The White-Tiger Enigma

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CHEDIAK-HIGASHI syndrome (C-HS) is an inherited autosomal simple recessive non-sex-linked gene disease of the membrane-bound organelles of various cell types. It occurs in certain blood-line albinos or partial albinos and has been reported in at least six relatively diverse animal species: man,[1,2] mink,[2-4] cattle,[2,5] American bison,[2] beige mice,[6,7] and a captive killer whale.[8]

In animals with C-HS, enlarged primary granules of leukocytes (neutrophils, lymphocytes, monocytes, and eosinophils) fuse into a few very large ones with crystalloids and a complement of smaller secondary granules. These enlarged peroxidase-positive granules are lysosomes found to be due to abnormal formation of primary granules in C-HS affected animals.[8] They are also acid phosphatase-positive. They have not been demonstrated in the leukocytes of white tigers.

It seems likely that a common basic cellular defect would cause production of these abnormal granules. Apparently, their presence within many cell types results in characteristic gross, histologic, and clinical manifestations seen in C-HS.[2]

In 1959, the National Zoological Park, Washington, D.C., acquired from India an unusual 2-year-old female Bengal tigress (*Panthera tigris*) named Mohini. This animal is white, has ice-blue eyes and the characteristic dark gray-brown stripes of normal tigers (*Figure 1*).

In 1963 Mohini was mated with Samson, a closely inbred relative (*Figure 2*). Three cubs were delivered on January 7, 1964. Of these, one male (Ramana) and one female (Ramani) had normal coloring. The third, a male (Rajkumar), was white. The yellow female cub died on August 17, 1965, and the white, blue-eyed male died on August 27, 1965. Both died of infectious feline panleukopenia. All three cubs had been properly vaccinated against this disease.

Two cubs, both female and of normal color, were later born to Mohini and Samson. One was stillborn. At this writing, the other (Kessari) is living and was mated to a yellow full brother (Ramana, of the first Mohini-

Figure 1—*Mohini*, mother of the strain of white tigers in the National Zoological Park, Washington, D.C. (Painting by Dr. Harry H. Berrier).

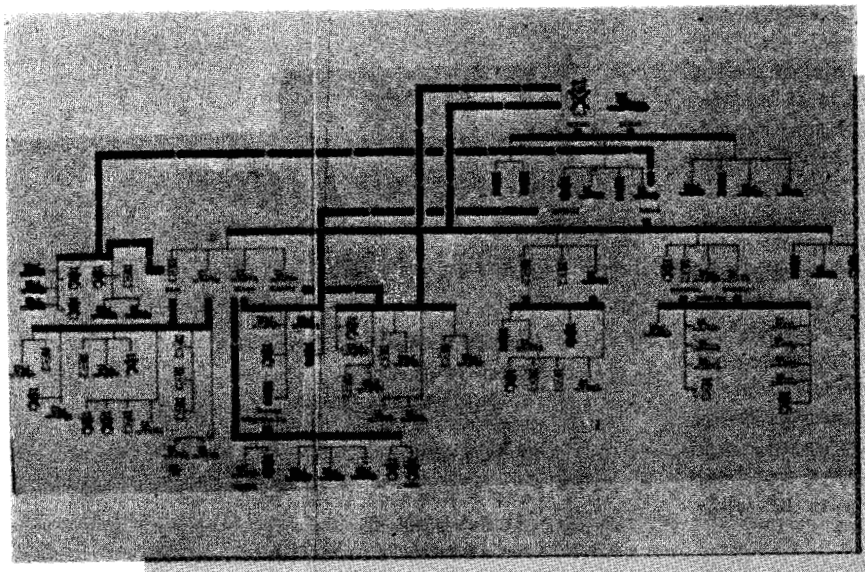


Figure 2
Family tree of the world's known white tigers illustrates how inbreeding makes white-coat genes dominant. Upright tigers are male, prone female. An X through a symbol means the tiger has died. *Mohan* was caught as a cub in the jungle preserve of the Maharaja of Rewa, where tigers seem to maintain the genetic capacity for whiteness. His mate, *Begum*, was wild and had normal coloring. Their mating (blue lines indicate matings) produced three litters, all yellow. Yet, since the cubs carried at least one

Figure 3 *(top left)*—Renal tubules of a mink with Chediak-Higashi syndrome (C-HS) showing deposits of PAS-positive material in cytoplasm (arrows). In mink, the material is most readily observed in collecting tubules (x400). (Courtesy *Am. J. Path.)*

Figure 4 *(center left)*—Renal tubules of a Hereford calf with C-HS, showing deposits of PAS-positive material (arrows) in cytoplasm (x400). (Courtesy *Am. J. Path.*)

Figure 5 *(lower left)*—Renal tubules of child with C-HS, showing deposits of PAS-positive material (arrows) in cytoplasm (x400). (Courtesy *Am. J. Path.*)

Figure 6 *(near right)*—Renal tubules of a white tiger (*Rajkumar*), showing deposits of PAS-positive material (arrows) in cytoplasm (x575).

