EXPERIMENTAL OBSERVATIONS ON THE USE OF RUBBER IN THE TREATMENT OF CRANIOSYNOSTOSIS

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(Received for publication September 26, 1957)

The surgical treatment of craniosynostosis by the wrapping of inert foreign material around the edges of linear craniectomies parallel to fused cranial suture lines was first reported by Simmons and Peyton in 1947, who used tantalum foil in 2 infants. Prior to this, Lannelongue in France in 1890, and Lane in the United States in 1892, had advocated the use of simple linear craniectomies. However, their method of treatment rapidly became unpopular because of indefinite indications for the operation. In 1927 and again in 1943, Faber and Towne re-introduced the use of linear craniectomy in craniosynostosis.

In 1948 Ingraham et al. carried out extensive experimental studies on the use of fibrin film, oxidized cellulose gauze (Oxycel), tantalum, methyl methacrylate (Lucite), and polyethylene (Polythene). They studied the tissue reaction to these substances when placed between the margins of artificially created channels in the cranial vaults of dogs and monkeys with survivals from 32 to 315 days. Control linear craniectomies were placed on the opposite side of the cranium in each animal. Bony fusion was found in all control saw cuts examined after 100 days. They concluded that polyethylene, because of its flexibility, transparency, and availability in various sizes of tubing and film, was particularly adaptable for introduction into the gap of artificially made sutures in the cranium in order to inhibit bony healing. They observed that its tolerance by the tissues was equal to that of tantalum or Lucite. They found that fibrin film and Oxycel failed to inhibit bony union across the saw cuts. Tantalum and Lucite were found to be inert and to inhibit bony fusion. However, the weight and opacity of the tantalum to roentgen rays and the rigidity, brittleness and difficulty in molding of the Lucite made the use of these substances difficult.

Following the study by Ingraham et al. there were no unfavorable reports regarding the use of polyethylene in the treatment of craniosynostosis until 1956 when Anderson and Johnson noted a reaction to polyethylene film in 2 patients, necessitating its postoperative removal. They were compelled to search for a new method to prevent bony regrowth across a linear craniectomy. They described the use of a thorough application of Zenker's acetic fixative or of a 7 per cent tincture of iodine on the surgically exposed...
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It has been the general experience in this clinic that polyethylene material which has been embedded in human tissues has a tendency to become brittle and to crack. Experimental studies by Oppenheimer et al.\textsuperscript{13,14} and Bering et al.\textsuperscript{4} have revealed that numerous implanted plastic materials, including pure polyethylene, have induced the development of sarcomas in rats and mice in from 400 to 650 days. These observations noted above have prompted us to consider the use of a soft, pliable, resilient, relatively inert material such as rubber in the treatment of craniosynostosis. This report is concerned with observations on the use of rubber material in chronic animal experiments.

MATERIALS AND METHODS

Fourteen mature cats weighing approximately 2 to 4 kg. were used. Anesthesia was obtained with pentobarbital sodium (U.S.P.) in a solution of 10 per cent alcohol injected either intravenously or intraperitoneally in the approximate dosage of 25 mg. per kg. of body weight. The hair of the scalp was clipped with small animal clippers. The operative procedures were carried out with aseptic technique and were essentially the same as described by Ingraham et al.\textsuperscript{10} The cranium was exposed through a midline sagittal incision. The pericranium was elevated from the mid frontoparietal areas. Two bi-frontoparietal and bi-parietal burr holes 1 cm. in size were made approximately 2 mm. from the midline. The bi-frontoparietal burr holes usually bisected the coronal sutures and were about 2 to 2.5 cm. anterior to the bi-parietal burr holes. The burr holes were connected unilaterally with Gigli saw cuts, the edges of which were trimmed to right angles, leaving bilateral linear craniectomy defects averaging approximately 2 mm. in width. No bone wax was used in these experiments. Bleeding from the bone was allowed to stop spontaneously.

One linear craniectomy was used as the control and was left untouched following its completion. On the side in which the tested material was used, 2 holes were made with a 1-mm. dental drill, approximately 2 mm. from the lateral edge of the saw cut at each end of the cut. Three types of rubber material were used: 1) latex surgical tubing;\textsuperscript{*} 2) Penrose rubber drains;\textsuperscript{†} and 3) condom rubber.\textsuperscript{†}

The material to be tested was then wrapped around the lateral edge of the linear craniectomy and held in place with No. 40 stainless steel wire sutures passed through the dental drill holes. The dura mater was not opened. The galea and the skin were closed with interrupted 0000 black silk sutures. There were no operative deaths. One cat in which Penrose rubber had been implanted died 11 days postoperatively with a purulent wound infection. It was autopsied and studied although it was not used in the final consideration of these results.

