The activities of CL-peptidase and DAP-IV in the sera from normal controls, from patients with rheumatoid arthritis and from patients with apoplexia are shown in the table. The activities of CL-peptidase and DAP-IV were significantly lower in patients with rheumatoid arthritis. The lowered activities are probably not due to decreased ADL, since patients with apoplexia, with a similar degree of decreased ADL, did not show any significant decrease in the two enzyme activities.

Significant positive correlation was found between the activity of CL-peptidase and that of DAP-IV in patients with rheumatoid arthritis or apoplexia (fig.) ($r = 0.655$, $p < 0.01$). There was no significant correlation between serum CL-peptidase activity and age (from 35 years to 80 years).

These results indicate that the activities of CL-peptidase and DAP-IV are decreased in the serum of patients with rheumatoid arthritis. This suggests that the degradation of collagen may be decreased in rheumatoid arthritis.

1 Correspondence should be addressed to T.N., Laboratory of Cell Physiology, Department of Life Chemistry, Graduate School at Nagatsuta, Tokyo Institute of Technology, Yokohama 227 (Japan).

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Sympathectomy enhances the substance P-mediated breakdown of the blood-aqueous barrier in response to infrared irradiation of the rabbit iris[1]

G. Bynke, A. Bruun and R. Håkanson[2]

Departments of Experimental Ophthalmology and Pharmacology, University of Lund, S-22362 Lund (Sweden), 17 April 1984

Summary. Rabbits were subjected to infrared irradiation of the iris 1 month after unilateral cervical sympathectomy. The resulting breakdown of the blood-aqueous barrier was greatly enhanced on the sympathectomized side. In contrast, the response to intravitreally injected substance P (SP) was the same in both eyes. The enhancement of the response to IR irradiation could be abolished by pretreatment with an SP antagonist, (D-Pro^2, D-Trp^{7,9})-SP.

Key words. Rabbit iris; cervical sympathectomy, blood-aqueous barrier; infrared irradiation; substance P antagonist; miosis.

The response of the eye to local injury includes miosis (constriction of the pupil) and breakdown of the blood-aqueous barrier, with consequent leakage of protein into the aqueous humor.

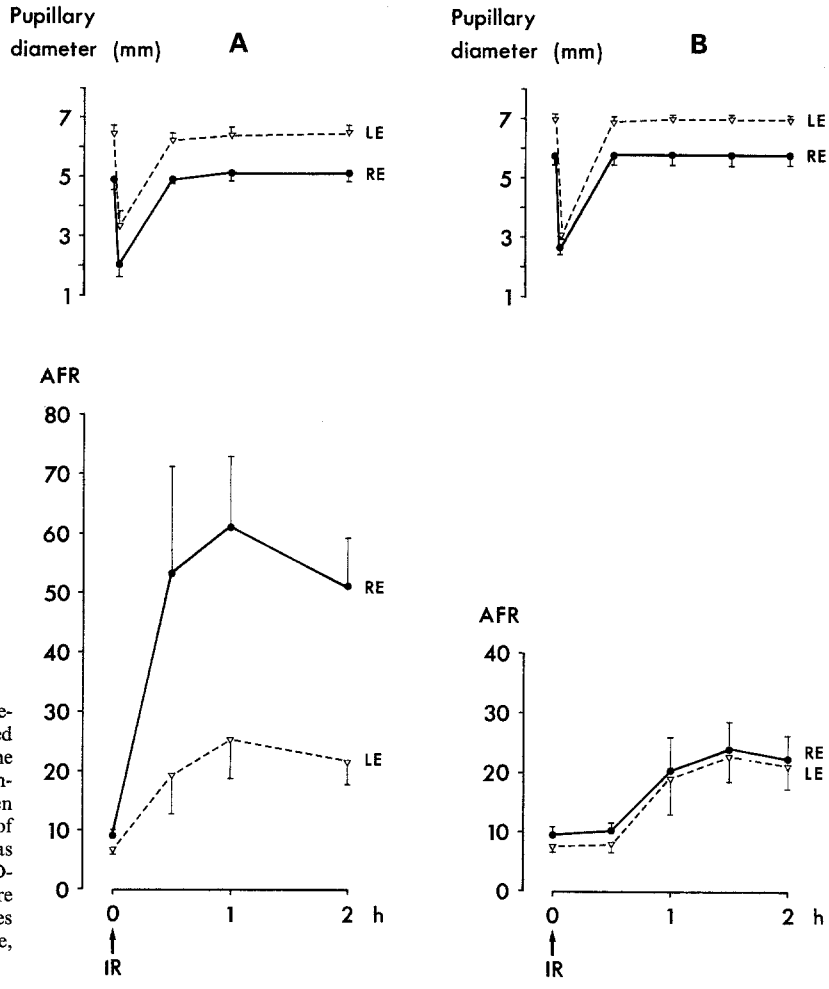
The response of the rabbit eye to laser irradiation of the pigmented iris appears to be mediated partly by E-type prostaglandins (PGs) and partly by a noncholinergic neurogenic factor[3,4]. Similar mechanisms seem to be involved in the breakdown of the blood-aqueous barrier evoked by infrared irradiation (IR) of the rabbit iris, since this breakdown is reduced after topical or retrobulbar anesthesia[5] and after indomethacin[6]. However, Butler and Hammond[7] emphasized the key role of the neurogenic pathway in the response to all types of noxious stimuli, since trigeminal denervation was found to abolish the response not only to laser irradiation of the iris[8] but also to PGE_1. The response to substance P (SP) was not abolished. SP has been put forward as a candidate mediator of the ocular response to injury, since it evokes symptoms of ocular injury[9–11], and since it exists in the trigeminal nerve from which it is released into the aqueous humor upon stimulation[9]. Moreover, destruction of the trigeminal ganglion is followed by reduced SP levels in the uvea[12]. Also, a substance P antagonist, (D-Pro^2, D-Trp^{7,9})-SP, has been shown to reduce the breakdown of the blood-aqueous barrier to IR of the iris[11] and to PGE_2[13] and PGE_1[14].

