Carrier State in Human Acatalasemia

Abstract. The heterozygous carrier state of a rare hereditary disease, acatalasemia, has been defined biochemically. Affected homozygotes have no blood catalase activity, whereas heterozygotes show activities intermediate between this inactivity and the activity of normal controls, without overlap. Pedigrees show a high frequency of consanguineous marriages.

In 1949 Takahara and Miyamoto (*1*) reported four siblings with progressive gangrenous gingivitis in whom catalase activity was not demonstrable in the peripheral blood. In this and subsequent communications (*2–4*), these authors described and elaborated upon the syndrome and coined the term *acatalasemia,* since the level of catalase activity in the tissues other than blood could not be ascertained.

At the time of our preliminary report (*5*), 38 cases of acatalasemia in 17 families had been documented by various investigators in Japan (*6*). In all but three families, two or more siblings were affected. A history of consanguineous marriage was obtained from 16 families. Among the parents of the acatalasemic individuals were ten instances of first-cousin marriages and two marriages involving not only first cousins but additional degrees of relationships as well; three sets of parents were more remotely related, and information on the others was uncertain. Takahara *et al.* (*3*) have suggested that the disorder is transmitted as a monogenetic recessive character; however, in these previous studies the genotypic characteristics were not investigated in the related family members in whom definite catalase activity has been demonstrated.

After review of the levels of catalase activity reported by Takahara (*4*), it occurred to one of us (E. T. N.) that the mean value of blood catalase activity among the positive catalase reactors of the acatalasemia families seemed to be lower than that noted for the control group. This was interpreted to indicate that certain members of the acatalasemia family probably had significantly low levels of catalase activity, while others had higher values, comparable to the control series.

To investigate this possibility (*7*), heparinized blood samples were obtained from five families previously studied by the Okayama University group. A modification of the method used by Herbert (*8*) was employed for the determination of blood catalase activity. The activity, which is expressed as the reaction velocity constant $K_{cat.}$ ($K_1 \times 10^3$), was determined for randomly selected Japanese subjects in Hiroshima and Nagasaki: the mean value was 5.54 (range, 3.91 to 7.10) in 206 individuals (*9*). In Fig. 1, of the 66 cases of positive catalase reactors in the five acatalasemia families examined, 30 had $K_{cat.}$ values which were definitely below those of the controls: the mean was 2.15 (range, 1.48 to 2.89), and there was no overlap with values for the controls. This phenomenon of low blood catalase activity is referred to below as *hypocatalasemia.* One can, apparently, with this biochemical technique, readily separate the hypocatalasemic from the normal and the acatalasemic states.

As Fig. 2 shows, certain members of the families of acatalasemic subjects are hypocatalasemic while others possess normal blood catalase values. It appears that (i) the parents of acatalasemic children are hypocatalasemic, (ii) the siblings of acatalasemic individuals may be either hypocatalasemic or normal, and (iii) an acatalasemic parent has hypocatalasemic children when mated to a normal individual. The possibility that an acatalasemic-hypocatalasemic parent combination may produce acatalasemic and hypocatalasemic children has not yet been demonstrated. Genetically, the hypocatalasemic state may be thought of as a carrier state for acatalasemia. Sawin and Glick (*10*) have described a similar genetic pattern for the enzyme atropine esterase, in rabbits. They ascribed the difference in the amount of enzyme activity to incomplete dominance—that is, ability to produce the enzyme is dominant over absence of this ability.

The results of the study reported here

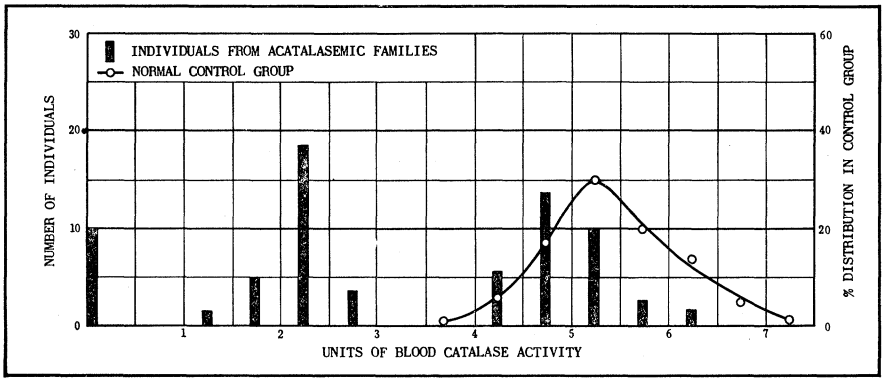

Fig. 1. Distribution of catalase values for members of the five acatalasemia families and comparison with a percentage distribution curve of values from a normal control group.

