COMMUNICATIONS

PHOTOCOAGULATION OF THE RETINA*

OPHTHALMOSCOPIC AND HISTOLOGICAL FINDINGS

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SINCE the introduction of the photocoagulator by Meyer-Schwickerath (1954), the clinical application of this method has developed rapidly, but there have been relatively few experimental reports on the histological effects of photocoagulation (Nover, 1961; Kissen, Delaney, and Wachtel, 1961). The immediate and long-term histological effects of different intensities of photocoagulation are of great importance, and an attempt has been made to correlate the progressive clinical pictures with microscopic findings after photocoagulation of the rabbit's retina.

Material

Five adult normally-pigmented rabbits were used. In each eye three photocoagulations were done at different times, so as to study the histological appearance from 1 hour to 54 days after the photocoagulation. The animals were observed daily until the time when they were killed.

Method

The majority of coagulations were done with the intensity used in the clinic for cases of retinal holes and retinal detachment (Size diaphragm 6, Iris (intensity diaphragm) 2, Time $\frac{1}{2}$ sec. lower switch I, 45 amps, 22 volts). For comparison a few coagulations were done with a higher intensity (Size diaphragm 6, Iris (intensity diaphragm) 2, Time $\frac{1}{2}$ sec. upper switch I, 68 amps, 26 volts). The pupils were kept dilated with atropine 1 per cent., scopolamine 0.25 per cent., and neosynephrine 10 per cent. After the animals had been killed, the enucleated eyes were fixed in formalin. After coronal section of the globe, the fundal lesions were identified by slit-lamp examination and trephined out for histological sectioning and staining with haemalum and eosin.

One human eye with malignant melanoma of the choroid was also examined histologically 8 days after experimental photocoagulation of a normal portion of the fundus with a low-intensity dose.

Observations

Clinical

Immediately after the coagulation a white, raised area appears, which becomes

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surrounded by a transparent pinkish ring; this is easily visible 6 hours after the coagulation (Fig. 1).

One day after the coagulation the white centre is still visible, the pink ring around it becomes brownish, and the whole becomes surrounded by a very delicate pigmented ring.

Between the 2nd and the 7th day pigment appears in the centre of the white area; this is very delicate to begin with but becomes progressively coarser and advances towards the periphery of the lesion. Simultaneously the pigmented ring in the periphery becomes coarser and wider.

Between the 7th and the 14th day the white area becomes less and less visible under the pigment covering. This area sometimes becomes atrophic before being covered by the central pigment.

From the 14th to the 21st day the pigment becomes denser and, in some cases, it is dispersed in the vicinity of the focus of coagulation. From the end of the 3rd week, no clinical changes in the fundus picture occur.

This description is very similar to that reported in the rabbit by Nover (1961), and it also resembles the changes observed after photocoagulation in pigmented human eyes.

Histological

After 1 Hour (Fig. 2).—The retina is several times thicker than normal. The outer nuclear layer and the rod and cone layer appear to be folded or shrunken inwards, displacing the inner part of the retina towards the vitreous. The nerve fibre layer shows marked oedema, suggesting that the fine vessels of the retina have been affected by the rise in temperature of the retinal tissues.

FIG. 2.—Lesion 1 hour after coagulation. $\times 75$.

FIG. 1.—Clinical appearances of lesion produced by photocoagulation:

1. Immediately after coagulation.
2. 6 hours after coagulation.
3. 1 day after coagulation.
4. 2-7 days after coagulation.
5. 7-14 days after coagulation.
6. After the 14th day.

There is oedema and cellular infiltration of the choroid. The raised white area observed clinically is no doubt evidence of both the retinal oedema and the cellular infiltration of the choroid.

The inner part of the sclera shows some loss of acidophilic staining.

The vitreous overlying the lesion shows little if any change.

After 1 Day (Fig. 3).—The apparent thinness of the retina is probably an artefact caused by the tearing of the internal limiting membrane during the histological preparation (Fig. 3A). The marked oedema of the affected retina is well seen at the edges of the lesion, photographed with high power (Fig. 3B, 3C).

FIG. 3.
(A) Lesion after 1 day. $\times 26$.

FIG. 3.
(B) Margin of (A). $\times 100$.

