Another phenomenon which has been thought to depend on the transverse tubular system was also noted to be absent in these treated fibers. The large, prolonged after-depolarization following a train of action potentials (the late afterpotential) has been attributed to an accumulation of potassium in an extracellular compartment which was thought to be the lumen of the transverse tubules (*6*). In muscle fibers with disrupted transverse tubules, no late afterpotential was seen.

In the experiment illustrated in Fig. 2 a series of action potentials was elicited by a train of short depolarizing pulses at 100 pulses per second. The upper trace of Fig. 2 shows a train of eight action potentials displayed at low voltage gain and high sweep speed. The same record is shown below at ten times the voltage gain and one-tenth the sweep speed. Even at this high voltage gain there is no sign of the normal late afterpotential. The disappearance of the late afterpotential in muscle fibers with disrupted transverse tubules indicates that the extracellular compartment thought to be responsible for the potential is indeed the lumen of the transverse tubules.

The lower trace of Fig. 2 shows a miniature endplate potential which suggests that release of the transmitter is unimpaired. In fact, in muscle fibers with disrupted transverse tubules, endplate potentials with a time course that is shorter than normal can still be elicited by nerve stimulation (see *7*). The treatment with glycerol apparently does not damage the nerve trunk or the nerve terminals, nor does it disrupt the mechanism for transmitter secretion.

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Haptoglobin Levels in Serum of Various Strains of Mice

Abstract. *Only a single type of haptoglobin was found in the serum of 11 strains of mice, but there were wide variations between strains with respect to the amount of haptoglobin found. In the AKR and C3H strains, in which haptoglobin was low or absent, various agents stimulated production of high levels of haptoglobin. Serum haptoglobin rose in association with the development of leukemia in AKR mice, but remained low when C3H mice developed mammary tumors.*

In man, the relative risk of developing leukemia may be associated with haptoglobin type (*1*), and accordingly it was of interest to determine whether an analogous situation might exist with respect to certain strains of inbred mice for which the relative risk of acquiring leukemia or another malignancy is under known genetic control. Genetically controlled variations in the molecular structure of serum haptoglobins, well documented in man, are not known to exist in other species where only a single protein has been described (*2*).

We have found that the quantitative level of serum haptoglobin differs markedly in several strains of mice. A preliminary examination of the serum of eight mice from each of 11 strains of inbred mice showed considerable variation with respect to the numbers in each strain which had haptoglobin levels exceeding the sensitivity of the analytical method (*3*) as follows: AKR, 0; C3H, 2; BALB/c, 3; A, 3; SWR, 3; NBL, 3; C57BL/6, 4; C57BL/An, 6; C58, 7; DD, 7; DBA/2, 8. More extensive studies were carried out on female AKR, C3H, and DBA/2 mice with the following result: AKR, 0/100; C3H, 31/183; DBA/2, 23/24 mice possessed clearly demonstrable haptoglobins.

The AKR and C3H strains are similar in having very low values for serum haptoglobin; indeed, most mice in these two strains have haptoglobin levels beneath the detectable limit. They differ clearly from the DBA/2 strain, where high values (50 to 150 mg of hemoglobin bound per 100 ml) are most common. The AKR and DBA/2 strains represent extremes with respect to percentage of mice having haptoglobins; other strains studied appear to occupy intermediate positions.

When found at all, the presence of haptoglobin in the serum of C3H mice is transient. Fifteen C3H mice, which on first examination had some haptoglobin, were reexamined 3 to 4 weeks later. Eight had small (approximately 30 mg of hemoglobin bound per 100 ml) amounts of haptoglobin in their serum; but the other seven had lost their haptoglobin and were negative.

Subcutaneous injections of turpentine regularly cause rises in serum haptoglobin (*2*). All of the animals that were tested by subcutaneous injections of 0.1 ml of turpentine responded by a marked increase in the amount of serum haptoglobin, whether or not the particular mouse's haptoglobin had been detectable prior to treatment. The stimulating effect of turpentine was studied in both AKR and C3H mice, where the levels rose from 5 to 10 mg of hemoglobin bound per 100 ml to a maximum of 150 to 250 mg of hemoglobin bound per 100 ml and persisted for 5 days. Other agents that provoked a rise of serum haptoglobin level were talcum powder, India ink, corn oil, and paraffin oil. These latter agents were not effective on all mice tested, nor was the response as long lasting as with turpentine. Injections of 0.85 percent NaCl did not result in changes in the serum levels. In all cases where haptoglobin could be observed, there was a single major protein, analogous to the human 1-1 protein, migrating with the same mobility in all strains. In most cases where mice had elevated haptoglobin levels, there were several additional slower moving bands (Fig. 1). The electrophoretic patterns of the mice which normally have higher levels

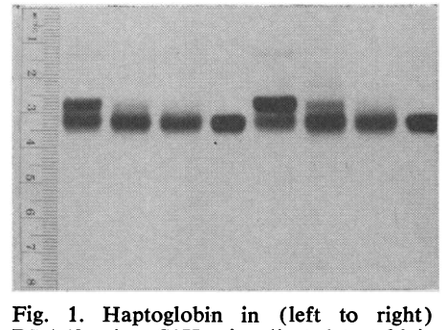

Fig. 1. Haptoglobin in (left to right) DBA/2 mice, C3H mice (just detectable), AKR mice (negative), human hemoglobin, AKR (turpentine stimulated), DBA/2, C3H (negative), human hemoglobin. The origin is at the zero index, and the migration is towards the anode at the bottom of the figure. Human hemoglobin was added to each serum to form the haptoglobin-hemoglobin complex; guaiacol was used to stain the complex (major band at 2.8 cm). Unbound hemoglobin migrated at 3.3 cm.

