Brit. J. Ophthal. (1968) **52**, 453

NECROGRANULOMATOUS SCLERITIS*

EFFECTS ON THE SCLERA OF VASCULAR DEPRIVATION

BY

DAVID SEVEL†

Department of Pathology, Institute of Ophthalmology, University of London

THE histological appearance of necrogranulomatous scleritis is characterized by a central focus of scleral necrosis (sequestroid) which disintegrates, forming an area of smudgy necrosis. This sequestroid is surrounded by a wall of polymorphonuclear leucocytes, eosinophils, plasma cells, lymphocytes, epithelioid cells, and occasional giant cells. These inflammatory cells may be arranged in palisade formation. The reaction is self-perpetuating, since the deep scleral reaction acts as a stimulant for further proliferative response and accounts for the chronic nature of the condition (Sevel, 1965).

The characteristic histological appearance suggests that the primary focus is the scleral necrosis, around which the granulomatous reaction occurs. It is therefore of importance to establish whether the scleral necrosis is a specific change or whether it is primarily due to vascular occlusion. The sclera lies between two vascular strata—the choroid and the episclera—and probably derives its low nutritional requirements from these two sources.

First the blood supply of the sclera will be described and then the effect of isolating it from the choroid and episclera will be considered.

BLOOD SUPPLY OF THE SCLERA

Material and Methods

Rabbit and Cat

The animals were deeply anaesthetized with intravenous nembutal; immediately before death, the thorax was opened, the descending aorta clipped with artery forceps, and the left ventricle punctured with a wide-bore needle to which was attached a 50 ml. syringe. The corneae were then punctured in order to allow aqueous humour to escape, thus lowering the intra-ocular pressure and facilitating filling of the blood vessels. The right auricle was opened and the circulatory system irrigated with approximately 200 ml. 0·2 per cent. sodium nitrate solution. When the fluid from the right auricle was clear, 10 ml. Pelikan Indian ink (CII/143a) were injected, followed by approximately 1,000 ml. Rowney Kandahar black Indian ink (28). The size of the carbon particles in the Pelikan ink is small and therefore most of the vessels were filled.

Man

Eyes excised *post mortem* were injected with Indian ink (in the same sequence as in rabbit and cat) according to the technique of Ashton (1952).

* Received for publication May 22, 1967.

† Present address for reprints: Department of Ophthalmology, University of Cape Town, Groote Schuur Hospital, Cape Town, South Africa.

Clearing of the Sclera

A disc of cornea was excised and the intra-ocular contents were removed. The episclera was then dissected off the sclera. Each scleral shell was bleached in 0·1 per cent. potassium permanganate solution for 24 hours, and then washed with 2 per cent. oxalic acid solution until the red discoloration had been removed. This was followed by a wash with distilled water. The sclera was transferred to 70 per cent. alcohol for a few minutes and then put into pure glycerine at 37°C. for 2 hours before being finally placed in pure glycerine.

The rabbit and cat sclera became transparent within 1 hour, probably because it is thin, but it was impossible to render the human sclera entirely clear because of its relative thickness. With the aid of transillumination, however, the vessels in the human sclera were clearly observed.

Results

In the rabbit, the cat, and in man, the short and long posterior ciliary arteries together with the vorticose veins were observed to course through scleral channels without giving off branches or receiving tributaries. In man, however, capillaries were occasionally found in the sclera at the site of the insertions of the recti and inferior oblique muscles.

Apart from these vessels, the sclera was avascular except for the area anterior to the insertions of the recti and especially in the limbal region where a dense capillary system was observed.

In man, this vascular complex is considered to be important as it is related to the canal of Schlemm, but in the rabbit and the cat, where this canal is replaced by a plexus of vessels, the vascular complex is of less importance.

There were, however, some individual variations of this vascular complex in the rabbit, the cat, and in man.

In the rabbit, the vascular complex is formed by the anterior ciliary artery and is confined to the region of the limbus. It is a narrow plexus about 1 mm. wide and the arrangement is such that the vessels lie parallel to the axis of the limbus in both the superficial and deep aspects of the sclera (Fig. 1).

