Genetical Analysis of the Stroke in Spontaneously Hypertensive Rats

Akinobu NAGAOKA, Hisashi IWATSUKA, and Ziro SUZUOKI

In 1972, Okamoto and his colleagues segregated the spontaneously hypertensive rats (SHR) into several sublines, some of which had a tendency to develop stroke (Jap Circulat J 36: 461, 1972). Recently, from these sublines "stroke-prone SHR" was established by successive selective inbreeding (Okamoto, Yamori, and Nagaoka: Circulat Res 34-35: Suppl 143, 1974).

A mode of inheritance of stroke or its related pathological changes, cerebral hemorrhage and/or infarction, in SHR was investigated using stroke-prone SHR (A_3), stroke-resistant SHR (C), and their hybrids: hybrid of A_3 and C (F_1), offspring of $F_1 \times F_1$ (F_2), that of $F_1 \times A_3$ ($BC(F_1 \times A_3)$), and that of $F_1 \times C$ ($BC(F_1 \times C)$).

The average blood pressure became higher in the following order: $C < BC(F_1 \times C) < F_2 \div F_1 < BC(F_1 \times A_3) < A_3$. The values of F_2 hybrids ranged from C to A_3 , although the average was similar to that of F_1 . These findings suggest a possibility that polygenic inheritance participates in the blood pressure determination in either A_3 or C, and the difference in the pressure between A_3 and C is accounted for by that in gene concentration. Loading 1% salt solution resulted in increasing the blood pressure level and exaggerating the onset of stroke in all groups of SHR. Under the condition, there was no significant difference in the pressure level among 5 groups except A_3 , the level of which was the highest, but the incidence of stroke became lower in the following order: $A_3 > BC(F_1 \times A_3) > F_2 \div F_1 > BC(F_1 \times C) > C$. The effects of the salt solution were observed in another series of hybrid rats of A_3 and normal Wistar/Kyoto rats (WK). The incidence of stroke even in offspring of back-crossing $F_1(A_3 \times WK)$ to A_3 was lower than that in C. From these findings, the onset of stroke, as well as hypertension, appears to be subjected to polygenic inheritance. However, there is no evidence to indicate that the same genetic factors participate in predisposition to either hypertension or stroke.

From the Biological Research Laboratories, Central Research Division, Takeda Chemical Industries, Ltd., Osaka.