Hypertensive Eye Lesions in the Rat. Effect of Carotid Ligation

It has previously been reported that the hypertensive encephalopathy produced by chronic administration of desoxycorticosterone acetate (DCA) can be prevented by ligation of both carotid arteries[1]. When one artery is tied, the cerebral hemisphere on the same side is protected, whereas the contralateral hemisphere is edematous and shows extensive hemorrhages. Protection has been ascribed to the failure of the blood pressure to rise in the head area after ligation.

The present paper describes the eye lesions seen in hypertensive rats and the influence of ligation of one or both carotid arteries on their development.

Materials and Methods. 75 female rats of the Upjohn strain (originally from Sprague-Dawley) of an average body weight of 50 g were divided into four groups as follows:

Group I: 8 rats, untreated controls;
Group II: 20 rats, DCA + sham left carotid ligation;
Group III: 21 rats, DCA + left carotid ligation;
Group IV: 26 rats, DCA + bilateral carotid ligation.

On *day 0* the right kidney was removed in all animals and NaCl 0·9% given as drinking fluid, to sensitize the animals to the hypertensive effect of DCA. In groups II, III and IV a DCA pellet of 25 mg was implanted subcutaneously in the dorsal region. In groups III and IV the left common carotid artery was ligated whereas in group II the same vessel was exposed but not tied. All these operations were performed under ether anesthesia in a single step. On *day 10* a second pellet was implanted subcutaneously under ether anesthesia in animals of groups II, III and IV. Implantation of DCA pellets has been shown repeatedly to produce in rats a syndrome of malignant hypertension[2]. Finally on *day 12*, the right carotid artery in group IV was ligated. The fluid intake was measured daily. Special care was taken to note any ocular changes. The experiment was terminated after 42 days. At autopsy, both eyes were removed and, after gentle extraction of the lens, were fixed in formaldehyde 10% for histological examination.

Results. Mortality Rate. Animals of group II (DCA without ligation) began to die earlier than those of groups III and IV, which had a unilateral and bilateral ligation respectively, and at the end of the experiment a significantly higher percentage of rats had died in this group as compared to the last two (Table II). This confirms earlier results showing the marked protection afforded by carotid ligation in hypertensive animals[1]. Most of the DCA-treated rats showed advanced nephrosclerosis and myocarditis in addition to widespread periarteritis nodosa.

Brain Lesions. Table I summarizes the brain changes. It can be seen that in the unligated DCA-treated rats (group II) the lesions (edema and hemorrhage) were distributed on both sides and these were mostly on the surface of the brain. On the other hand, in the rats ligated on the left side (group III), only the right hemisphere showed lesions; finally, the brain was normal in animals having a bilateral ligation (group IV). This demonstrates the effectiveness of this surgical procedure to counteract hypertensive organic lesions in a given territory.

[1] A. ROBERT, Circulation Research *4*, 527 (1956).

[2] H. SELYE, C. E. HALL, and E. N. ROWLEY, Canad. med. Ass. J. *49*, 88 (1943). – F. M. FRIEDMAN, C. L. FRIEDMAN, and G. R. POLLEY, Amer. J. Physiol. *153*, 226 (1948). – E. SALGADO, Endocrinol. *55*, 377 (1954).

Table I
Effect of Carotid Ligation on the Development of Hypertensive Encephalopathy*

Group No. Rats	DCA 20	DCA + Left 21	DCA + Both 26
Edema			
Left hemisphere	18	0	0
Right hemisphere	18	17	0
Hemorrhage			
Left hemisphere only	6	0	0
Right hemisphere only	2	17	0
Both hemispheres	7	0	0
Total	15	17	0