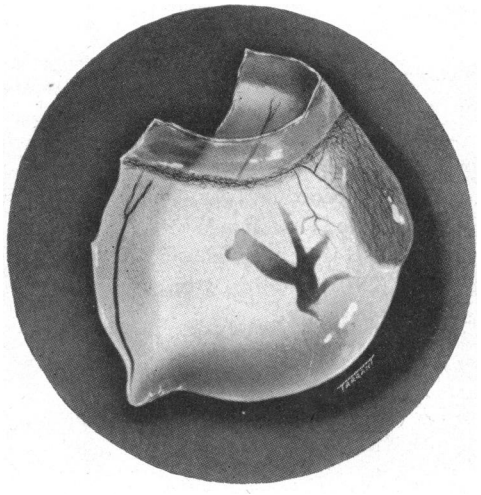

FIG. 1.—Anterior vascular complex in the rabbit confined to the immediate limbus.

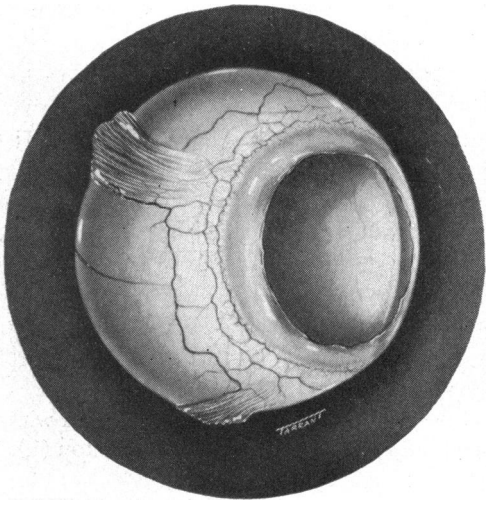

FIG. 2.—Anterior vascular complex in the cat, showing the three arcades.

In the cat, the complex arises from the anterior and posterior ciliary arteries. The anterior ciliary arteries form a primary arcade to which the long posterior ciliary arteries contribute. Two finer and less well-developed arcades are formed on the limbal side of this primary arcade and are connected by a superficial and a deep plexus, while fine capillaries emerge from the third arcade at right-angles to the limbus (Fig. 2, previous page).

In man, the vascular complex is formed by the tortuous anterior and posterior ciliary arteries. The anterior ciliary arteries form an arcade parallel to the limbus, from which a net-like plexus of superficial and deep vessels arises (Fig. 3). The posterior ciliary artery merges with this plexus, which is particularly dense in relation to the canal of Schlemm where an incomplete arterial circle is formed (arterial circle of the canal of Schlemm).

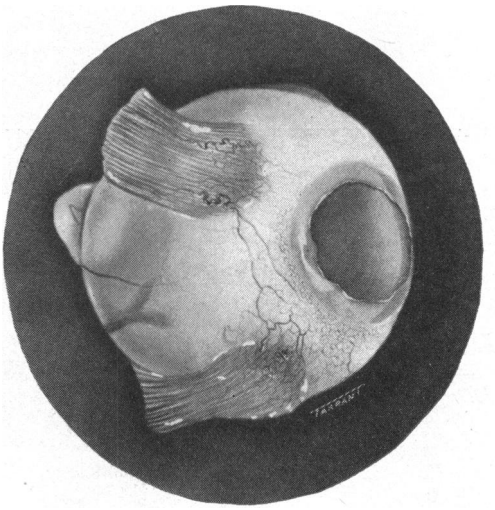

FIG. 3.—Anterior vascular complex in man, showing the primary arcade and the broad limbal plexus.

In addition, the essential drainage from the anterior chamber runs through the intrascleral plexus of veins into the anterior ciliary veins. Varicose collector channels arise from the outer aspect of the canal of Schlemm to form the deep scleral plexus, from which intrascleral branches pass to the episcleral plexus, while aqueous veins also pass directly from the ciliary venous plexus through the sclera, to empty directly into the episcleral venous plexus (Ashton, 1951, 1952a, b; Ashton and Smith, 1953).

