BRITISH MEDICAL JOURNAL

LONDON SATURDAY MARCH 30 1940

A NEW METHOD OF PREVENTING ADHESIONS

THE USE OF AMNIOPLASTIN AFTER CRANIOTOMY

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(WITH SPECIAL PLATE)

Laceration of the brain which is the outcome of gunshot wounds of the head, depressed fracture of the skull, and cranio-cerebral operations results in meningo-cerebral adhesion. The adjacent brain comes to be vascularized through a scar from extracerebral blood vessels. This is a most important element in the production of post-traumatic epilepsy.

Following the last war Wagstaffe (1928) made a critical study of the end-results in a series of soldiers who had received severe head injuries. He found that 1.6 per cent. of these patients became epileptic when the dura had not been penetrated, whereas 18.7 per cent. of those whose dura had been perforated developed post-traumatic epilepsy. It seemed obvious from his figures that penetration of the dura rendered epileptiform seizures ten times more likely to occur. Steinthal and Nagel (1926) concluded that severe injury to the brain resulted in frank epilepsy in 28.9 per cent. and lesser forms of epilepsy in 35.5 per cent., making a total of 64.4 per cent. In the scars that result from such injuries must lie the secret of the high incidence of post-traumatic epilepsy, which may appear at any time up to ten or fifteen years after the injury (Penfield, 1924, 1927). Head injury without penetration of the dura rarely results in epilepsy, although the brain damage may be, and often is, greater. In such cases adhesions, if they form at all, are much less severe, and blood vessels rarely grow down through the scar and into the brain.

The need for a method to exclude the brain from superficial scars is apparent—a method of restoring the subdural space that separates with a thin layer of fluid the pachymeninx from the leptomeninx. The use of amniotic membrane prepared as described below (amnio-plastin) seems to solve this problem.

Experimental Study

In a series of cats the bone and dura were removed over the cerebral hemispheres. The underlying pia was then injured by multiple needle pricks or by actual laceration of the brain. The material to be tested was laid upon this area of brain and the temporal muscle closed

over it. Animals were then sacrificed at intervals of from ten to sixty days, and gross and microscopical studies were made. In the case of "amnioplastin" and "insultoin" the test was made more severe by cauterization or removal of cerebral tissue down to the ventricles and the emplacement there of excised bits of muscle.

In the following table the results are indicated briefly. In general the non-absorbable materials prevented adhesions from forming through them, but they produced

Comparison of Materials used for Prevention of Adhesions

Material	Gross Adhesions	Cellular Reaction
Cargile membrane	+++	Moderate
Fat	+++	Severe
Aluminium foil	+++	Mild
Silver foil	++++	Severe
Mica	+++	Moderate
Nickel plate	+++	Severe
Stainless steel plate	+++	Fibrous capsule
Cellophane	+++	Mild
Fascia lata	++	Moderate
Plain catgut membrane	++	Moderate
Insultoin membrane (allantoic) ..	+	Mild
Human amnion	+	Very mild
Amnioplastin	0	Phagocytosis and meningeal restoration

dense adhesions between the dura and pia at the periphery of each inset and they became covered with a dense connective-tissue envelope. The under wall of this envelope formed part of an intracerebral scar, and the outer sheet of the envelope a new and very thick dura. Cellular reaction with the appearance of foreign-body giant cells and evidence of actual cerebral destruction was most marked in the case of silver foil and nickel plate and least noticeable about the thin steel plates and celloidin sheets.

In general the sheets of animal tissue (fascia, catgut, and fat) became incorporated in a new-formed brain

covering which replaced dura and incorporated pia without the formation of separate meningeal linings. The conclusion of the initial experiments was that of all the animal tissue used fat produced the most severe cellular reaction and human amniotic membrane the least. Cargile membrane,* which is at present in use in a number of neurosurgical clinics to place over the brain at the close of operation, gave a comparatively poor result. When this membrane was placed over pia that had been slightly injured dense adhesions resulted.

Preparation of Amniotic Membrane †

Membranes received from the delivery room were washed and then placed in 75 per cent. alcohol for seven days before use. Later the membranes were boiled before being preserved in alcohol. At the time of use the chorion was stripped off the amnion as completely as possible. Thus prepared the membrane compared favourably with other materials, but there was still slight evidence of irritation. Consequently the following method of preparing what we have called "amnioplastin" from amniotic membrane is now recommended.

Preparation of Amnioplastin

The fresh membranes as received from the delivery room are washed in water in order to remove as much of the blood and mucus as possible. By finger dissection the inner membrane (the amnion) is freed from the outer membrane (the chorion). It is possible to remove the entire inner membrane, even that portion over the surface of the placenta. The membrane is again washed in water and placed in 70 per cent. alcohol. The thin membrane is then stretched and dried in sheets of convenient size. This is accomplished by stretching on a smooth glass plate which has previously been rubbed over with mineral oil. It is then dried in a drying oven or in the open air. To remove the membrane from the plate moisten with 70 per cent. alcohol and allow to stand a few moments and then peel it off. These sheets may be preserved dry or in 70 per cent. alcohol until such time as final sterilization can be carried out. It is also to be noted that, from this point on, the procedure may be taken over by a nursing sister in the operating clinic.