* Values indicate number of rats showing the pathological change

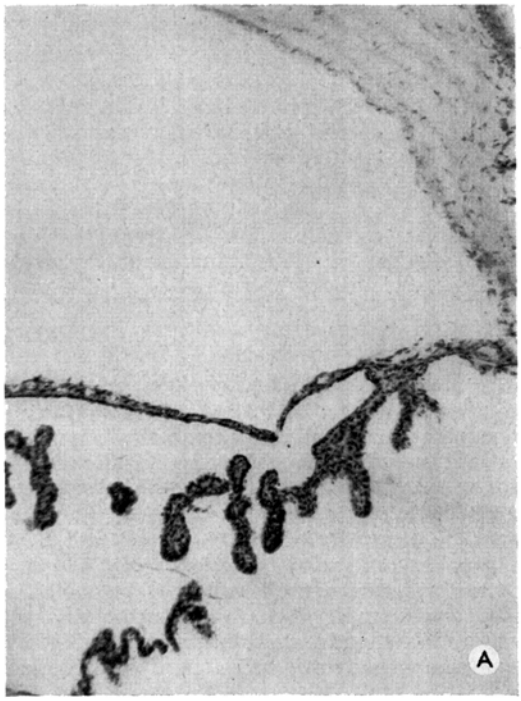
Eye Changes. Pathological changes in the *iris* were noted in a high percentage of DCA-treated animals. The lesion appeared first either as small white spots or as a rather large patchy area extending to about ⅓ of the corneal surface through which it could be seen. In some cases, almost all the iris became involved. The pupil was deformed and usually eccentric. Sometimes the white spots were accompanied by red streaks and in other instances there was a frank hemorrhage within the eye. Frequently the anterior chamber contained a big clot (Fig. 1 *B*). Histological examination showed in the iris and the ciliary body the presence of scar tissue which was probably formed as a consequence of hemorrhage in these organs. Usually, the vessels of the iris arterial circle were found to be hyalinized and their wall partially necrotic (Fig. 1 *C*). This lesion of arteriolonecrosis was of the same type as that seen in other areas, with the differences that there was a less marked periarteritic reaction as in the case of the mesenteric or renal arteries. In many animals, large, often multiple cystic formations appeared within the iris, markedly distending its structure; these cavities contained blood and were obviously the result of intrairidal hemorrhages. When there had been extensive hemorrhage in the anterior chamber of the eye, the cornea was inflamed (Fig. 1 *C*). The retina in most cases appeared normal. Only in a few instances were the arterioles of the retina thickened and their wall slightly hyalinized. This change was by far less frequent than the lesions in the iris and the ciliary body and it is noteworthy that it never led to hemorrhage. This is in contrast with the hypertensive lesions seen in man which are localized in the retinal vessels. All these changes (arteriolonecrosis and hemorrhage in the iris and ciliary body) were present in either eye in unligated rats (group II) and often bilaterally, but they appeared *only on the right side* in the animals of group III which had their left carotid artery ligated. Finally, the eyes remained normal in bilaterally ligated rats (group IV) in spite of the fact that extensive hypertensive vascular

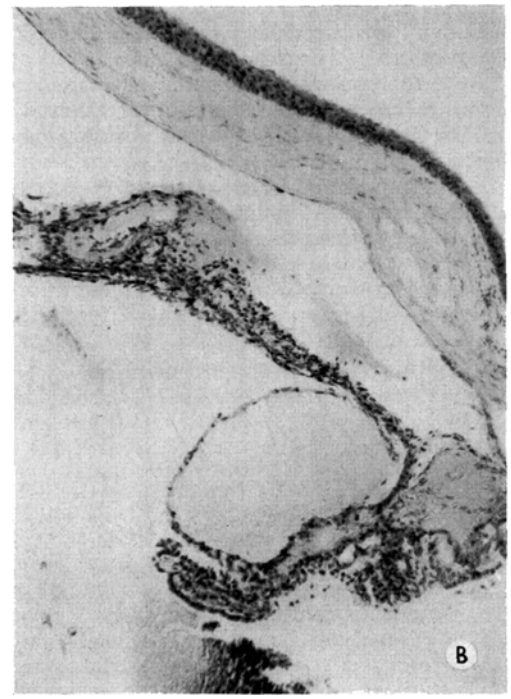
Table II
Mortality Rate and Incidence of Eye Lesions on the 38th Day

Group	Mortality Rate %	Incidence of Eye Lesions %
Group II, DCA	60	56
Group III, DCA with unilateral ligation	28	73

lesions were found in organs situated below the site of ligation, e.g., nephrosclerosis, periarteritis nodosa.