EFFECTS OF EXPERIMENTAL OCCLUSION OF THE VASCULAR SUPPLY OF THE SCLERA

Material and Methods

Dutch rabbits with an average weight of 1,500 g. were used. Intravenous nembutal and inhalation of ether were given for general anaesthesia and amethocaine 1 per cent. was instilled into the eye.

A conjunctival flap based on the fornix was made and Tenon's capsule together with the episclera was reflected. Two incisions, 2·5 mm. long and 7·5 mm. apart, were made in the sclera between the superior and medial rectus muscles. A modified cyclodialysis spatula was used to detach the choroid from the sclera and a silicone plate 5 × 5 × 0·5 mm. was placed in the suprachoroidal space and sutured to the sclera. A similar silicone plate was secured to the episcleral side, thus isolating an area of sclera 5 mm. square from both the choroid and the episclera (Fig. 4, overleaf).

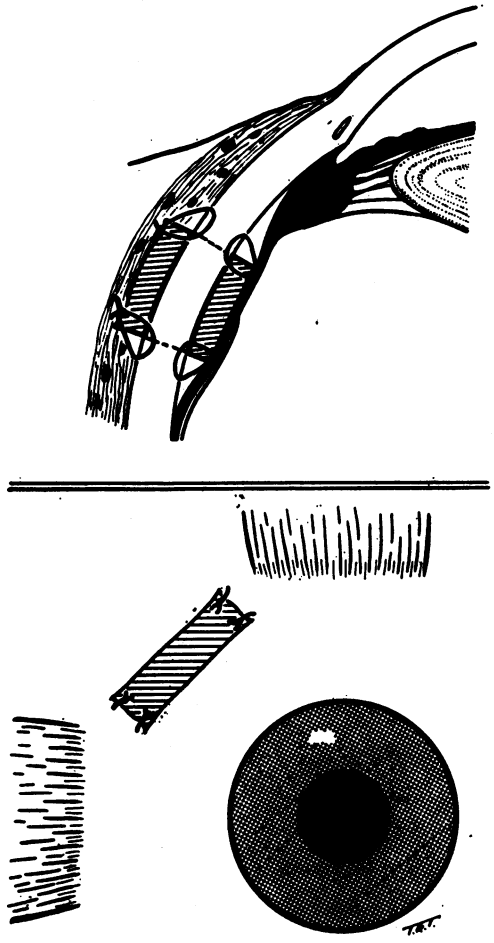

FIG. 4.—(1) Silicone plates in suprachoroidal space and in episclera sandwiching a scleral segment.

(2) Silicone plate between the superior and medial rectus muscles.

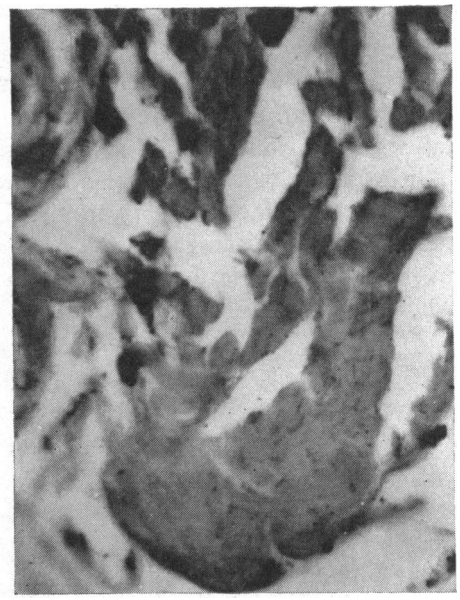

FIG. 5.—Occlusion of vascular supply to sclera for 1 week, showing hyaline change, malalignment of the scleral fibres, and apparent absence of the scleral nuclei. Haematoxylin and eosin. ×346.

Achromycin ointment and 1 ml. intramuscular Crystamycin were administered postoperatively daily for the first week and then twice weekly.

The rabbits were killed at intervals of 1, 2, 5, and 8 weeks, and the eyes were enucleated immediately after death. The portions of sandwiched sclera were removed and fixed in formol saline, and paraffin sections were examined histologically.

Results and Conclusions

One week after the operation, sections of sclera showed a hyaline appearance and with polarized light there was seen to be an apparent malalignment of the scleral fibres (Fig. 5). Later developments, however, indicated that these changes were not degenerative, but were probably due to altered hydration of the sclera following an initial inflammatory reaction to the operative procedure.