\textsuperscript{*} Manufactured by Rubber-Latex Products, Inc., Cuyahoga Falls, Ohio, U.S.A. No. 200, size \textfrac{1}{4} inch I.D., Wall Amber. The manufacturer states that the tubing “contains approximately 95 per cent pure latex rubber, the balance being made up of small quantities of zinc oxide, sulphur, wax and an aliphatic amine.”

\textsuperscript{†} Manufactured by Sterling Rubber Co., Ltd., Guelph, Canada. The rubber is a centrifuged, clarified, prevulcanized, natural latex. The manufacturer lists a 2 per cent chemical content made up of the following ingredients: “Sulphur, Accelerator 552, zinc oxide, Antioxidant 2446, El-Sixty, soap stabilizer, Butyl Zimate, casein stabilizer, ammonia, and caustic potash.”

\textsuperscript{††} Manufactured by Julius Schmidt, Inc., New York. The rubber is a natural latex containing only a trace of free sulphur. It was generously supplied by the manufacturer in a powder-free state for use in this experiment.
**Pathological Studies.** The animals were sacrificed at intervals from 1 to 369 days with pentobarbital sodium (U.S.P.). Immediately after death, the operative areas were inspected and the character of the implanted rubber was noted. The operative area with adjacent brain was then removed *en bloc* by making 2 coronal cuts with an electric autopsy saw, one anterior to the coronal suture, and the other at the level of the lambdoid suture. A transverse cut was then made at the level of the inferior surface of the cerebral hemispheres.

The specimen was placed in a 4 per cent solution of formaldehyde for about 3 weeks. The specimens were then carefully examined under the dissecting microscope. Roentgenographs were taken of the cranial vaults of animals surviving longer than 3 months. Most of the brains, including all specimens with survival periods of 92 days or longer, were then sectioned in coronal slices beneath the operative areas. Adjacent slices were taken for microscopic study. The posterior slices were embedded in paraffin and stained with hematoxylin, phloxine and saffron; Laidlaw’s method for connective tissue; Mallory’s phosphotungstic acid; and Luxol-fast blue and cresyl violet for myelin sheaths and cellular detail. The anterior slices were placed in Cajal’s formol-ammonium-bromide solution for at least 1 week. Sections were cut on the freezing microtome at 20 μ, and were stained for astrocytes by Cajal’s gold chloride sublimate method, for oligodendroglia and microglia by Hortega’s silver carbonate, and for fat with the Scharlach-R stain.

The rubber material was carefully dissected free from the operative site, and the skulls with attached dura mater were decalcified in nitric acid (20 per cent) and phloroglucinol (1 per cent) and embedded in 8 per cent celloidin. Sections were cut at 35 to 60 μ, and stained with the hematoxylin van Gieson method.

**RESULTS (Table 1)**

**Controls.** In 7 cats examined within the first 19 days there was no bony fusion. The 7 cats examined after 92 days all showed solid bony union across the saw cuts. This was demonstrated both grossly and microscopically (Fig. 1), and roentgenologically. The control craniectomy, 369 days after operation, presented gross and microscopic evidence of solid bony fusion. However, the roentgenogram (Fig. 4) revealed only scattered points of bony union.

**Rubber Tubing.** Latex surgical tubing was used in 2 cats examined at 92 and 369 days (Fig. 2). In both animals the rubber had changed in color from light tan to an opaque tannish-white. The rubber was completely intact and had probably lost a slight degree of its normal resiliency. The tubing was well encapsulated in each case by a tough, white, slightly shiny, fibrous capsule. The underlying dural layers were intimately connected to the connective tissue surrounding the rubber and were moderately thickened. There was a complete prevention of bone formation across the saw cuts. Histological sections in each case revealed the thick fibrous capsule made up of parallel connective-tissue fibers, fibroblasts, and phagocytes. The capsules were intimately merged with the underlying dura mater and the overlying muscle and fascial tissues. The outer layer of the capsules contained a few small blood vessels. New bone was not observed to penetrate the capsules or to have formed from the underlying dura mater or overlying soft tissues.
**TABLE 1**

