Cardiac Hypertrophy in Spontaneously Hypertensive Rats (Further Study)

Hitoshi Tanijiri, M.D., Masakazu Ikeda, M.D., Chujiro Kashii, M.D., and Tadasu Takatsu, M.D.

A chronological observation of the development of cardiac hypertrophy in the spontaneously hypertensive rat (SHR) by the light and electron microscopy and by histochemical methods was reported previously at the 7th annual meeting (1971). In this study further experiments were performed to resolve the question whether the increased activity of $\beta$-hydroxybutiric dehydrogenase ($\beta$-HBDH), which was seen in the myocardium of SHR at the age of 5 to 17 weeks, might participate in the development of hypertrophy or might be present only as a strain-specific character.

An additional chronological observation: Materials and methods were the same as in the last experiment with the exception of the age of rats. While in the last experiment the SHR at the age of 5 to 21 weeks were used, the suckling SHR, at the age of 2 to 4 weeks, and the elder SHR, at the age of 23 weeks and 1 year, were examined in this study. In the suckling rats, at the age of 2 to 4 weeks, no differences were found in the activities of glucose-6-phosphate dehydrogenase (G6PDH), lactic dehydrogenase (LDH), succinic dehydrogenase (SDH), isocitric dehydrogenase (IDH), ATPase and monoamine oxidase (MAO) between SHR and the control rats. The activity of $\beta$-HBDH, which was found to increase significantly in SHR throughout the last experimental period, began to increase in the 4th week after birth. At the age of 23 weeks and 1 year, no differences were found in the activities of all enzymes but MAO between SHR and the controls. The activity of MAO was slightly increased in SHR in those periods. By electron microscopy, no differences were found at the age of 2 weeks between SHR and the control rats. At the age of 1 year, remarkable accumulation and destruction of the mitochondria accompanied with scarcity of the myofibrils were seen in SHR, whereas almost normal structures were maintained in the normal controls. The ratio of area occupied by myofibrils to that occupied by mitochondria decreased down to 0.55 at the age of 1 year.

A chemical assay of the activity of $\beta$-HBDH: To compensate for the drawback of histochemical method, by which a quantification is difficult, a chemical assay was applied for the determination of the activity of $\beta$-HBDH.

From the Third Division, Department of Internal Medicine, Osaka Medical College, Takatsuki.
The heart, removed immediately after decapitation, was homogenized with 0.25 M sucrose. The homogenate was centrifuged for 10 min at 600 × g at −5°C. The supernatant suspension, containing mitochondria, was used for the assay. The activity of β-HBDH was determined by spectrophotometrically following enzymic reduction of NAD by β-hydroxybutyrate. The reaction was monitored by observing the change in absorbancy at 340 mµ in a quartz cuvette, with 1 cm light path. By this method it was found that the activity of β-HBDB in the heart of SHR, at the age of 10 weeks, was 1.5 to 2.0 times as high as that of control rats of the corresponding age.

The effect of the inhibition of the development of hypertension and cardiac hypertrophy on the activity of β-HBDH in the heart of SHR: To evaluate the role of β-HBDH in the development of cardiac hypertrophy the following experiments were undertaken. Two SHR were given drinking water containing antihypertensive agents (reserpine, hydralazine and chlorothiazide) for 2 weeks starting immediately after weaning, while the 2 control litter mates received only tap water without drugs. After the treatment for 2 weeks they were sacrificed, and their hearts were examined histochemically. There found no differences in the activity of β-HBDH between treated and untreated rats, although the blood pressure in the former was lower than that in the latter. Since the period of the experiment was not long enough to evaluate the effect of this treatment, a long term experiment was started and is now in progress.

Discussion and summary: Supplementary experiments to the previous one were performed to complete the chronological observation of the development of cardiac hypertrophy in SHR from birth to the age of 1 year. So far, the increased activity of β-HBDH in SHR seems not to be a genetic strain-specific character, but to be pertinent to the development of its cardiac hypertrophy, because the activity of β-HBDH was not increased in the early suckling SHR, and its increased activity was also seen in the elder control rats.