Specimens of sclera examined after the second and fifth weeks did not show necrosis or malalignment of the scleral fibres, and there appeared to be no reduction in the number of intrascleral cells (Figs 6 and 7, opposite).

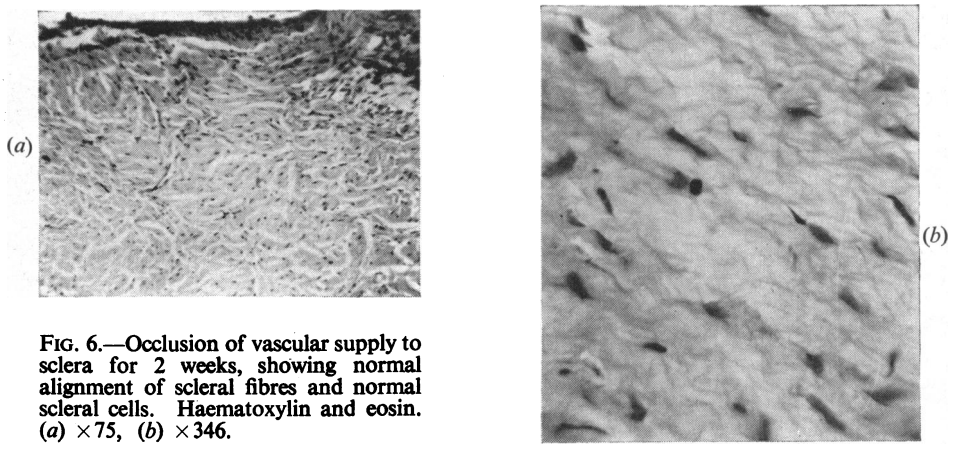

FIG. 6.—Occlusion of vascular supply to sclera for 2 weeks, showing normal alignment of scleral fibres and normal scleral cells. Haematoxylin and eosin. (*a*) ×75, (*b*) ×346.

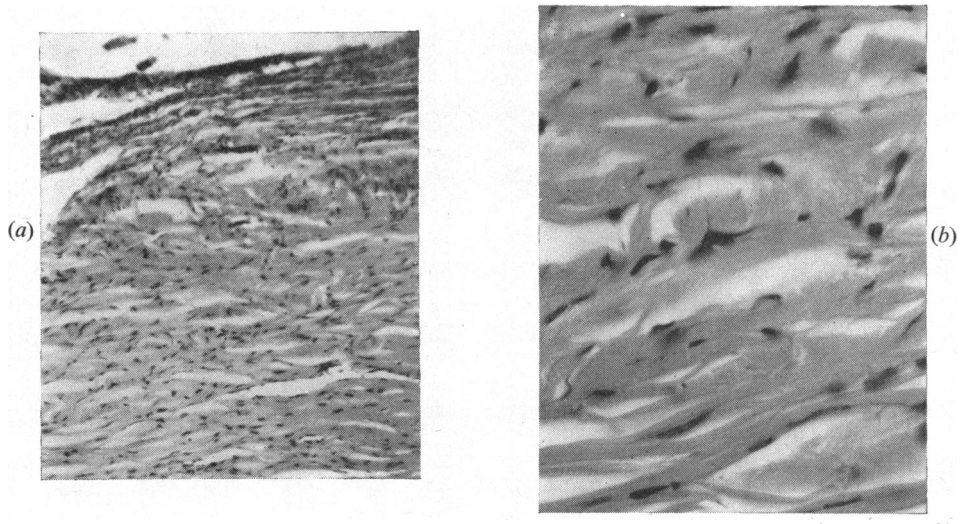

FIG. 7.—Occlusion of vascular supply to sclera for 5 weeks, showing normal alignment of the sclera, fibres, and normal scleral cells. Haematoxylin and eosin. (*a*) ×75, (*b*) ×346.

Specimens of sclera examined after 8 weeks showed thinning but no necrosis (Fig. 8, overleaf).