FIG. 3.
(C) Margin of (A). $\times 100$.

The rod and cone layer does not show the normal striation, and is of a generally necrotic appearance. The nuclear layers are compressed together, the outer molecular layer being absent in most places. On the other hand the inner molecular layer is relatively well represented. The nerve fibre layer is markedly oedematous, and the ganglion cell layer is represented by a few shrunk-en nuclei. Locally the retina and choroid are slightly separated from each other by oedematous fluid (Fig. 3D).

FIG. 3.

(D) The retina and choroid are slightly separated from each other.

The local choroid shows polymorph infiltration. The sclera shows distinct loss of nuclear staining. The vitreous shows some mild changes localized to the lesion.

The circle of delicate pigment noted clinically after 1 day could not be definitively identified histologically, but no doubt represents a reaction by the pigment layer. The persistence of retinal oedema noted after one hour can be observed at this stage chiefly in the nerve fibre layer.

After 4 Days.

(a) LOW INTENSITY (Fig. 4).—The retina is thinned because of the lessening of the oedema. The rod and cone layer is amorphous. The few ganglion cells which can be seen are small and shrunken.

FIG. 4.—Lesion after 4 days (low intensity). $\times 60$.

The choroid locally appears to be oedematous. There is adhesion between the retina and choroid, and perhaps between choroid and sclera. The sclera appears to have more nuclei than on the first day, but still less than normal. The adhesion is shown by an artefact, a local separation of the retina.

(b) HIGH INTENSITY (Fig. 5A, B).—The retina is thinned because of the lessening of the oedema. It has lost its architecture and its outer part shows some pigment clumps, which are more concentrated in the centre of the lesion, corresponding to the clinical picture.

FIG. 5.—Lesion after 4 days (high intensity).

(A) Retina and choroid adherent to one another. $\times 38$.

(B) Cavitation in sclera. $\times 100$.

The choroid and retina are very closely adherent over a large area, and it is very difficult to detect the line of demarcation between them. The local choroidal

vessels are dilated for a short distance on each side of the lesion. There is a loss of tissue, appearing as a cavitation, in the sclera. The vitreous opposite the focus shows no gross changes.

After 6 Days.—The loss of retinal oedema has continued, and the retina is reduced to a very thin layer (Fig. 6). There is a gross proliferation of the pigment epithelium, especially at the central part of the lesion. At the edge of the area can be seen the shelving nature of the retinal destruction. The most extensive change in the retina is the loss of the rod and cone and the nuclear layers, particularly the outer nuclear layer. The limiting membranes seem to be the most resistant tissues.

The choroidal vessels cannot be seen in the scar. There is marked local pigmentation of the choroid. The sclera has returned to its normal appearance.

FIG. 6.—Lesion after 6 days, showing pigmentation at the margin and in the centre. $\times 100$.

After 9 Days.—This is similar to the 6-day-old-lesion, except that the clumps of pigment are bigger and rounder (Fig. 7).

FIG. 7.—Lesion after 9 days (low intensity). $\times 100$.

The pigmentation is more marked if the intensity of light is greater (Fig. 8, opposite). The pigment is of two types: proliferation of pigment epithelium *in situ*, and migration of pigment into the retinal scar.

A few narrow choroidal vessels are visible. A fine, delicate scar tissue is present throughout the affected choroid.

FIG. 8.—Lesion after 9 days (high intensity). $\times 100$.

After 18 Days.—The atrophy of the retina has progressed until it is reduced almost to the internal and external limiting membranes, with contained pigment clumps (Figs 9 and 10). The retina remains densely attached to the choroid.

FIG. 9.—Lesion after 18 days. $\times 100$.

FIG. 10.—Lesion after 18 days. $\times 100$.

After 23 Days.—The retina is reduced to a thin heavily pigmented layer, in which no architecture can be observed. It is strongly adherent at the edge of the lesion to the pigment epithelium, which is thickened. The choroid opposite the scar shows few blood vessels.

After 31 Days.—The atrophied retina is now almost completely filled with pigment (Fig. 11).

FIG. 11.—Lesion after 31 days. $\times 118$.

After 54 Days.—The static atrophic pigmented state of the retina is well seen in Fig. 12.

