130. *Acatalasemia. III.* *On the Heredity of Acatalasemia.*

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While the relation between enzyme and genetical factor has in the recent years been drawing keen attention as a subject of much debate and discussion, we have fortunately discovered cases of acatalasemia or the absence of catalase ferment in the blood, and have prepared detailed pedigree charts and other data of three families involved. Adding thereto the data of two families reported on by M. Yoshiya of the Tokyo Medico-Dental College, we have looked into the heredity of acatalasemia in the five pedigrees. The enquiry so conducted has resulted in our conclusion that acatalasemia is due to recessive monogenetic inheritance. Below is our report on the data and their study and interpretation. It is our wish that it be commented upon by our interested readers.

Investigation.

Methodical description of the investigation:

Quantitative estimation of catalase in the blood was conducted in our department on 90 members of three involved pedigrees (Nakayama, Fukutake, and Abe) by utilization of Inoue's quantitative estimation method of catalase, together with Stern's method and Warburg's method. Hydrogen peroxide test (direct addition of hydrogen peroxide on the blood) was also carried out. M. Yoshiya had utilized Euler-Josephson's quantitative estimation for catalase in the blood of 17 members of his two pedigrees (Yoshikawa and Kaneko).

In our department, in addition to the quantitative and qualitative estimation for catalase in the blood of the individuals involved, we ascertained their blood type, measured their number of erythrocytes, amount of hemoglobin (Sahli's test), number and percentage of leucocytes, and carried out their peroxidase test. Like individuals with normal blood, the cases of acatalasemia showed nothing abnormal in the results of the above tests.

Results of investigation (pedigree charts):

Below are the pedigree charts of both Yoshikawa and Kaneko families as reported by M. Yoshiya:

In the above five pedigrees, there were marriages between first cousins once removed, between first cousin once removed and first cousin twice removed, and between first cousins twice removed. These crossings are extracted and shown below:

The five pedigrees had nine consanguineous marriages. For the sake of simplicity, these consanguineous marriages are represented in the following observation with ciphers I through IX, in the order of the pedigrees Nakayama, Fukutake, Abe, Yoshikawa, and Kaneko.

Discussion.

The factor contributing to acatalasemia is represented with "Ac", and its allelomorph with "ac". If the factor for acatalasemia should

be dominant or if those with acatalasemia be individuals of genotype $AcAc$ or $Acac$, this supposition would be denied for the following reasoning:

As a crossing that will for its next generation produce an $AcAc$ individual, the parental generation must be of no other combination than $AcAc \times AcAc$, $AcAc \times Acac$, $Acac \times AcAc$, or $Acac \times Acac$. The parents must thus be with acatalasemia. A crossing that will produce an $Acac$ individual for its next generation requires the parental generation to be of no other combination than $AcAc \times Acac$, $Acac \times AcAc$, $Acac \times Acac$, $AcAc \times acac$, $acac \times AcAc$, $Acac \times acac$, or $acac \times Acac$. This means at least one of the parents must be with acatalasemia.

Of the five marriages with acatalasemia in the pedigree charts, parental investigation could be carried out on three of them, I, VIII, and IX where the parents were alive and available for examination. Of these three, there was not even a single parent with acatalasemia. This led to a conclusion that acatalasemia is not a dominant inheritance.

It consequently follows that acatalasemia must be ascribed to recessive factor; and, for that matter, the genotype of this disease is limited to recessive homozygosis of $acac$. A crossing in a parental generation that will produce an $acac$ individual for its next generation is limited to $acac \times acac$, $Acac \times acac$, $acac \times Acac$, or $Acac \times Acac$. From the fact that there was no acatalasemia present in any of the parents of the marriages I, VIII, and IX, we can rule out the possibility of $acac \times acac$, $Acac \times acac$, or $acac \times Acac$. And the pedigree charts of these can be accounted for only when the parents are of an $Acac \times Acac$ combination.

Let us then study whether or not the inheritance of acatalasemia is of monogenic type. Excluding 4 individuals unavailable for examination because of death (3 individuals) or other reasons (1 individual), 27 brothers and sisters of acatalasemia cases (including acatalasemia cases) in these five families were examined. Thirteen of them were found with acatalasemia and 14 had the normal blood. On the basis of these findings, let us here regard acatalasemia as of recessive monogenetic inheritance. Then the proportion of $acac$ appearing in crossings $Acac \times Acac$ is one-quarter, and its test of goodness of fit (X^2 -test) shows $X^2=7.71$. This value, according to the X^2 table, is of lower probability than 0.01 (probability would be 0.01 if $X^2=6.63$). This is a deviation which is statistically significant. It means that something else than an incidental cause must be regarded to be responsible for that deviation. Conceivable as thus responsible is that the number of cases available was rather too small and also that among such marriages as IV and V where the father had died

and was therefore unavailable for examination, there may possibly have been crossings of $Acac \times acac$ type. So long as the observation ratio is 14:13, the expectation ratio may be regraded to be 1:1. X^2 test on the basis of this expectation ratio gave X^2 value as 0.037 and probability over 0.7 (probability would be 0.7 if $X^2=0.15$). This value of the X^2 test obviously satisfies the segregation ratio 1:1. If crossings contributory to the segregation ratio of 1:1 in recessive monogenetic inheritance are present, then $Acac \times acac$ and $acac \times Acac$ are possible. These crossings are obviously one of various forms of recessive monogenetic inheritance. If they were to be regarded as polygenetic inheritance, the expectation ratio of the appearance of acatalasemia would theoretically be smaller than 3:1. Within the scope of the data so far available, we may rightly conclude, as already stated, that the heredity of acatalasemia comes from recessive monogenetic inheritance.

While the mother of the marriage VI was $acac$, the father had an $Acac$ aunt, which latter fact means a possibility for an $Acac$ genotype. If the father be $Acac$, $acac$ may appear in their children at the rate of one-half. Children who may be born of the marriage VI have a possibility of developing acatalasemia and further observation on the new born children should be followed with great interest.

Conclusion.

On the basis of the detailed pedigree charts prepared on five families (including two reported by Yoshiya) wherein acatalasemia was detected, we examined the kin for lack of catalase in the blood. There were some unavailable because of death or other reasons; therefore, we could examine only 27 individuals (including acatalasemia cases) all of whom were brothers and sisters of acatalasemia cases. Thirteen of these 27 were acatalasemia cases. On the basis of these findings, we consider that acatalasemia is due to recessive monogenetic inheritance.

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References.

- 1) S. Takahara: Proc. Japan Acad., **27**, No. 6, 1951.
- 2) S. Takahara, S. Mihara, K. Tsugawa, and M. Doi: Proc. Japan Acad., **28**, No. 7, 1952.
- 3) S. Takahara: Okayama Igakukai Zasshi, **63**, No. 1, 1951.
- 4) S. Takahara and H. Miyamoto: Jibinkoka, **21**, No. 2, 1949.
- 5) H. Sato, M. Doi, S. Mihara, K. Tsugawa, and Y. Ogura: Acta Haematologica Japonica, **15**, No. 4, 1952.
- 6) H. Nakamura, M. Yoshiya, K. Kaziro, and G. Kikuchi: Proc. Japan Acad., **28**, No. 1, 1952.
- 7) K. Yoshiya: Kōkubyō Gakkai Zasshi, **19**, No. 1, 1952.