Fig. 2, which gives the incidence of eye lesions in groups II and III, shows that the changes appeared first between the second and third week. Until the 32nd day, the incidence of animals showing the lesions was almost identical in both groups. From the 33rd day on, there was an increased tendency of the animals with unilateral ligation to develop the lesions but, as said before, on the unligated side only. Since these eye lesions appear late in the course of DCA treatment, their higher incidence in group III is likely to be due to the fact that in this group more animals were living during the latter part of the experiment, thus allowing more





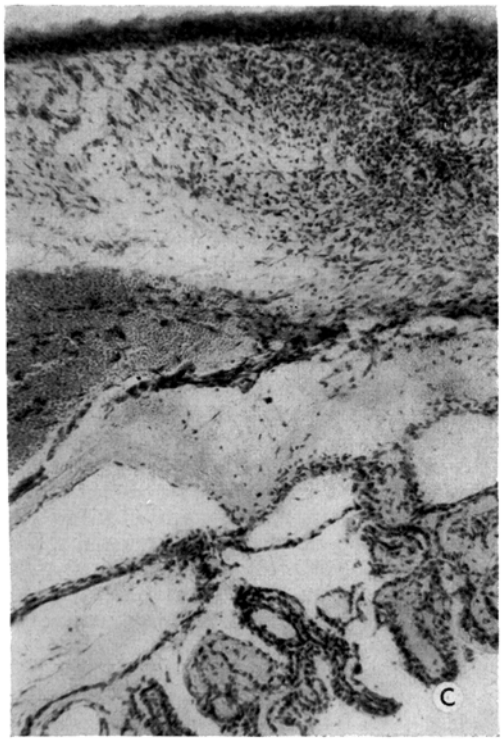


Fig. 1.—On top, the cornea; on the bottom, the iris. Magnification: 110 ×. *A* Normal eye. *B* and *C* Eyes of animals treated with DCA for 42 days. *B* Note hyalinization of arteries in the ciliary body and in the iris. Also, cystic formations due to intra-iridal hemorrhage. Cornea is normal. *C* Massive hemorrhage in the anterior chamber of the eye with secondary corneal inflammation. Marked arteriolonecrosis in the iris as in B.

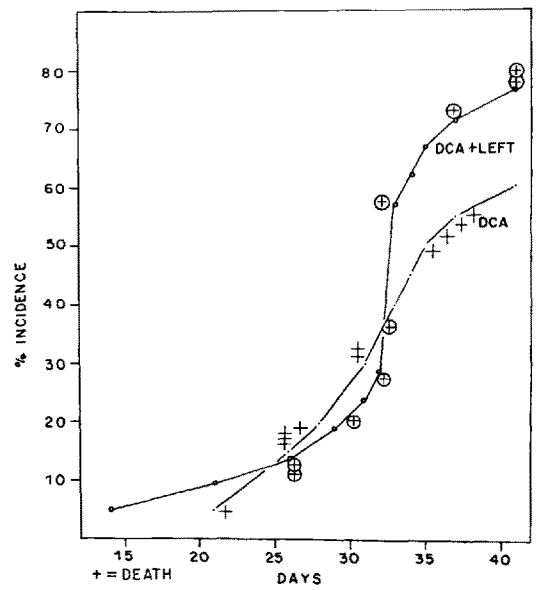


Fig. 2.—Incidence of eye lesions in DCA-treated animals, with and without carotid ligation. There is increased incidence after unilateral ligation but only on the opposite side. At the same time the survival rate is prolonged after an unilateral ligation. Each plus (+) indicates the death of an animal.

time for the pathological changes to develop in the unprotected eye. This is best illustrated by a correlation between mortality rate and incidence of eye lesions. For instance, on day 38, at a time when ocular changes were almost maximum, the relation was as indicated in Table II. It is also possible that the systemic blood pressure–which was not determined–was higher in group III than in group II; if this were the case, this may have contributed to a greater incidence of eye lesions in group III.

Discussion. It is evident that carotid ligation significantly protected the animals against some of the most serious complications of malignant hypertension. The protection seems to be due to the fact that by ligating the artery, the blood pressure could not rise in the head area following administration of DCA. Therefore, it is likely that the mere elevation in blood pressure plays a prominent role in the pathogenesis of vascular lesions found in the eye and the brain in malignant hypertension. It is too early to know what practical application could be made of such a treatment.

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A. ROBERT and J. E. NEZAMIS

Department of Endocrinology, The Upjohn Company, Kalamazoo (Michigan), May 22, 1957.