EFFECTS OF OTHER CAUSES OF OCCLUSION OF THE VESSELS OF THE SCLERA (Table, overleaf)

(1) Extensive Diathermy

To assess further the effect on the sclera of vascular occlusion, thirty eyes were examined from patients who had extensive diathermy for retinal detachment. In two of these cases cautery puncture had also been carried out and in four cases there had been a lamellar scleral resection.

(2) Irradiation

Eighteen eyes, which had been irradiated for malignant tumours, were examined. An average of 3,000–4,000 rads had been employed for retinoblastomata and 5,000–6,000 rads

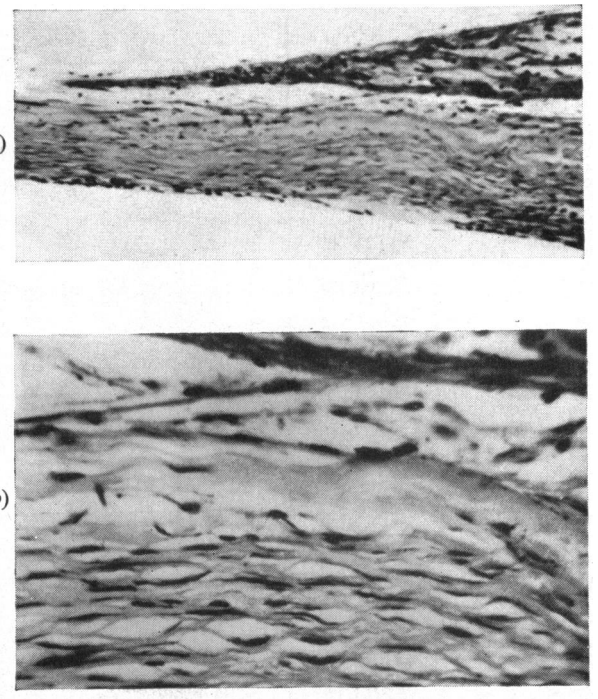

FIG. 8.—Occlusion of vascular supply to sclera for 8 weeks, showing scleral thinning, but normal alignment of scleral fibres and normal scleral nuclei. Haematoxylin and eosin. (*a*) ×75, (*b*) ×346.

TABLE
EFFECTS OF DIATHERMY AND IRRADIATION ON THE SCLERA

Procedure		No. with Granulomatous Reaction around Suture Material	No. with Scleral Scarring	No. with No Obvious Change
Surface Diathermy for Retinal Detachment (30)		1	16	14
Irradiation for	Retinoblastoma (13)	1	5	8
	Malignant melanoma (5)	—	1	4

for malignant melanomata. It is known that thrombosis may be produced in medium-sized vessels by a dosage of between 1,000 and 2,000 rads and that vessels in the vicinity of diseased tissue are probably more sensitive to irradiation.

Results

Examination of the sclera at the site of diathermy and irradiation showed that, although thinning was present in association with scarring, true scleral necrosis, as observed in necrogranulomatous scleritis, did not occur.

Discussion

Both clinical and experimental observations indicate that occlusion of vessels supplying a segment of sclera does not result in sequestroid or smudgy necrosis.

Scleral necrosis has been described by Girard and Beltranena (1960) at the original insertions of the rectus muscles which have been recessed after squint operations, but examination of the micrographs in the article shows that the altered scleral morphology is more likely to be due to scleral scarring (this complication was observed more frequently in adults than in children). Boniuk (1965) and Boniuk and Zimmerman (1961), however, examined 150 eyes which had been enucleated for complications after operations for retinal detachment and did not observe scleral necrosis.

Berman, Zauberman, and Michaelson (1966) found that in the adult cat the choroid could be stripped from the sclera by the injection of liquid silicone into the suprachoroidal space. Radioactive sulphate was then administered and after 5 minutes the animal was killed and both eyes enucleated. There was little difference in the radioactivity found where the choroid was detached as compared to the intact portions of sclera. These authors concluded that in the eye of the adult cat the choroid did not contribute to the nutrition of the sclera.

Sequestroid and smudgy necrosis do not occur after the exclusion of the choroidal and episcleral blood supply to a segment of sclera for 8 weeks, but it is possible that the segment of "sandwiched" sclera may obtain nutrition from its bordering attached ends, for Bill (1965) has shown that albumen and dextran are able to diffuse through the sclera.