FIG. 12.—Lesion after 54 days. $\times 63$.

The pigment epithelium cells show no tendency to infiltrate the choroid. There are many fibroblasts in the choroidal scar (Fig. 13, opposite).

FIG. 13.—Lesion after 54 days, showing fibroblasts within choroidal scar. $\times 330$.

Human Eye

Fig. 14 is taken from the human eye, 8 days after low-intensity photocoagulation. The picture is similar to those of the 6th and 9th day in the rabbit (see Figs 6 and 7).

The pigment epithelium has proliferated and is seen to be invading a retina which appears to be otherwise empty.

FIG. 14.—Human eye; 8 days after coagulation (low intensity). $\times 100$.

Bruch's membrane is interrupted in places and shows loss of its normal straightness (Fig. 15, overleaf). Unlike the rabbit choroid the human choroid shows a gross enlargement of the vessels, including the chorio-capillaris. There is much noncellular infiltration between the vessels.

FIG. 15.—Human eye; 8 days after coagulation, showing irregularity of Bruch's membrane. $\times 280$.

Discussion

The histological changes described above suggest that the pattern of evolution in the retina consists of two stages; one of immediate tissue destruction and oedema, and the other of progressive lessening of oedema and infiltration of the atrophic retina with pigment. The first stage is visible until the 4th day, and the second stage progresses until the end of the 3rd week, after which the condition of the retina is more or less static.

It is possible that the first-stage oedema is caused by a lesion of the capillaries in the inner part of the retina as well as of the chorio-capillaris. The capillary changes and the tissue destruction result from the heating of the pigment epithelium, which absorbs the radiations.

Although there is a slight separation of the retina and choroid on the first day this has disappeared by the 4th day, and the demarcation between retina and choroid is hard to see. This is similar to the findings of Kissen and others (1961). The firmness of the retino-choroidal adhesion on the 4th day is shown in Fig. 4, where the artificial retinal separation resulting from the sectioning, does not involve the coagulated area.

The changes in the choroid may also be divided into two stages; the first lasts until about the 4th day, and consists of vascular engorgement, oedema, and cellular infiltration. The second includes more or less complete obliteration of the choroidal vessels, with formation of scar tissue. New vessel formation in the scar could not be determined.

In the human eye the first stage appears to last longer than in the rabbit.

The scleral changes also appear to be divided into two stages; the first, lasting until the 6th day, consists of a loss of staining of the stroma and of nuclear staining, and the second shows a gradual recovery to a normal appearance. With higher intensity the first stage may show cavitation.

The vitreous shows no definite histological changes.

The histological cause of the raised white opacity seen immediately after coagulation is coagulation necrosis of the retinal tissue, oedema of the retina which raises the internal limiting membrane, and cellular infiltration of the choroid. The red halo surrounding the white opacity probably represents dilatation of the choroidal vessels. The fine peripheral pigment line seen clinically for the first day or two could not, as already stated, be identified histologically. The central pigment clumps seen between the 2nd and 7th day are due to proliferation of the pigment epithelium. The progressive pigment changes, beginning between the 7th and 14th day and continuing for a week or two beyond this period, represent the filling of the atrophic retina contained between the internal and external limiting membranes, by invading pigment clumps.

An important decision in the treatment of patients with photocoagulation concerns the time when the patient should leave hospital. It is probably wise that this should be delayed until the oedema of the retina and choroid has passed, and until a fine adhesion has formed between the retina and choroid. The above findings suggest that these changes are complete by about the 4th day.

A further point of clinical importance is the decision regarding the patient's return to normal life. The migration of pigment into the retina, as compared with its proliferation, probably indicates that the adhesion between the retina and the choroid is strongly formed. This was found to be in progress by the 9th day, in man as well as in the rabbit (Figs 7 and 15). It would therefore appear to be safe, in at least the less severe cases, to permit the patient to return to normal life at the end of the second week.

Summary

1. The evolving clinical picture in photocoagulation of the rabbit fundus is described and is correlated with the histological changes.
2. The similarity between the clinical and histological pattern in the rabbit and man is shown.
3. Conclusions are drawn regarding the time when the patient may be permitted to leave hospital and return to a normal life.

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