Cellolite (Merocel): a new form of neurosurgical patty
Evaluation of histological responses in rats

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Cellolite and cottonoid were compared with regard to histological reactions provoked when they were left in contact with the rat brain. Pieces of each material were implanted in 27 rats either extra- or intracerebrally for 48 hours or 28 days. Histological findings suggest that the use of Cellolite for neurosurgery would be unlikely to cause adverse reactions any worse than those caused by cottonoid.

KEY WORDS • surgical patty • biocompatibility • cottonoid • polyvinyl alcohol formaldehyde • Cellolite • Merocel

In the course of surgery, neurosurgeons make frequent use of cottonoid patties (or "paddies") to stem hemorrhage and to protect the exposed brain. During these surgical procedures, patties are often in contact with the brain for a long time, sometimes for hours. Before the end of an operation, surgeons take meticulous care to remove all the patties used, except on rare occasions when it is undesirable to remove a particular one. It is essential that a patty should not have unacceptable consequences however long it remains in contact with the brain. Extensive searches indicate that very little has been published concerning the effects of cottonoid on the brain. However, it is generally agreed that this material is suitable for making patties for use in neurosurgical procedures.

A form of patty material (Cellolite*) has been produced as an alternative to cottonoid. Cellolite is made of a polyvinyl alcohol foam cross-linked with formaldehyde and impregnated with particles of barium sulfate. If this material is to be considered for neurosurgical use, it is desirable to ensure that it causes no cerebral reactions that are greater than those provoked by cottonoid.

With this in mind, we undertook the present study to compare Cellolite and cottonoid with respect to the pathological changes that ensue when these materials are placed on or into the rat brain for a short time (48 hours) or longer (28 days).

Materials and Methods

Each rat had a piece of Cellolite implanted on one side of the head and a piece of cottonoid on the other. Cards individually numbered for each rat† were placed in a box. The cards were drawn at random to determine the sides (left or right) and the sites (extracerebral or intracerebral) for the implanted materials, and also the period (48 hours or 28 days) for which the brain was to be exposed to them. Small pieces of Cellolite and cottonoid‡ were cut and, depending on the results of the draw, were placed upon or within the brains of 27 male rats (age range 3 to 6 months) weighing 290 to 415 gm (mean 370 gm).

*Cellolite, supplied by Smith and Nephew Research Ltd., Gilston Park, Harlow, Essex, England, is also known as Merocel, produced by Americal Corp., Mystic, Connecticut.

†Wistar strain rats, outbred, obtained from Animal Supplies (London) Ltd., Roebuck Farm, Pottersheath, Welwyn, Hertfordshire, England.

‡Cottonoid patties sold commercially by Downs Surgical Ltd., Church Path, Mitcham, Surrey, England.
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Operation

Each rat was anesthetized with intraperitoneal phenobarbitone and allowed to breathe spontaneously throughout the procedure. Employing aseptic techniques, the vertex of the skull was exposed through a sagittal incision in the midline of the scalp. Bilateral craniectomies and later stages of the procedure were performed with the aid of an operating microscope.

In 13 animals, the patty material was placed on the surface of the thin transparent meninx corresponding to the dura mater overlying the exposed brain. Cottonoid was placed on one side and Cellolite on the other. Each material was inserted and kept in place by tucking its periphery under the bone edges of the craniectomy. One animal from this group died during surgery (presumably from hypoxia), leaving 12 survivors.

In 14 animals, a tenotome held perpendicular to the cerebral surface was used to make a coronal incision in the exposed brain to a depth of 2 to 3 mm. The material appropriate to a given side was then inserted into the incision so that it lay entirely within the cerebral substance. A small piece of patty material similar to the buried piece was placed on the superficial surface of the exposed brain with its periphery tuckied under the edges of the craniectomy.

When the implants were completed, the scalp incisions were closed with metal staples. The craniectomy defects were left unfilled.

Postoperative Course

Except for the one animal that died during the operation, all others recovered from the procedure in an unremarkable fashion and remained in good health until the time of sacrifice. Throughout the study the rats were given a standard diet.

Results

Short Survival (48 hours)

Group 1. Six rats underwent the extracerebral application of the material. For both types of materials, the cerebral changes varied from minimal superficial depression of the cortex at the sites of the implants (Fig. 1 upper left) to edema, necrosis, and mild to moderate monocellular reaction either in the meninx or in the underlying brain.

In each of three rats, the local histological response to cottonoid and to Cellolite was equal in degree. In the remaining three rats, cottonoid produced a reaction more severe than that provoked by Cellolite.

Group 2. Six rats underwent the intracerebral implantation of the material. For both materials, the meninx, when preserved in the section, showed thickening due to mild proliferation of meningeal cells. In the brain adjacent to either material, there was vascular congestion and gliosis, together with small numbers of mononuclear cells with foamy and hemosiderin-containing macrophages in some of the specimens.