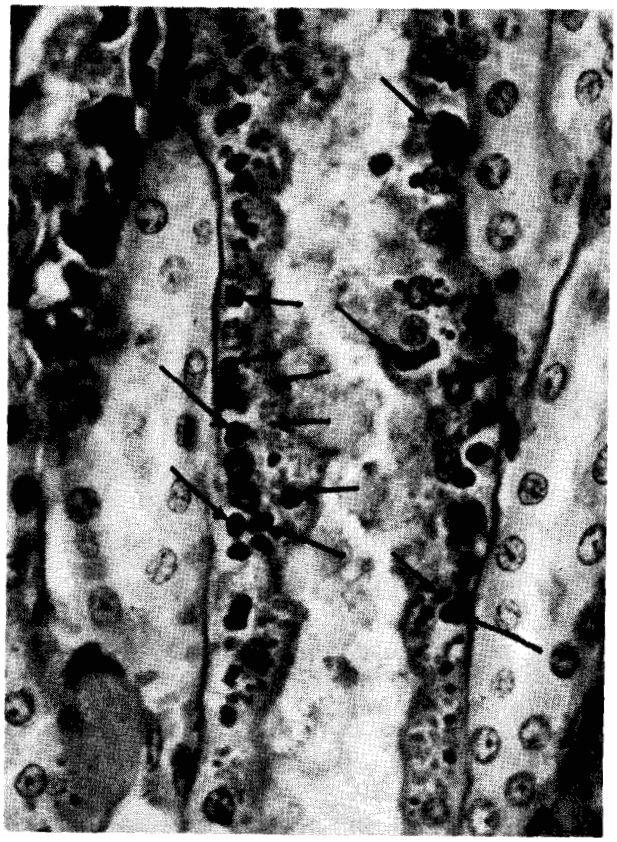
Figure 7 *(far right)*—Renal tubules of a white tiger (*Moni*), showing deposits of PAS-positive material (arrows) in cytoplasm (x575).

white gene from *Mohan*, his next mating to his daughter, *Radha*, produced 11 white cubs in four litters. *Mohan's* blood line (red) then joins a mating line with *Sukeshi*. All cubs from this mating are white. His yellow son, *Samson*, mated with *Mohini*, building Washington's white-tiger dynasty. *Mohan's* son and daughter, *Champak* and *Chameli I*, mated to start the Bristol Zoo family in England. His other progeny maintain the Indian line. (Courtesy Smithsonian Associates, Washington, D.C. Art by Paul Reed.)

Samson mating). Ramana died of a kidney infection on June 18, 1974, before the litter was born on June 20, 1974. In this litter were four cubs. Three were white and one was yellow. At this writing all are still living.

Mortality rate among patients with C-HS is approximately one-third.[9] Age at death is usually early, ranging in children from about 5.4 to 8.4 years, in cattle 12.4 months (most dying before 6 months old), and in mink within the first year.[2] On the white tiger genealogy chart (*Figure 2*) the death rate exceeds 43% for animals of both colors carrying white genes. In 1965 Mohini aborted one cub produced by the second mating with Samson.

Mohini's first surviving son (Ramana) who was of normal color but carried the white gene, was mated with Mohini. They



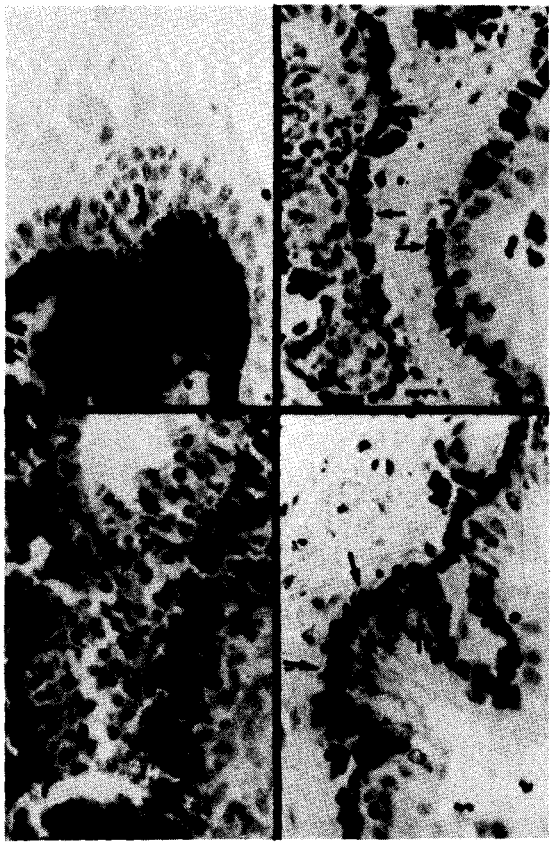


Figure 8 *(far left)*—Ciliary process of a normal Hereford. Note the small size of the melanin granules (arrows) and amount of pigment. The iris in the normal animal is dark brown or black (x300). (Courtesy *Am. J. Path.*)

