbits with coronary occlusion.

Fig. 2 to be remarkably reduced to 1.35 mcg/gm in the infarcted area, and to 1.10 mcg/gm in the non-infarcted area 6 hours after the coronary ligation. The further diminution followed down to 0.5 mcg/gm in the former on 14th day. In the non-infarcted area the greater reduction was seen within 3 days after the coronary obstruction and followed by restoration to the previous level on 14th day. The results stated above can make it understandable that the myocardial catecholamine was lesser in the non-infarcted area than in the infarcted in the autopsy case with the coronary occlusion.

Catecholamine content of the adrenal gland was remarkably decreased in the first three days and hardly found to restore, if any, in the course of 14 day observation. It would be suggested that catecholamine in the adrenal gland is released almost as much amount as produced for supplementing the myocardial storage which was considerably depleted following myocardial damage. Therefore, the delayed restoration of catecholamine store in the adrenal gland can be considered as an effect of homeostatic mechanism. The hypothesis would be supported by the fact that catecholamine content in the spleen which is not affected by ligating the coronary artery got increased from seventh day of the coronary obstruction, indicating uptake of released catecholamine from the adrenal gland. Another example can be shown for supporting the hypothesis. Replacement of circulating catecholamine with adrenaline takes place associated with inevitable augmentation in urinary excretion of adrenaline together with resultant decrease in noradrenaline when adrenaline is infused at a rate of 5 to 20 mcg/min to healthy persons.⁵⁾ From about it would be reasonable to conclude that the non-infarcted area restores its function by repleting with noradrenaline synthesized in its own tissue to the storage which was depleted of catecholamine for 3 days after the concerning obstruction.

Further example can be taken concerning the regulation mechanism of catecholamine. Myocardial catecholamine was 0.5 mcg/gm on the first day in the newborn rabbits, increasing up to 1.8 mcg/gm in one month. It is suggested that the hearts of the newborn animal are

obliged to release a great deal of amount of⁶⁾ catecholamine to meet the demand provided by the changeable environment after birth. It is questionable whether their hearts can afford the capacity of meeting the demand. On the other hand, the adrenal gland was found to contain an excess amount of catecholamine at birth which was reduced to the normal level in one month. It is reasonable to say that the adrenal gland in newborn rabbit contains sufficient amount of catecholamine, releasing its store to meet the bodily demand with resultant reduction in the first one month after birth, during the period of which the heart can store its own requirement.

CONCLUSION

- 1) Catecholamine content has been measured in the organs using various animals like the rat, rabbit and dog.
- 2) Distribution of catecholamine in the heart has been presented.
- 3) Myocardial content of catecholamine has been demonstrated in 6 autopsy cases in three hours after death.
- 4) It is proved by the experimental study that no great postmortem change in myocardial catecholamine is found in three hours after death.
- 5) Myocardial catecholamine has been discussed in non-infarcted and infarcted area in man and in animal subjected to ligation of the coronary artery.
- 6) Myocardial catecholamine has been demonstrated in the specimen taken from the right atrium of the congenital and acquired heart disease at the cardiac surgery.

REFERENCES

1. CROUT, J. R. CREVELING, C. R. AND UDEN-FIEND, S.: *J. Pharmacol. exp. Therap.* **132**: 269, 1961.
2. SHORE, P. A. et al.: *Nature, Lond.* **181**: 848, 1958.
3. ANTON, A. H. AND SAYRE, D. F.: *J. Pharmacol.* **138**: 360, 1962.
4. MUSCHOLL, E.: *Arch. exper. Path. u. Pharmacol.* **237**: 350, 1959.
5. CHIDSEY, C. A., BRAUNWALD, E. AND MORROW, A. G.: *Amer. J. Med.* **39**: 442, 1965.
6. TOMOMATSU, T. et al.: *Jap. Heart J.* **8**: 242, 1967.
7. TOMOMATSU, T. AND UEBA, Y.: *Jap. J. Geriatr.* **7**: 36, 1970.