The cottonoid tended to produce greater mechanical damage. It was found within defects shaped like clefts or craters, with edema and necrosis of the adjacent gray and white matter (Fig. 1 upper right). On the other hand, Cellolite produced smaller cavities with ragged edges often mixed with fibrin and red cells. The cottonoid also caused a moderately severe foreign-body giant-cell reaction that was not found with Cellolite.
Fig. 1. Cross sections of the implantation sites. The hole in the sections indicates the right side of the specimen. Cellolite is indicated by the single arrowhead, and cottonoid by the double arrowhead. For microscopic description see text. Upper Left: Group 1 rat brain shows a bilateral superficial cortical depression. Luxol fast blue, × 5.5. Upper Right: Group 2 rat brain shows greater disruption associated with cottonoid. Luxol fast blue, × 5.5. Lower Left: Group 3 rat brain shows a patch of chronic granulomatous reaction to cottonoid. Luxol fast blue, × 5.5. Lower Right: Group 4 rat brain. The cavity about the cottonoid is larger than that about the Cellolite. H & E, × 8.

**Longer Survival (28 days)**

Group 3. Six rats underwent the extracerebral application of the material. In this group, the local cellular reaction varied from minimal changes, such as localized areas of necrosis or edema, to a foreign-body giant-cell reaction of moderate degree surrounding the implanted material (Fig. 1 lower left). There was some local reaction in every specimen examined.

In three rats, the reaction to Cellolite was of similar degree to that produced by cottonoid. In two rats, the response to Cellolite was more severe than that to cottonoid, and in one rat cottonoid provoked the greater response.

Group 4. Eight rats underwent the intracerebral implantation of the material. For both Cellolite and cottonoid, the reaction included the presence of lymphocytes, plasma cells, foamy and hemosiderin macrophages, and foreign-body giant cells. In general, the cellular inflammatory reaction to the test materials was more marked for rats in this group than for the intracerebral implants in the rats of Group 2. The changes were less marked about the Cellolite than about the cottonoid implants. For either material, the implant tended to lie within a smaller cavity than was seen in Group 2, but generally the cottonoid elicited a denser gliotic reaction in the adjacent brain. The cottonoid was not invaded by cells or fibrin. However, at the same stage after surgery, fibrin and cells were clearly woven within the interstices of Cellolite (Fig. 1 lower right).

**Discussion**

Animals are commonly used to study the biological response to foreign materials that may be implanted in
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human subjects during surgical procedures. At present, no published guidelines exist for testing materials used for neurosurgical patties, although guidelines are available for testing surgical materials used in other parts of the body. The present experiment conforms in general with the guidelines suggested in this publication, although the latter does not specifically cover implants in the brain.

The pieces of material implanted were gross in relation to the size of the rat brain so that our results may exaggerate the mechanical effects of small patties when implanted intracranially in humans. However, the rat brain appears to provide a suitable means of assessing the histological changes when these materials are implanted in contact with the brain.

Forty-eight hours after the extra- or intracerebral application of patty material, the mechanical damage to the brain and the cellular response were a little less severe with Cellolite compared with cottonoid. Twenty-eight days after implantation within the brain, the Cellolite and cottonoid had both elicited the acute and chronic inflammatory changes that occur in response to foreign material. This cellular response and the accompanying glial reaction were less marked in the vicinity of Cellolite than in the region immediately surrounding the cottonoid. This finding may reflect differences between the two materials in their composition and physical structure. According to the manufacturers, Cellolite is a polyvinyl alcohol foam, cross-linked with formaldehyde and having particles of barium sulfate embedded in the final product. The cottonoid supplied consists of regenerated cellulose fiber (cottonoid is not “cotton” any more). In cottonoid, the fibers are closely packed, while Cellolite has a looser matrix with larger interstices. The initial impression is that Cellolite is softer and more flexible. Differences such as these probably account for the finding that implanted cottonoid leads to greater immediate cerebral damage than does Cellolite from local pressure applied to the adjacent brain.

Twenty-eight days after intracerebral implantation, cottonoid also appears to provoke greater reaction than does Cellolite in the adjacent brain. However, whereas cottonoid tends to be walled off by this response, the process of repair and organization seems to involve the Cellolite itself, which had fibrin and cells woven into it in the later specimens.

In summary, the present findings indicate that if Cellolite were used in human neurosurgery it would be unlikely to cause adverse reactions any worse than those caused by cottonoid. We intend in no way to comment on the relative merits of Cellolite with respect to its absorbency, its ease of handling with surgical instruments, or its ability to conform to the surface of the brain or blood vessels, although, in addition to the histological response provoked by Cellolite, these considerations are extremely important in deciding its suitability for neurosurgical practice.

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Reference


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