Figure 9 *(near left)*—Ciliary process of a Hereford with C-HS. Many melanin granules are large (arrows), but some are of approximately normal size. The iris of the animal with C-HS is gray (x300). (Courtesy *Am. J. Path.*)

Figure 10 *(far left)*—Ciliary process of a standard dark mink. Note the small size of the melanine granules (arrows) and amount of pigment. The iris of the normal animal is black (x300). (Courtesy *Am. J. Path.*)

Figure 11 *(near left)*—Ciliary process of a Hope color-phase mink with C-HS. Note the large melanin granules (arrows) as compared to those of approximately normal size. The iris of the mink with C-HS is light pink or red (x300). (Courtesy *Am. J. Path.*)

produced two litters. In the first was one white female (Rewati) and one yellow male. The latter died of brain damage within 48 hours of birth. In the second litter, there were three females of normal color and two white males. Two of the females and one white male were crushed while the mother labored to deliver the third female cub (retained stillborn). Moni, the remaining male cub died of shock at the age of 16 months. The cause of shock is unknown.

On arrival at the National Zoological Park from India, stained blood films of Mohini were examined at Washington State University for C-HS-like inclusion bodies in the leukocytes. No abnormal granules were found. Mohini was pronounced negative for C-HS.[10]

Stained films of blood taken from the first white cub (Rajkumar) when it was about 2 months of age were also studied for C-HS-like inclusion bodies in the leukocytes. None were seen. These slides were compared with those made from blood of a nonrelated normal-colored 2-month-old tiger cub. No differences were observed.

Comparative studies of C-HS in man, mink, and cattle have been described.[11] Large periodic acid Schiff (PAS)-positive inclusions were observed in renal tubular epithelial cells in all three species (*Figures 3-5*). It appears that identical PAS-positive bodies have been found in renal tubular epithelial cells of beige mice with C-HS.[12,13] Large PAS-positive inclusions were also present in renal tubular epithelial cells of the two white tiger cubs, Rajkumar and Moni, (*Figures 6 & 7*).

Ciliary processes in eyes of cattle and mink with C-HS were found to contain abnormally large clumps of melanin granules (*Figures 8-11*) as compared to those in eyes from normal animals of the species.[11] Unfortunately, the eyes of Rajkumar were not available for study, but ciliary processes in

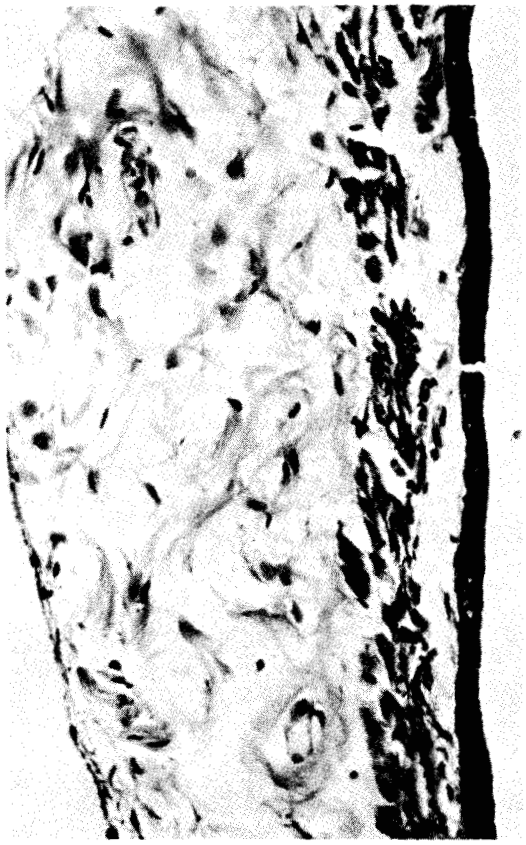


Figure 12 *(left)*
Iris of a white tiger (*Moni*). Note the scant amount of pigment as compared to that in the normal Siberian tiger cub shown in Figure 13 (x300). The iris of the white tiger (*Figure 1*) is blue in the center, fading to gray at the periphery.