Sterilization.—If the sheets have been preserved in alcohol they are again dried and laid between the strips of gauze in a large Petri dish or some such covered receptacle, and are autoclaved for twenty minutes at 250° F. with 120 lb. pressure. After autoclaving, the sheets may be placed directly in sterile Ringer's or saline solution for immediate use. They may, if desired, be kept dry and sterile for later use or they may be kept in 70 per cent. alcohol. An alternative method of sterilization is to boil the sheets in distilled water for twenty minutes. After boiling they are placed in the 70 per cent. alcohol or may be taken direct from the water and washed thoroughly in saline solution, when they are ready for use. Boiling, however, causes somewhat more shrinkage than sterilization in the autoclave. By either method of sterilization a thin, pliable, transparent membrane is produced in which there is no cellular structure. The operating nurse should leave a sheet of amnioplastin in Ringer's or saline solution for at least twenty minutes before she flattens it out on a glass plate as described below.

* Cargile membrane is ox peritoneum in dry sterile sheets, prepared commercially under that name.

† We are much indebted to Professor John Fraser for providing us with this material from the delivery rooms of the Royal Victoria Montreal Maternity Hospital.

Experiments with Amnioplastin

In a second series of similar experiments the animals were sacrificed at intervals varying from ten to sixty days after the surface of the lacerated brain had been covered with this membrane. It was found at necropsy that a new-formed dura had appeared on the under surface of the muscle. This was not disturbed but was removed with the brain. Inspection of the inner surface of dura was made only in those cases not used for microscopical study. In the group studied microscopically the freedom from adhesions made it necessary to hold the dura down to the underlying brain with thread ties until the process of embedding the tissue was completed.

The results were consistently as follows. In no instance was there evidence of gross adhesion. The amnioplastin sheet progressively disappeared. In the ten-day animals a mucoid material which represented the membrane was found in the space between injured cortex and re-forming dura. When the brain was placed in fixative this material washed away for the most part. On gross inspection at twenty days there was slight evidence of the substance, except for a very small amount of the same mucoid material. At thirty days no gross or microscopical evidence of membrane could be found.

Microscopically in the ten-day group there was no evidence of any foreign-body reaction, and no organized adhesions. It may be said that the growth of fibroblasts beneath and above the membrane was a reaction to the presence of a vanishing foreign body. Remains of the amnioplastin could be seen as an amorphous substance without cellular structure. There was evidence of beginning regeneration of the dura and pia. By twenty days the dural defect had completely filled in, the pia had partially closed over the destroyed brain, and the membrane between the two was represented by a thin amorphous material. Panel A of Fig. 1 (see Plate) is from such a twenty-day preparation. In it the dura is labelled d, membrane m, and pia p. The area of brain which had been traumatized is easily seen and the superficial cell growth which is the precursor to new pia.

In panel B of the same figure is shown a section from an animal of thirty days' standing. It will be noted that there is no evidence whatsoever of any membrane, that the dura and pia have both regained their continuity, and that there is no sign of any adhesive bands even over the area of brain injury. In panel C of Fig. 1 is shown a section from an animal sacrificed fifty days after operation. Here is seen complete restoration of both dural and pial coverings, the latter over damaged cortex, with no evidence of any adhesion. It seems fair to assume that the subdural space is now filled with a thin layer of fluid as under normal conditions and, further, that no element is present which could produce adhesions after this sixty-day period.

Previous Work

Following the war of 1914–18 much work was done on the problem of meningo-cerebral adhesions because of the prevalence of post-traumatic epilepsy in those who had recovered from wounds of the brain. After such seizures had become habitual futile efforts were made to stop them by opening the skull and placing upon the brain scar such substances as fat, fascia, celloidin, and metal plates in the hope of lessening or abolishing adhesions. These attempts failed for two reasons: first, because the substances did not prevent re-formation of adhesions; and, secondly, because such seizures cannot

be stopped until the cicatrix within the brain is excised. The latter cause of failure is probably the more important, as was pointed out by Foerster and Penfield (1930). Nevertheless, a membrane that will really prevent adhesions after a radical operation for post-traumatic epilepsy should improve the results of such operations.

On the other hand, to present a method of preventing the formation of such adhesions at the time of the original injury is the aim of this communication. Harvey and Burr (1926) pointed out that injury to the pia arachnoid was invariably followed by adhesions involving the pachymeninges and brain. This is due not to the peculiarity of the pia but to the fact that the central nervous system when deprived of its normal covering becomes the site of marked cellular reaction, both neuroglial and fibroblastic. Any portion of the nervous system, if it loses its proper covering, calls forth violent reaction from the surrounding tissue, as pointed out by Trotter (1926). This is as true of peripheral nerves as it is of the brain, and there would seem to be no reason why amnioplastin should not be used to surround a recent nerve suture to prevent much of the fibroblastic reaction ordinarily produced by the bared nervous tissue. Furthermore, it might well be found useful to envelop a recently sutured tendon and perhaps also to produce gliding surfaces so necessary in joints and about injured areas of peritoneum.