A central focus of necrosis (fibrinoid, sequestroid, or smudgy) surrounded by a granulomatous reaction (polymorphonuclear leucocytes, eosinophils, lymphocytes, plasma cells, epithelioid cells, and giant cells) is a common feature of the necrotizing vasculitis group of diseases, particularly rheumatoid arthritis, polyarteritis nodosa, and Wegener's granulomatosis. These pathological features are also characteristic of negrocranulomatous scleritis and this suggests that the latter, as well as these three systemic diseases, may be in some way related and may reflect the same disease process despite the diversity of their clinical courses.

The appearance of fibrinoid necrosis surrounded by a granulomatous reaction is, however, not pathognomonic of the necrotizing vasculitis group of diseases (Klemperer, 1950). Askanazy (1921) demonstrated fibrinoid necrosis and inflammation at the base of gastric ulcers, and Wu (1937) observed similar changes in the vicinity of pancreatic necrosis after mechanical injury. Wilson and Pickering (1938) and Goldblatt (1937) reported that in animals made hypertensive by Goldblatt's technique, typical necrotizing arteritis commonly appeared in many organs. Byrom and Dodson (1948) found that increased intravascular tension was directly concerned in causing arterial necrosis in the hypertensive animal, and by inference, in human hypertensive disease.

It is not possible at present to be sure whether or not the necrosis in necrogranulomatous scleritis is a specific degeneration. A better understanding of the connective tissue diseases may give the answer.

Summary

(1) The blood supply of the sclera was demonstrated in rabbit, cat, and man, using injection techniques.

(2) A segment of sclera was "sandwiched" between two plates of silicone, to assess the effects of vascular deprivation. Neither sequestroid nor smudgy necrosis was observed.

(3) The sclera was also examined both at the site of surface diathermy (30 cases) for retinal detachment, and at the site of irradiation for retinoblastoma (13 cases) and malignant melanoma (5 cases). Scleral necrosis was not observed in the sections examined.

(4) It was concluded that the specific type of necrosis observed with necrogranulomatous scleritis was not due to ischaemia alone.

I should like to thank Prof. Norman Ashton for his invaluable advice and encouragement during the preparation of this investigation, and I am grateful to Miss E. M. FitzGerald for secretarial help and to Mr. A. McNeil and Mr. V. J. Elwood for their technical assistance.

This work was carried out during the tenure of the Alexander Pigott Wernher Memorial Trust Fellowship (administered by the Medical Research Council).

REFERENCES

ASHTON, N. (1951). *Brit. J. Ophthal.*, **35**, 291.
——— (1952a). *Ibid.*, **36**, 265.
——— (1952b). *Ibid.*, **36**, 465.
——— and SMITH, R. (1953). *Ibid.*, **37**, 577.
ASKANAZY, M. (1921). *Virchows Arch. path. Anat.*, **234**, 111.
BERMAN, E., ZAUBERMAN, C., and MICHAELSON, I. C. (1966). *Cited by* Michaelson, I. C. (1965). *Invest. Ophthal.*, **4**, 1004.
BILL, A. (1965). *Arch. Ophthal. (Chicago)*, **74**, 248.
BONIUK, M. (1965). Personal communication.
——— and ZIMMERMAN, L. E. (1961). *Arch. Ophthal. (Chicago)*, **66**, 318.
BYROM, F. B., and DODSON, L. F. (1948). *J. Path. Bact.*, **60**, 357.
GIRARD, L. J., and BELTRANENA, F. (1960). *Arch. Ophthal. (Chicago)*, **64**, 576.
GOLDBLATT, H. (1937). *J. exp. Med.*, **65**, 671.
KLEMPENER, P. (1950). *Amer. J. Path.*, **26**, 505.
SEVEL, D. (1965). *Trans. ophthal. Soc. U.K.*, **85**, 357.
WILSON, C., and PICKERING, G. W. (1938). *Clin. Sci.*, **3**, 343.
WU, T. T. (1937). *Virchows Arch. path. Anat.*, **300**, 373.