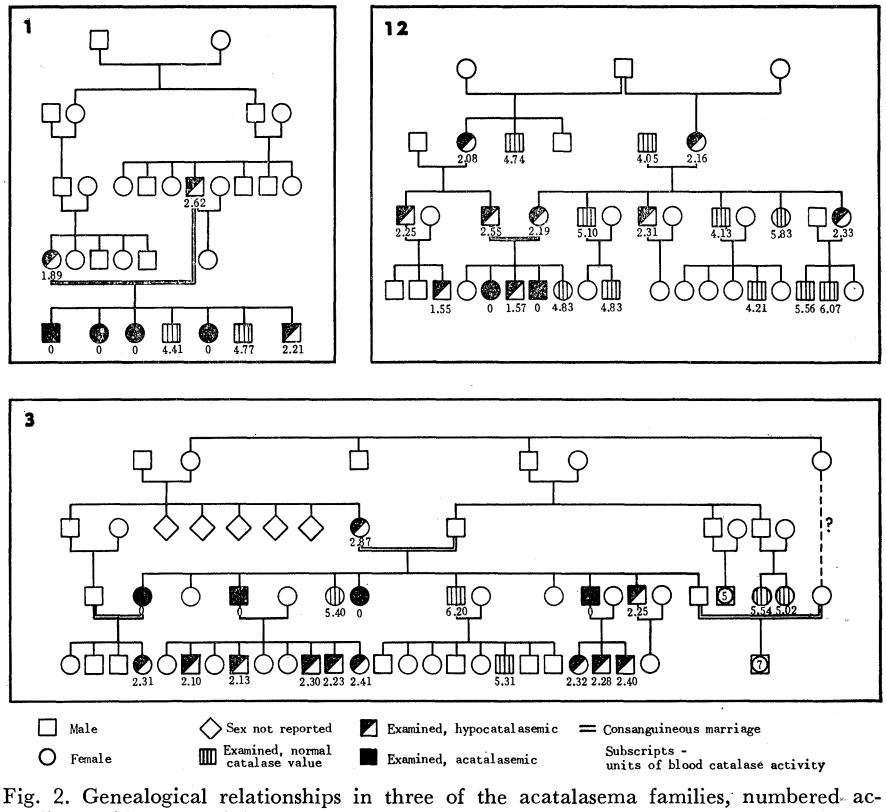

Fig. 2. Genealogical relationships in three of the acatalasema families, numbered according to Takahara (*6*).

resemble the data reported by these investigators and suggest that in this respect the underlying genetic phenomenon may be similar. The exact nature of the defect in acatalasemia is at present not clear.

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6. S. Takahara and K. Doi, *Nihon Jibi Inkoka Gakkai Kaiho (Japan. J. Otolaryngol.)* 61, 1727 (1958) (in Japanese with English summary).
7. These data were collected under the auspices of (i) the Atomic Bomb Casualty Commission, a field research agency of the U.S. National Academy of Sciences–National Research Council, with financial support from the U.S. Atomic Energy Commission, administered in cooperation with the National Institute of Health of the Japanese Ministry of Health and Welfare, and (ii) the Department of Otorhinolaryngology of Okayama University Medical School, Okayama, Japan.
8. D. Herbert in *Methods in Enzymology*, S. P. Colowick and N. O. Kaplan, Eds. (Academic Press, New York, 1955–57), vol. 2, p. 784.
9. Determinations were performed on non-irradiated individuals over 11 years of age.
10. P. B. Sawin and D. Glick, *Proc. Natl. Acad. Sci. U.S.* 29, 55 (1943).

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Presence of Myoglobin in "Cartilage" of the Marine Snail Busycon

Abstract. The odontophore of the snail *Busycon* has been found to contain myoglobin. The red pigment is readily extracted with water, and spectrophotometric analysis shows the characteristic peaks of myoglobin at 575 and 539 mμ. Although the odontophore is considered to be cartilaginous, it contains, not a chondroitin sulfate, but a polyhexose sulfate. This unusual chemical composition may be responsible for the absorption of myoglobin by the odontophore.

