68) Effects of High-Fat and -Cholesterol Feeding on Lipoprotein and Apolipoprotein Concentrations and Distributions in Old SHRSP. Hiroshi Ogawa, Tomoyo Nishikawa and Sukenari Sasagawa. Department of Hygiene, Kinki University School of Medicine, Osaka-fu 589.

In our previous paper, we reported that age-related increase of serum apo-lipoprotein(apo-) A-I content in SHRSP may be closely related to the elevation of high density lipoprotein(HDL)-cholesterol in old SHRSP. It seems to be of particular interest to evaluate the influence of the elevation of HDL-cholesterol on lipoprotein metabolism in SHRSP which is relatively prone to develop hypercholesterolemia by the feeding of high-fat and -cholesterol diet(HFC diet) in comparison with WKY, since HDL is generally recognized as anti-atherogenic factor. In the present paper, we investigated changes in the concentration and the distribution of serum lipoproteins and apolipoproteins by the feeding of HFC diet in about 8 month-old SHRSP showing nearly the same serum apo A-I content as that in age-matched WKY.

MATERIALS AND METHODS: Male SHRSP at the age of 33 weeks and the age-matched male WKY were used and fed HFC diet prepared as reported previously or laboratory chow(CE-2, Clea Japan Inc.) with food and water available at all times for 7 weeks. Blood pressure was measured by tail-pulse pickup method. Serum was obtained from jugular vein under light ether anesthesia after fasting overnight. Serum various lipoprotein fractions were isolated by ultracentrifugation at various densities(VLDL; $d < 1.006$, IDL; $d: 1.006-1.020$, LDL; $d: 1.020-1.063$ and HDL; $d: 1.063-1.210$). Cholesterol concentration was determined enzymatically, and concentrations of apo A-I, A-IV and E were measured by modified Laurell rocket immunoelectrophoresis. Profile of lipoproteins was examined by 4/30 gradient slab-PAGE and that of apolipoproteins by SDS-8/23 gradient slab-PAGE.

RESULTS AND DISCUSSION: At the age of 33 weeks, serum apo A-I concentrations in WKY and SHRSP were 56.2 ± 2.1 mg/dl and 53.1 ± 1.8 mg/dl ($M \pm SE$) respectively. By the feeding of HFC diet for 7 weeks, neither body weight nor blood pressure were affected significantly in both strains. Serum total cholesterol(TC) in WKY increased about 2.5-fold(275 ± 8 mg/dl vs. 116 ± 11 mg/dl), associated with a remarkable increase in serum apo Bs and a significant increase in serum apo A-I and A-IV. On the other hand, serum TC in SHRSP increased about 3.5-fold(304 ± 21 mg/dl vs. 90 ± 2 mg/dl), associated with a remarkable increase in serum apo Bs, a significant increase in serum apo A-IV and a significant reduction in serum apo E. To investigate further this difference of response between WKY and SHRSP against the feeding of HFC diet, we examined the distributions of cholesterol and apolipoproteins among the isolated various lipoprotein fractions. In VLDL and IDL fractions, a drastic elevation of cholesterol content due to the production of β -VLDL, associated with a remarkable increase in apo Bs and E, was observed in both strains, yet much greater extent in SHRSP than in WKY. In LDL fraction, cholesterol content considerably increased and showed nearly the same level in both strains, nevertheless HDL_c rich in cholesterol and apo E in addition to native LDL were main constituents of LDL fraction in WKY, while only native LDL was main constituent in SHRSP. In HDL fraction, cholesterol content in WKY remained unchanged although some increase in apo A-I and A-IV and a significant decrease in apo E were observed, while that in SHRSP was significantly lowered with a moderate decrease in apo A-I and A-IV and a marked decrease in apo E, but the change in HDL fraction of old SHRSP was not so remarkable as that of adult SHRSP. Consequently, these changes in various lipoprotein fractions were similar to those reported previously(Ogawa et al. Jpn Heart J, 26:674, 1985) and confirmed the accelerated production of β -VLDL, the reduced level of HDL rich in apo E and the significant decrease of HDL fraction in SHRSP fed HFC diet. In addition, the increased level of apo A-I may be effective to some extent for prevention of the decrease of HDL fraction in SHRSP, yet apo E in HDL fraction may play much more important role for development of hypercholesterolemia rather than apo A-I in HDL fraction.