Johnson (1937), after the investigation of the fate of various absorbable substances when buried in muscle, came to the conclusion that bovine allantoic membrane† was the least irritating and caused by far the least reaction. On the basis of his findings he scarified the bowel wall and peritoneum in animals, and found that a covering of allantoic membrane prevented the formation of adhesions. Davis and Aries (1937) also stated that they were able to restore a practically normal gliding mechanism after repair of nerve or tendon if the nerve or tendon was protected by allantoic membrane.

We have found that this foetal membrane serves fairly well over the brain, as is shown by reference to the table, but that amnioplastin had definite advantages. It is possible that allantoic membrane might be much improved if prepared after the manner of amnioplastin.

Clinical Applications

When a craniotomy is carried out and the brain exposed for a considerable length of time, or when the brain is injured as by the removal of a tumour (Fig. 2), amnioplastin is recommended as a routine covering to be interposed between dura and brain, both where the brain is intact and where it is lacerated, as shown in Fig. 3. We have used it for this purpose and are under the impression that local post-operative oedema is thereby lessened. Certainly there is no increase in immediate cellular reaction in the spinal fluid. It has not as yet been employed long enough to determine its effect upon the incidence of post-operative epilepsy.

Treatment of Brain Wounds.—Wounds of the brain should be treated according to the principle of careful débridement that applies to other tissues. All destroyed brain tissue should be removed or sucked out. Foreign bodies should be removed and bone fragments elevated or removed. Débridement thoroughly and carefully done is the most important procedure for the immediate preservation of life, prevention of infection, and avoidance of subsequent focal epilepsy (Penfield, 1936). Added to

this, amnioplastin should be spread over the wounded surface in order to prevent adhesion. If there is a defect in the dura as well as the pia the use of amnioplastin will provide for the re-formation of dura and pia as separate layers. For such cases large sheets should be used. A sheet may be lifted by the operating nurse from the saline or Ringer's solution on her table and placed on a piece of clean glass of suitable size. She should then smooth out all wrinkles. With the membrane still moist she may then place another piece of glass on the top so that the membrane is kept flat and moist between the two glass sheets. When thus covered the membrane may be kept an hour or two with no fear of drying. When the field is prepared the surgeon can then remove the upper glass and use instruments to lift the membrane by two of its corners. When he places the membrane upon the wet surface of the brain it adheres at once and is not easily displaced.

Conclusion

Amnioplastin is a thin sheet which may be easily prepared from the membranes available in the delivery room of any obstetrical hospital. It may be boiled or autoclaved before use. It is recommended as a preventive of meningo-cerebral adhesions and as an adjunct to the radical surgery necessary to prevent post-traumatic and post-operative epilepsy. This membrane allows regrowth of leptomeninges over the brain even after cerebral laceration and re-formation of an overlying dura mater. It thus provides for restoration of the subdural space.

Amnioplastin remains a foreign body for a short time, but is completely absorbed within a period of thirty days. It should serve in other surgical fields to prevent adhesions in the peritoneal and joint cavities and also about tendons and sutured nerves. It may therefore be recommended for use in many of the operative procedures of military and civil surgery.

LEGENDS TO PLATE

FIG. 1.—Photomicrographs to show re-formation of meninges over lacerated area of cerebral cortex. d = dura mater; m = amnioplastin; p = pia mater. Panel A, twenty days after wound of cortex, shows pia re-forming over the area of laceration. The membrane has partly washed away, but may be made out. The dura is re-forming. Panel B, thirty days after wound, shows pia re-formed actually over the injured area, where no true cortical structure is now to be seen; membrane gone. Panel C, after fifty days: complete absence of adhesions.

FIG. 2.—Operative photograph showing the brain of a young man and the excavated area from which a glioma (astrocytoma) has just been removed. The tickets A and H lie on the precentral gyrus, as proved by electrical stimulation. Membrane may be seen at one side ready to be placed in position.

FIG. 3.—Operative photograph of same case as Fig. 2. The brain and excavated area are being covered with a sheet of amnioplastin. No weakness followed this operation, and there was a minimum of post-operative reaction of any sort.

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† Insultic membrane, prepared commercially by the Lewis Manufacturing Company, Walpole, Mass., U.S.A.

H. H. Schuman (*Amer. J. Dis. Child.*, 1939, 58, 564) illustrates the rarity of chicken-pox in the newborn by the fact that he has found only six cases, to which he adds the seventh. In five of the six cases the disease had a mild course, and only one was fatal, though it is not clear whether chicken-pox was the cause of death. In Schuman's case the rash appeared on the twentieth day of life of the child, whose mother had the disease at the time. The attack was mild and no complications occurred.

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(For Legends, see Text)

FIG. 1

FIG. 2

FIG. 3

C. K. VARTAN AND G. DISCOMBE: DEATH FROM QUININE POISONING

FIG. 1.—Section through cortex of kidney. The glomeruli are seen to be for the most part unaffected.

FIG. 2.—Section through tubular portion of kidney. The collecting tubules are seen to be choked by a granular amorphous deposit.