The occurrence of myoglobin in the marine snail *Busycon caniculatum* was first noted by Ball and Meyerhof (*1*), who studied the myoglobin and respiratory enzymes of the muscles associated with the radula of this snail. Since the blood pigment of *Busycon* is hemocyanin, it is of interest to note the occurrence of an additional oxygen-carrying pigment. In recent studies on the cartilage-like tissues of some marine invertebrates it was noted that the odontophore (the supporting rod for the radula in the proboscis) of *Busycon* contained a bright red pigment. This pigment was readily extracted with water, and subsequent analysis of the aqueous solution of pigment in a Beckman model DU spectrophotometer proved it to be myoglobin. This solution of pigment gave an α peak at 574 mμ and a β peak at 538 to 539 mμ. These peaks are in agreement with the data of Ball and Meyerhof (*1*) for the muscle myoglobin of *Busycon*.

Myoglobins have a higher oxygen-carrying capacity and are more soluble than hemocyanin. Therefore, myoglobin would probably be a more efficient respiratory pigment in the comparatively active movements of the radular apparatus. The radular musculature is rich in myoglobin, and so is the odontophore, to which the muscles are attached. The fact that the odontophores of young snails do not contain myoglobin and that those of older snails do accumulate the pigment suggests that myoglobin is stored there and is not essential to the metabolism of the tissue.

The odontophores of snails are frequently thought of as being cartilage tissue. With the advent of biochemical analysis, cartilage is currently defined as tissue which contains one or more of the chondroitin sulfates and which, upon hydrolysis, yields a hexosamine (D-galactosamine), a uronic acid, and sulfuric acid. Alkaline extracts of the odontophore extracted with potassium chloride and potassium carbonate (*2*) yielded a material which, upon ionophoresis (borate buffer, *p*H 10.0; potential gradient, 18 v/cm), produced a spot which stained metachromatically with alcoholic thionin (0.15 percent in 65-percent ethanol). This metachromatic material had an ionophoretic mobility (−12.2) slightly greater than that of chondroitin sulfate (−11.8). Pronounced streaking of the material during ionophoresis indicated that the extracted material was badly degraded. On improving the methods of extraction by use of trypsin digestion (*3*), an extract was obtained which gave no indication of being degraded. This extract was strongly metachromatic and had an ionophoretic mobility similar to that of the alkaline extract.

Upon acid hydrolysis (4.0*N* HCl for 18 hours or 1.0*N* H_2SO_4 for 4 hours in sealed glass tubes) and subsequent chromatography (butanol:acetic acid:water, 3:2:1), neither hexosamine nor uronic acid was detected. The only hydrolyzate product detected was glucose. Sulfate analysis (*4*) indicated that the extract contained ester sulfate. The polysaccharide of the odontophore is therefore a polyglucose sulfate and not one of the mucopolysaccharides normally found in cartilage (*5*). Since the odontophore does not contain the polysaccharides characteristic of cartilage, it cannot be considered normal cartilage. A further analysis of the apparently unique chemical composition of the odontophore may help to explain why the myoglobin is absorbed by the chondroid matrix (*6*).

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5. A more detailed report on the identification of the polyglucose sulfate is in preparation.
6. This work was done while I was a Lalor Foundation fellow at Marine Biological Laboratory, Woods Hole, Mass.

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Notes on the Champlain Sea Episode in the St. Lawrence Lowlands, Quebec

Abstract. Palynological studies, coupled with geological investigations and radiocarbon dating, have shown that the Champlain Sea episode in the St. Lawrence lowlands is in part contemporaneous with the Two Creeks interstadial of the Wisconsin glaciation.

Recent studies made on Pleistocene deposits of the St. Lawrence lowlands, Quebec, involving stratigraphic studies by Gadd (*1*), Karrow (*2*), and McClintock (*3*), and palynological studies by Potzger (*4*), Potzger and Courtemanche (*5*), and me (*6*) have clarified the chronology of the late Pleistocene events in that area enough to warrant a reassessment of the previously accepted sequence of these events.

The palynological studies (Fig. 1) have indicated conclusively the regional presence of the postglacial pine period (Fig. 1, pollen zones III and IV), the hypsithermal interval (*7*), and the earlier spruce maximum (Fig. 1, pollen zone V) in post-Champlain Sea deposits of the St. Lawrence lowlands.

In sediments older than those showing the spruce maximum (zone V) the higher percentages of pine pollen (*Pinus banksiana*), accompanied by an increase of non-tree pollen, have been interpreted as evidence for a late-glacial episode (zone VI). The high percentages of pine pollen should, perhaps, be explained by over-representation due to the high pol-