FIBRIN FILM IN NEUROSURGERY, FURTHER STUDIES

THE INSERTION OF FIBRIN FILM BETWEEN THE SUTURED DURA AND THE INTACT LEPTOMENINGS; THE EFFECT OF ROENTGEN THERAPY ON TISSUE REACTIONS TO FIBRIN FILM*

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I. THE USE OF FIBRIN FILM IN CRANIOTOMIES

In previous experimental and clinical studies, it has been shown that fibrin film is a valuable dural substitute and is effective in the prevention of meningocerebral adhesions. Additional experiments have been carried out to determine whether there was any advantage in using fibrin film in craniotomies in which no dural defect is left. It also seemed desirable to study experimentally the effect of roentgen therapy on wounds in which fibrin film had been implanted, since the material has found a considerable place in the surgery of central nervous system tumors.

The selection of cases in which fibrin film should be used depends upon the expected probability of scar and adhesion formation. In operations where the brain and dura are traumatized or sections of dura are removed, it is desirable to close the dural defect with fibrin film. To test whether this material should be used following intracranial operations in which the dura is completely closed after little manipulation of the brain and leptomeninges, we have performed temporoparietal craniotomies in monkeys with and without insertion of fibrin film under the sutured dura.

It is generally thought that trauma to the leptomeninges is required for the formation of adherent meningocerebral scars. In the course of our studies with fibrin film we have made several observations suggesting that in monkeys no detectable injury is required. In our earlier experiments designed to show the effect of fibrin film in preventing meningocerebral adhesions, circular sections of the dura were removed and replaced with fibrin film. Adhesions did not form after implantation of fibrin film, whether or not the leptomeninges had been injured. In 3 control animals the fibrin film was omitted. Two of these developed firm adhesions between the brain and the temporal muscle even though the leptomeninges had not been visibly dam-

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aged. Further evidence that adhesions may form without apparent injury to the leptomeninges came from 2 of the animals in which fibrin film had been implanted. In each case the disc of fibrin film had slipped, leaving approximately one half of the dural defect uncovered. In both of these animals, adhesions formed in the area not covered by fibrin film even though trauma to the leptomeninges had been carefully avoided, but the portion in which the fibrin film remained in place was entirely free from adhesions.

Experiments. In 4 monkeys (Macaca mulatta) bilateral temporoparietal bone flaps were made. With the animal under nembutal anesthesia the scalp was prepared and a longitudinal midline incision was made extending from the brow to the external occipital protuberance. The scalp was mobilized and reflected downward, first on the left. A trapezoidal bone flap was made with four burr holes, its upper edge parallel with the longitudinal sinus (Fig. 1). The dura was then opened for a distance of about 6 cm. A rectangle of fibrin film was placed

Fig. 1. Craniotomy. The bone flap has been raised, exposing the dura.

Fig. 2. Brain and dura separated after fixation. A faint discoloration of the dura near the suture line was caused by the fibrin film.
under the edges of the dura after which closure was carried out with interrupted silk sutures. The bone flap was ligated in place and the temporal muscle and fascia were closed. An identical operation on the opposite side was performed without the insertion of fibrin film. The scalp was then closed with subcuticular sutures. Two of the 4 animals were sacrificed after 3 months and 2 were sacrificed 6 months following operation. The hemispheres of the brain were fixed intact within the skull.

Results. In no case had adhesions formed on the side where fibrin film had been inserted. A faint brownish color on the inner surface of the dura marked the site of the fibrin film (Fig. 2). On the opposite side, however, adhesions were present in all of the animals. A row of small firm adhesions underlay the interrupted sutures. When the brain was separated from the dura small fragments of the cortex were pulled out by several of the adhesions. Microscopic sections from one of the animals sacrificed after 6 months are shown in Fig. 3. Where fibrin film was used (Fig. 3a) the characteristic membrane produced by this material is seen to underlie the sectioned silk suture. On the opposite side (Fig. 3b) the suture is surrounded by a larger mass of inflammatory tissue which was adherent to the brain.

These experiments show that in the monkey small but firm adhesions may form between the brain and the dura where silk sutures used to close the dura lie in contact with leptomeninges. This is in agreement with the findings of Lear and Harvey. When fibrin film is placed under the sutured dura the adhesions do not form.
It is often desirable to use fibrin film in patients who may later require roentgen therapy. The possibility that roentgen rays may change the fibrin film itself or the reaction of tissues to it made it desirable to study the effect of roentgen rays on the tissue reaction to this material.

Physical Studies. Fibrin film is an insoluble protein which has been denatured by heat. This treatment is required to prevent quick absorption of the material and serves as a convenient means of sterilization. The degree of heating can be varied within moderate limits without affecting the tissue reactions to the fibrin film. The effect of roentgen rays on proteins in general is to cause denaturation and flocculation. Chemical changes in certain amino acids have been observed but changes in previously denatured proteins have not been recognized. These substances are thought to be unaffected by moderate exposure to roentgen rays. To confirm this impression for the special case of fibrin film, a strip of sterilized fibrin film was moistened with saline and was then exposed to the contact roentgen therapy apparatus which provides for maximum absorption in the first few mm. The time of exposure was 10 minutes; the apparatus was operated at 50 kV. and 2 mA. with an aluminum filter of 1.0 mm., target distance of 21 mm. and a 3 cm. portal of entry. The half-value layer of this radiation was 0.88 aluminum. The total roentgen dosage was 8,000 r (measured in air). The quantity absorbed by the fibrin film should exceed by a factor of at least 10 the amount absorbed when