Résumé

1° Un syndrome d'hypertension maligne a été reproduit chez le rat par l'administration d'acétate de désoxycorticostérone (DCA). Ce traitement produisit de l'artériolonécrose des vaisseaux de l'iris et du corps ciliaire, des hémorrhagies dans la chambre antérieure de l'œil ainsi que de l'œdème et des hémorrhagies cérébraux. 2° Ces lésions, oculaires et cérébrales, furent complètement prévenues par une ligature bilatérale de l'artère carotide primitive, probablement par suite d'une diminution de pression sanguine dans la région de la tête. Après une ligature unilatérale, l'œil homolatéral restait normal tandis que les lésions apparaissaient dans l'autre œil; de même, l'hémisphère cérébral homolatéral était normal alors que l'hémisphère contralatéral montrait un œdème marqué et de nombreuses hémorrhagies. 3° Le rôle pathogénique de l'hypertension *per se* est discuté brièvement.

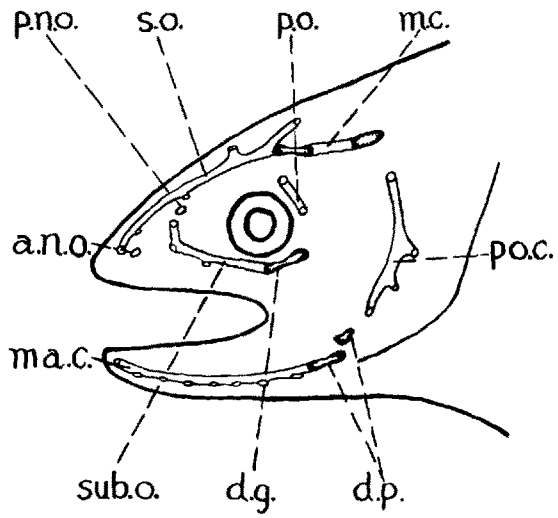
Sensory Canals of the Head in *Wallagonia attu* (Day)

All available descriptions of the sensory canals of the head in Siluroid fishes indicate a general pattern of their disposition. The author has, however, noted certain features in *Wallagonia attu* which differ from the types hitherto described and which appear exceptional. The following description of the distribution of the main canals is based on studies of specimens measuring 25 mm to 28 mm in length.

(1) The infra-orbital canal consists of (a) the sub-orbital, and (b) the post-orbital parts.

(a) The sub-orbital part starts with a pore below the posterior nasal opening, runs downwards for a short distance and then opens to the outside by a pore. The first sense organ is lodged in this region. Beyond this pore, it turns posteriorly and after running for some distance, communicates with the exterior by another pore. The second and third sense organs are located on either sides of this pore. Continuing further backwards below the eye, it finally passes over as an open dermal groove, until it loses its existence below the posterior limits of the orbit. The fourth and the last sense organ of the sub-orbital part is located in the region of the open dermal groove.

(b) The post-orbital part is a short canal, running obliquely behind the eye. It opens by two pores along its course and lodges one sense organ. There is no evidence, whatsoever, of any continuity between the sub-orbital and the post-orbital parts of the infra-orbital canal, or, between the latter and the supra-orbital canal.



Diagrammatic view of the head of a 28 mm long *Wallagonia attu*, showing the course of the sensory canals with their openings. *a.n.o.* anterior nasal opening; *d.g.* dermal groove; *d.p.* dermal pits; *ma. c.* mandibular canal; *m. c.* main canal; *po. c.* preopercular canal; *p.n.o.* posterior nasal opening; *p.o.* post-orbital part; *s.o.* supra-orbital canal; *sub.o.* sub-orbital part.

(2) The supra-orbital canal starts by a pore placed just anterior to and above the level of the anterior nasal tubular opening. It then takes a short oblique course dorsally and opens to the outside by a pore. The first sense organ is placed in this region. As it runs posteriorly, it gradually acquires a dorsal position and lodges three more sense organs. At its posterior extremity, it gives off a dorsal backwardly directed branch, which possesses one sense organ. After a short distance it opens and is subsequently lost.

The junction between the supra-orbital canal and the main canal of the head is marked by a large double pore. Beyond this point, a fully developed main canal is discernible, which lodges definite sense organs.

(3) The preoperculo-mandibular canal is also distinguishable into two parts -the mandibular and the preopercular, which are not continuous with each other. The mandibular part has eight pores and nine sense organs—the last two of which are situated in open dermal pits. Close to this point, a little dorsally, a pore leads into the preopercular canal, which at first runs obliquely along a postero-dorsal course, but soon turns abruptly in a dorso-vertical direction. Finally, it ends by a pore situated at some distance from the main canal. The preopercular canal possesses three sense organs in all and does not communicate with the main canal.