Following sympathectomy, the ocular response to laser irradiation of the iris is increased[15,16]. Concomitantly, the SP levels in the uvea of the rabbit are raised significantly[17]. This gives indirect support to the theory that SP plays a key role in the ocular response to injury.

In the present study, the miosis and breakdown of the blood-aqueous barrier caused by IR of the iris was studied after sympathectomy and the involvement of SP was tested by the use of an SP antagonist.

Methods. Five adult pigmented rabbits (3–5 kg) underwent extirpation of the right cervical ganglion during pentobarbital (Mebumal®) anesthesia. Successful sympathectomy was indicated 3 weeks later by the supersensitivity of the mydriatic response to topically applied phenylephrine (Neosynephrine®). 1 month after sympathectomy the rabbits were subjected to IR of the iris of both eyes for 2 min. For details see Dyster-Aas and Krakau[18]. The pupil diameter was measured with a transparent plastic ruler under standardized light conditions immediately after IR and then at 30-min intervals. The time course of the barrier damage was followed by photoelectric measurement[6] of the aqueous flare response (AFR) every 30 min. This response is a Tyndall phenomenon, reflecting protein leakage into the anterior chamber. A correlation between the AFR and the protein concentration has been established[19]. The results are expressed in arbitrary units with reference to a standard. A week later the right eye was pretreated with 300 nmoles (D-Pro^2, D-Trp^{7,9})-SP, topically every 15 min for 1.5 h before IR of the iris of both eyes, and the AFR was measured. 1 month later the same animals were given 30 pmoles (9 µl) SP intravitreally to both eyes.

Results. The pupil of the sympathectomized eye was significantly smaller than that in the control eye before IR of the iris, 4.9 mm ± 0.33 versus 6.5 ± 0.22, $p < 0.0025$ (Student's t-test). There was no significant difference in the IR-induced pupillary



A Aqueous flare response (AFR) and miotic response (mm) (mean ± SEM, vertical bars) to infrared irradiation (IR) of the iris of the left eye (LE) and the right eye)RE) in rabbits 1 month after cervical sympathectomy of the right side. The difference between the eyes is highly significant ($p < 0.001$, analysis of variance, two-way). *B* 1 week later, the right eye was pretreated with repeated applications of (D-Pro^2, D-Trp^{7,9})-SP before IR of the iris of both eyes. There was no longer any difference between the responses to IR in the two eyes ($p > 0.05$, analysis of variance, two-way).

constriction between the denervated and the control eye ($p > 0.25$) (Student's t-test) (fig. A). The AFR following IR of the iris was significantly greater in the denervated eye (fig. A). The miosis induced by intravitreally injected SP was not significantly different in the two eyes, the pupillary diameter after 4.5 h (maximal miosis) being 3.5 mm ± 0.79 mm in the denervated eye and 2.7 mm ± 0.62 mm in the control eye. After pretreatment with (D-Pro^2, D-Trp^{7,9})-SP of the denervated eye there was no longer any difference between the AFR following IR of the iris (fig. B). The miotic response to IRI was reduced by pretreatment with the SP antagonist but the reduction was not statistically significant ($p > 0.05$) (Student's t-test).

Discussion. Sympathectomy is known to increase the SP levels in the uvea[17] and to enhance the response to ocular injury[15,16]. This is suggestive of a causal relationship, SP being a proposed mediator of the inflammatory response. As anticipated, the AFR evoked by IR of the iris was enhanced 1 month after sympathectomy. The enhancement could be abolished by pretreatment with (D-Pro^2, D-Trp^{7,9})-SP. The effect of intravitreally applied SP was similar in the sympathectomized and in the control eye with respect to both miosis and aqueous flare. Hence, the enhancement following sympathectomy does not reflect an increased sensitivity to SP but rather supports the view that SP is the mediator of the aqueous flare response to injury and that the SP nerve supply to the uvea is increased following sympathectomy.

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2 Reprint requests to R. H., Farmakologiska institutionen, Sölvegatan 10, S-223 62 Lund (Sweden).
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