(for example, DBA/2) closely resembled the patterns obtained after turpentine stimulation of haptoglobin in other strains.

The fact that AKR and C3H strains may be stimulated to produce serum haptoglobins by nonspecific agents indicates that the normal deficiency or absence of this protein in these strains is not due to a lack of the genetic information required for haptoglobin synthesis, and suggests the possibility that the transient appearance of haptoglobin in C3H and AKR mice may be a result of unknown environmental stimuli. In contrast, deficiency of liver catalase in the C57BL/6 strain has been shown to be under genetic control (*4*).

The relation between the formation of spontaneous tumors and haptoglobin levels was studied in AKR and C3H mice. One hundred AKR female mice, born on the same day, were obtained as weanlings and, at age 3 months, were found uniformly to have no demonstrable haptoglobin. Two of 13 mice at age 5 months were found to have low levels of haptoglobin. At age 9½ months, when over 50 percent of the mice had died of leukemia, serum haptoglobin levels were estimated in the remaining 22 mice, which were then killed and autopsied (Table 1). In this group, 10 out of the 22 mice had definite histological evidence of leukemia. The haptoglobin values could be divided into three groups: (i) markedly elevated (> 100 mg of hemoglobin bound per 100 ml), (ii) moderately or slightly elevated (20 to 100 mg of hemoglobin bound per 100 ml), and (iii) absent (> 15 mg). Of ten mice with markedly elevated serum haptoglobin, seven had definite histologic evidence of leukemia, an increased spleen weight (> 150 mg), and large thymus. Of seven with moderately elevated serum haptoglobin levels, three had definite leukemia. Five animals without demonstrable haptoglobin had no leukemia. There is thus a strong tendency for elevated haptoglobin levels, elevated spleen weights, and positive histological diagnosis for leukemia to occur together.

All animals with leukemia had elevations of serum haptoglobin. On the other hand, seven animals had elevated serum haptoglobin levels, and had not yet developed histologic signs of leukemia. On the presumption that these animals will develop leukemia, the data suggest the possibility that elevation of serum haptoglobin precedes any of the present diagnostic criteria for leukemia in AKR mice.

In contrast to the elevations in serum haptoglobin that occurred when leukemia developed in the AKR mice, haptoglobin levels in C3H mice did not rise even when mammary tumors were pronounced. C3H mice having definite tumors and low or absent haptoglobins could be stimulated by turpentine to produce an elevated level of haptoglobin. It appears, therefore, that with respect to stimulation of haptoglobin synthesis, the two host-tumor situations are unlike.

The data indicate that there is a notable distinction between the serum haptoglobins of mice and men. In man, differences in types of haptoglobin are striking. Mice seem to differ only with respect to quantitative levels. These differences in haptoglobin levels may serve further to characterize strains of mice.

Table 1. Serum haptoglobin and autopsy data, AKR mice.

Thymus enlargement	Lymph nodes enlargement	Spleen weight (mg)	Organs with histologic leukemia
		Serum haptoglobin markedly elevated	
Great	Great	750	Thymus, lymph nodes, spleen, liver, kidney
Great	Great	670	Thymus, lymph nodes, spleen, liver
Great	Great	610	Thymus, lymph nodes, spleen, liver, kidney
Great	Great	600	Thymus, lymph nodes, spleen, liver, kidney
Great	Great	465	Thymus, lymph nodes, spleen, liver, kidney
Great	Slight	450	Thymus, lymph nodes, spleen, liver, kidney
Great	Normal	130	Thymus
Slight	Slight	150	None
Slight	Slight	150	None
Slight	Normal	120	None
		Serum haptoglobin moderately elevated	
Great	Slight	275	Thymus, lymph nodes, spleen
Normal	Normal	100	Thymus, lymph nodes, spleen, liver, kidney
Moderate	Slight	128	Thymus
Slight	Slight	130	None
Normal	Normal	100	None
Normal	Normal	100	None
Normal	Normal	100	None
		Serum haptoglobin not detectable	
Slight	Slight	120	None
Normal	Normal	100	None
Normal	Normal	100	None
Normal	Normal	100	None
Normal	Normal	100	None

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Dichoptic Viewing and Temporal Discrimination: An Attempted Replication

Robinson's observation (*1*) that dichoptic presentation of visual stimuli allows correct discrimination of order at interstimulus separations of only 5 msec is of particular import. No previous investigation has implied such rapid, veridical processing of successive stimuli by humans. If valid, this observation would demand a reorientation of theory regarding the relation of stimulus input to the temporal processing mechanism. It would also follow that dichoptic presentation may be adapted to facilitate other perceptual capabilities.

To test the observation, a replication study was conducted with the use of procedures described by Robinson. A three-channel Scientific Prototype tachistoscope was fitted with stimuli (a square and a triangular luminous patch, each subtending 1 degree of visual arc) and a red circular fixation patch. The placement of the stimuli as well as the luminance were approximately the same as Robinson reported. Opal dif-