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**CHART I**

<table>
<thead>
<tr>
<th>FILM</th>
<th>MAMS FIBRIN PER CM²</th>
<th>FIBRIN CONTENT SWOLLEN</th>
<th>TENSILE STRENGTH GMS. PER MM²</th>
<th>MAXIMUM ELONGATION PER CENT</th>
<th>DIGESTION TIME 1% TRYPSIN HHS 37°C</th>
<th>SWELLING INDEX</th>
</tr>
</thead>
<tbody>
<tr>
<td>STANDARD</td>
<td>12.5</td>
<td>6.02</td>
<td>780*</td>
<td>273*</td>
<td>1.6 at 4 HRS. 2.0 at 17 HRS.</td>
<td>3.9</td>
</tr>
<tr>
<td>ROENTGEN TREATED</td>
<td>15.5</td>
<td>6.07</td>
<td>873*</td>
<td>283*</td>
<td>1.8 at 4 HRS. 1.9 COMPLETELY DIGESTED</td>
<td>4.3</td>
</tr>
</tbody>
</table>

* Average of four estimations
* Weight in mams
* 1 Molar solution
deep roentgen therapy is given to patients with implanted fibrin film. This fibrin film was then submitted to the tests which have been used to standardize this material. Chart I shows the results of these tests compared with those for a standard sample of fibrin film. The difference between the two sets of figures are all within the range of experimental error and the roentgen rays could not be said to have changed the physical characteristics of the film. Since in heat modification of fibrin film, changes detectable by these tests appear before any change in the tissue response to fibrin film, it can be assumed that a very wide margin of safety exists in roentgen therapy as far as the effect on the fibrin film is concerned.

Living tissues, in contrast to such materials as denatured proteins, are highly sensitive to the effects of roentgen rays. The principal changes are those leading to cellular death and carcinogenesis, both thought to result from chromosome damage. Such functions as respiration, glycolysis, nitrogen and enzyme activity are not affected by even large doses of radiation. Chromosomes are especially sensitive because of their exact molecular structure where the shift of a single bond may greatly alter the genetic behavior of the cell. The inflammation commonly seen during roentgen therapy is caused by the reaction of the tissues to the presence of cells destroyed by roentgen rays. From this discussion it would appear that on theoretical grounds no specific change in the tissue reaction to materials like fibrin film could be expected with roentgen therapy. On the other hand, the presence of low-grade inflammation in the surrounding tissue might in some way alter the tissue response.

* We are indebted to Dr. John M. Newell of the Antitoxin and Vaccine Laboratory of the Massachusetts Department of Public Health for conducting these tests.
Experiments. Three experiments were performed, each with 2 monkeys (Macaca mulatta). Fibrin film was inserted through a subtemporal decompression in the first pair of animals after which roentgen therapy was given without operation. Fibrin film was implanted in the third pair but roentgen therapy was omitted. The operations and histological preparations were done by the technique previously described. Roentgen treatment was begun 10 days after the operations and a total of 3,000 r units was given to each of the treated animals through 2 portals sufficiently long to cover the operative field. For each treatment the K.B. was 200, M.A. 10, Filter 1.0 aluminum +0.5 mm. Cu, target distance 50 cm., H.V.L. 1.05 mm. Cu, and the period of exposure 11 minutes. One animal of each pair was sacrificed 2 weeks after the completion of roentgen therapy and the second after an interval of 2 months. In the animals that did not receive roentgen therapy the same time schedule was followed.

Results. Symptoms of roentgen ray sickness were not detected in any of the animals. The gross and microscopic appearance of the brains, meninges and fibrin film did not differ from that previously described in normal animals.

CHART III

<table>
<thead>
<tr>
<th>TECHNICAL DATA ON ROENTGEN THERAPY</th>
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<tr>
<td>J.D</td>
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<tr>
<td>-----------------</td>
</tr>
<tr>
<td>NUMBER OF PORTALS</td>
</tr>
<tr>
<td>NUMBER OF TREATMENTS</td>
</tr>
<tr>
<td>FREQUENCY OF TREATMENTS</td>
</tr>
<tr>
<td>SINGLE DOSE (R IN AIR)</td>
</tr>
<tr>
<td>TOTAL DOSE (R IN AIR)</td>
</tr>
<tr>
<td>KILOVOLTAGE</td>
</tr>
<tr>
<td>TARGET - TO - SKIN DISTANCE (CM)</td>
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<tr>
<td>MILLIAMPERAGE</td>
</tr>
<tr>
<td>FILTER (MM)</td>
</tr>
<tr>
<td>PORTAL SIZE (CM²)</td>
</tr>
<tr>
<td>HALF VALUE LAYER (MM) OF COPPER</td>
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</table>

Clinical Studies. Nineteen patients have received roentgen therapy following operations at which fibrin film was used. In none of these were clinical changes produced by the material. Five of the operative wounds were inspected after roentgen therapy, 3 at secondary operations and 2 at autopsy (Chart II). No change in the appearance of the fibrin film and its tissue response had been produced by the roentgen therapy. Chart III shows the technical data for the roentgen therapy in these cases.
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SUMMARY

1. Further studies of the behavior of fibrin film when used to cover the brain and leptomeninges are presented. In uncomplicated craniotomies performed on monkeys (Macaca mulatta) meningocerebral adhesions form under the sutures used to close the dura. Fibrin film prevents this complication.

2. Roentgen therapy in the doses used for treatment has no detectable effect on fibrin film or the reaction of the meninges to this material.

REFERENCES