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HÆMATOLOGY

Elevation of Serum Haptoglobin in Rabbits in Response to Experimental Inflammation

Normal human serum contains sufficient haptoglobin to bind approximately 130 mgm. of hæmoglobin per 100 ml. (ref. 1). A number of other mammalian species, including the rabbit, have much lower serum haptoglobin-levels[2]. In order to have available a plentiful source of rabbit haptoglobin a method was sought by which the normal serum level could be elevated. Observations on patients with various diseases suggested that tissue inflammation might provide a means to this end[3]. Accordingly, the effect of administering turpentine to rabbits was investigated.

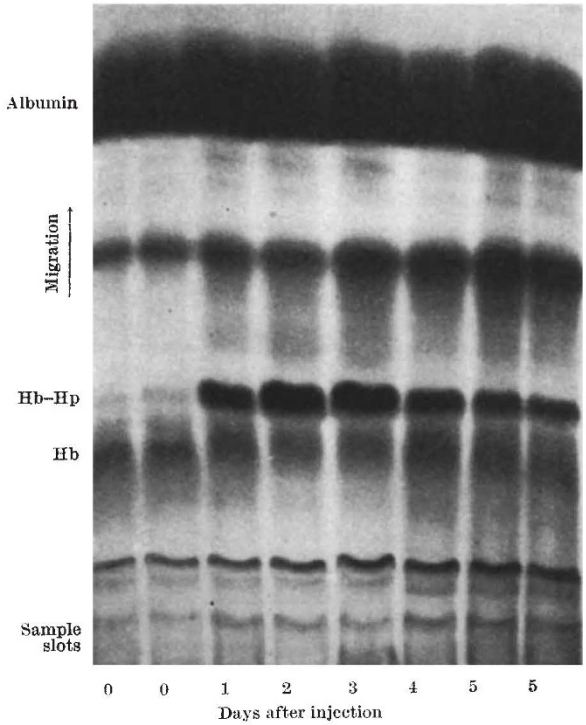

Fig. 1. Starch-gel electrophoresis (ref. 5) of serum samples from a rabbit following injection of turpentine. The buffer composition was 0·021 *M* boric acid 20 per cent neutralized with sodium hydroxide. Hæmoglobin was added to all samples in amounts sufficient to bind all free haptoglobin. The samples on the two edges of the gel are duplicates of the neighbouring samples. The position of the hæmoglobin zone is indicated by the symbol Hb, the hæmoglobin–haptoglobin zone by Hb–Hp

The range of serum haptoglobin concentration[4] in 32 rabbits was 2–35 mgm. with a mean of 10 mgm., expressed in milligrams hæmoglobin-binding capacity per 100 ml. Fifteen rabbits of various ages received a 1-ml. dose of turpentine injected subcutaneously in the dorsolumbar region. In these animals the serum haptoglobin concentration increased to 150–300 mgm. per 100 ml. The rise began at approximately 12 hr. after injection and reached a peak at 48 hr. The level afterwards decreased and fell to one-half of the maximum in 2½–3 days.

The changes in starch gel electrophoretic pattern[5] following turpentine injection are illustrated in Fig. 1. Although the increase and subsequent decrease in the hæmoglobin–haptoglobin zone is the most striking feature, there are changes in several other zones, particularly in those migrating between albumin and the hæmoglobin–haptoglobin complex. Analysis of serum samples for total protein-bound carbohydrate[6] and total protein[7] were also performed. Serum glycoprotein concentration doubled during the initial 48 hr. after injection. More than half the increase of the serum glycoprotein at 48 hr. could be attributed to haptoglobin. No appreciable changes in the total serum protein level were observed.

Whether the rise in haptoglobin represents net synthesis or liberation of pre-formed haptoglobin has not been elucidated. The site of synthesis or of liberation also remains unknown. However, it is unlikely for the following reasons that the haptoglobin is released into the blood at the site of injection: (1) the haptoglobin-level of exudate withdrawn from the site of injection at 24 and 48 hr. was found to be much lower than the haptoglobin-level of serum; (2) the injection of 2·0 *N* hydrochloric acid which caused local ulceration failed to produce marked elevation of serum haptoglobin; (3) when repeated daily injections of turpentine were administered to one rabbit at different sites, the maximum level of haptoglobin and the rate of disappearance were within the limits observed when only a single dose was given. These observations suggest that a tissue pool of haptoglobin may exist normally, possibly in the liver, and that the protein is released into the blood stream in response to inflammation.

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