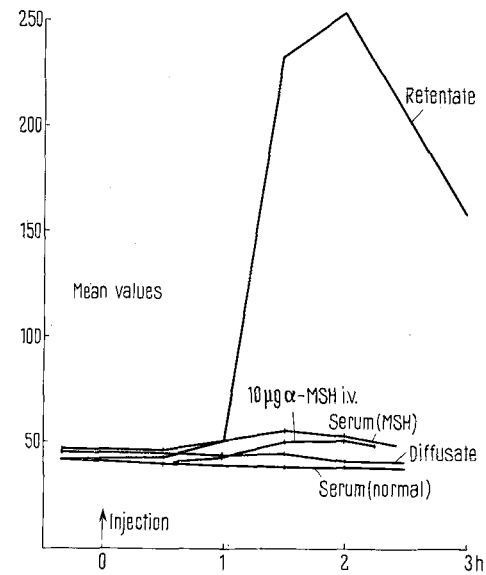
A MSH-Released Serum Factor Acting on the Blood-Aqueous Barrier of the Rabbit Eye

It has been shown that general administration of microgram doses of the synthetic melanocyte stimulating hormone (α-MSH) may cause an increase in the aqueous flare in the anterior chamber of the rabbit's eye[1]. This effect is due to damage in the blood aqueous barrier which permits serum protein in abnormally large amounts to enter the aqueous[2]. The permeability effect seems to be limited to the ciliary processes[3], and histological evidence is in favour of the hypothesis that the basal (pigmented) epithelial layer rather than the vessels in the ciliary processes are primarily affected[4].

On the other hand, the simple explanation that MSH acts directly on the epithelium is strongly contradicted by the fact that to elicit an effect at intraocular administration of MSH just as large amounts of the peptide are required as for general administration. Obviously a relatively high local concentration of MSH is not sufficient to influence the barrier. We have to presume that MSH releases some factor more directly responsible for the permeability effect. Some recent experiments have furnished support for this hypothesis. Rabbits known to have given an aqueous flare increase after MSH ('responsive') have been given 10 μg/kg synthetic α-MSH subcutaneously, and 90 min after the injection, when the flare effect has been well established, blood has been tapped. The serum in doses of 2 ml has then been given intravenously to 10 other responsive rabbits. These animals have shown a slight (30%) flare increase after a latency which does not seem to be significantly different from the effect after MSH itself. This effect can for several reasons hardly be caused by the small quantity of MSH possibly remaining in the tapped blood. Reckoning generously on about a 100-fold dilution in the donor's blood, we have given 0.1 μg MSH/kg intravenously to 6 of the rabbits in the previous group of rabbits. No flare effect was observed. Serum from animals which had not received MSH did not release any flare effect (15 animals). We have previously observed that some animals, especially young ones, may be refractory (non-responsive) to the flare effect by MSH. If serum was taken from such animals, after being given the usual dose of 10 μg/kg MSH, no effect could be elicited in 4 responsive rabbits either. If, on the other hand, serum from responsive animals was given to 16 non-responsive animals an effect was obtained. There seems to be a factor which is released by MSH in responsive but not in non-responsive animals. This factor is efficient in both responsive and non-responsive animals. A rough separation by dialysis of serum from responsive animals has been performed. 12 ml serum from rabbits which had been given MSH 90 min before tapping were dialysed against 50 ml of a physiological NaCl solution during 24 h in a refrigerator at + 4 °C. The diffusate was concentrated 5 times. 2 ml of this hypertonic solution were given intravenously to 5 responsive rabbits without any effect on the flare. The retentate was given in doses of 2 ml to the same 5 rabbits. The effect was in fact very striking. An extremely high increase in the flare density was observed, compared to which the effect of the undialysed serum was very feeble. As far as we can see the most probable explanation of this highly increased effect is that inhibitors of small molecular size are present in the serum, nearly balancing the permeability disturbing factor.

The increased effect is not induced merely by storing the serum. Serum from rabbits given MSH, kept for 24 h in a refrigerator without being dialysed, showed only an effect of the same order as the fresh serum.

The flare provoking factor is evidently the result of the MSH administration, since the retentate of dialysed serum from animals which had not received MSH was completely inefficient in causing a flare response. The dialysis properties make it most probable that a substance of a protein character is involved, as a genuine factor or as a carrier. Preliminary studies using gel filtration with Sephadex 200 have shown that the active factor is found in the first fraction containing large molecular components[5].



Effect on the aqueous flare intensity (ordinate, arbitrary units) of an intravenous injection of normal serum, serum from rabbits previously given MSH, retentate and diffusate of such serum, and 10 μg/kg α-MSH. The groups are represented by their mean values.

Résumé. L'injection sous-cutanée de l'hormone synthétique α-MSH en dose de 10 μg/kg peut produire chez le lapin une augmentation de la perméabilité dans l'œil. Le sérum qui a été prélevé à ces lapins contient un facteur non-dialysable et de grandes molécules. Injecté par voie intraveineuse à d'autres lapins, ce facteur augmente la perméabilité oculaire.

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