Figure 13 *(right)*
Iris of a normal Siberian cub. Note the greater amount of pigment as compared to that of the white tiger shown in Figure 12 (x300). The iris in normal tigers is dark red-orange. (Courtesy Dr. L. A. Griner, pathologist and director of research, San Diego Zoological Garden.)

the eyes of Moni were compared with apparently normal eyes of a normal-colored young Siberian tiger from the San Diego Zoological Garden, San Diego, California. In Moni's eyes there was a noticeable decrease in thickness of the pigmented layer of the posterior surface of the iris (*Figure 12*) as compared to the normal eye (*Figure 13*). Also, retinal pigment epithelium and choroid were not as heavily pigmented in Moni's eyes (*Figures 14 & 15*).

Pigment granules of both neural-crest and optic-cup origin have been described as being affected in mutant beige mice.[7,14] Giant and bizarre melanin granules were found in the medulla and cortex of hairs and in retinal and choroidal melanocytes of beige mice.[6] As yet, this factor has not been studied in white tigers.

PAS-positive material with the same distribution as that seen in children with C-HS was also present in neurons of the central nervous system and cells of the reticuloendothelial system in cattle with C-HS. All mink with C-HS had deposits in neurons but only 15 of 23 had PAS-positive material in renal tubular epithelium.[11] No PAS-positive material has been seen in neurons in either of the two white tiger cubs.

Cellular infiltrate (lymphocytes and histiocytes) consistently seen in children was not observed in cattle or mink with C-HS.[11] Studies of this aspect have not been performed on the white tigers.

The defense mechanism in man, cattle and mink with C-HS appears to respond normally. However, this response seems to give the patient little or no protection, at least during early age. Death is usually caused by massive hemorrhage, pneumonia or generalized infections which usually are recurring clinical problems. It has been generally known for many years that the defense mechanisms of albinos or partial albinos are not as functional as those of normally-colored man and other animals.

Other problems associated with some albinos or partial albinos are nystagmus

and/or crossed eyes. Siamese cats, white tigers, pearl mink and albino rats all exhibit an array of genetic anomalies in which some form of reduced pigmentation is combined with a congenital abnormality of the central visual pathways: some of the optic nerve fibers go to the wrong side of the brain. This abnormality can be associated with crossed eyes.[15] The eyes of Rewati and Moni were probably weakened by close inbreeding to maintain the white-tiger color.

There is not sufficient evidence to call the white-tiger enigma Chediak-Higashi syndrome. However, it appears there is sufficient evidence of a genetic defect in the blood line of the white tigers in the National Zoological Park, Washington, D. C., to warrant a complete scientific investigation. A colony of white tigers possibly could be established for further study of this genetic condition. Other albino or partial albino animals, including man, could perhaps benefit from such studies.

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Figure 14—Choroid of a white tiger (*Moni*). Note the scant thickness of pigment as compared to that in the choroid of the normal Siberian tiger cub shown in Figure 15 (x300).

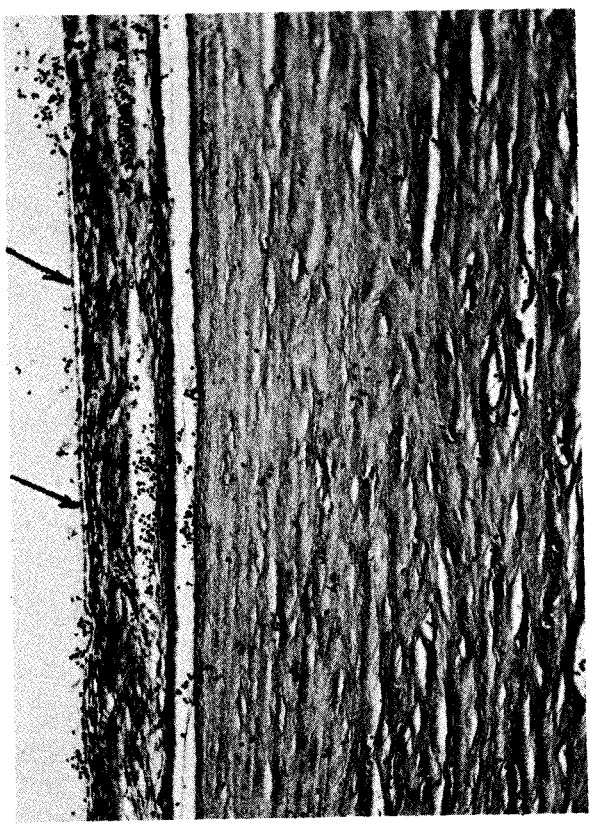

Figure 15—Choroid of a normal Siberian tiger cub. The pigment layer is thicker than that of the white tiger shown in Figure 14 (x300).