**Summary of experimental data**

<table>
<thead>
<tr>
<th>Cat</th>
<th>Survival Time in Days</th>
<th>Material Used</th>
<th>Preservation of Rubber</th>
<th>Encapsulation</th>
<th>Dural Thickening</th>
<th>Evidence of Bony Union on Tested Side</th>
<th>Evidence of Bony Union on Control Side</th>
<th>Underlying Brain</th>
<th>Remarks</th>
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<tbody>
<tr>
<td>P55-246</td>
<td>92</td>
<td>latex surgical tubing</td>
<td>good</td>
<td>thick</td>
<td>very slight</td>
<td>none</td>
<td>moderate</td>
<td>very slight gliosis</td>
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<td>369</td>
<td>latex surgical tubing</td>
<td>good</td>
<td>thick</td>
<td>very slight</td>
<td>none</td>
<td>moderate</td>
<td>no changes noted</td>
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<td>P55-240</td>
<td>5</td>
<td>Penrose rubber drain</td>
<td>good</td>
<td>very slight</td>
<td>very slight</td>
<td>none</td>
<td>none</td>
<td>no changes noted</td>
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<td>11</td>
<td>Penrose rubber drain</td>
<td></td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
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<td>none</td>
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<td>none</td>
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<td>moderately thick</td>
<td>very slight</td>
<td>none</td>
<td>marked</td>
<td>no changes noted</td>
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<tr>
<td>P55-261</td>
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<td>Penrose rubber drain</td>
<td>good</td>
<td>moderately thick</td>
<td>very slight</td>
<td>none</td>
<td>marked</td>
<td>meningo-cerebral cicatrix</td>
<td>dura mater and brain wounded at operation</td>
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<td>1</td>
<td>condom rubber</td>
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<td>none</td>
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<td>marked</td>
<td>meningo-cerebral cicatrix</td>
<td>dura mater and brain wounded at operation</td>
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<tr>
<td>P55-259</td>
<td>365</td>
<td>condom rubber</td>
<td>good</td>
<td>moderately thick</td>
<td>very slight</td>
<td>none</td>
<td>moderate</td>
<td>no changes noted</td>
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</tbody>
</table>

**Fig. 1.** Cat P55-246. Cross section through control linear craniectomy at 92 days. Bone formation is solid across inferior half of the gap. Hematoxylin van Gieson, X15.
The edge of the bone enclosed in the rubber tubing (Fig. 3) presented a moderate underlying cut-in defect. The underlying brain at 92 days had a slight indentation in which region the Cajal gold chloride sublimate stain revealed a slight condensation of astrocytes in the white matter. No significant histological abnormalities were noted in the brain 369 days after operation.

A roentgenogram of the 369-day specimen (Fig. 4) suggested slight bony resorption of the edges of the craniectomy along which the rubber tubing had been placed.

Penrose Rubber. Penrose rubber was placed in 6 cats with survivals of 5, 11, 13, 19, 313, and 368 days. The animal surviving 11 days died with a purulent wound infection and the gross and histological observations are not included in this analysis. The rubber was intact and had changed from a translucent reddish-tan appearance to an opaque yellowish-white appearance in each instance. At 5, 13, and 19 days, a thin layer of loosely organized fibrinous material was noted on the rubber. It was loosely adherent and was readily wiped away.

At 313 and 368 days (Fig. 5) there was a moderately thick grayish-white, slightly shiny, fibrous capsule completely enclosing each piece of rubber. The capsule was intimately attached to the underlying dura mater and to the overlying muscle and fascial tissues. In all animals there was complete prevention of bony union across the saw cuts.

Histological examination at 313 and 368 days revealed a well defined capsular formation of densely packed parallel connective-tissue fibers, fibroblasts, and phagocytes. The capsules were not as thick as those observed around the rubber tubing. There was no evidence of new bone formation invading these fibrous capsules. However, at 313 days there was a finger of bone formation projecting beneath the capsule along the outer layer of the dura mater. After 368 days, the edge of the bone which was enclosed with
Penrose rubber showed a marked cut-in defect, apparently produced by the rubber.

The underlying brains appeared normal in every case except that of the 368-day animal. In that experiment the dura mater had been inadvertently lacerated and there was a healed meningoencephalic cicatrix.

Roentgenograms of the 313-day (Fig. 6) and 368-day specimens revealed an absence of bony fusion at any point along the saw cuts around which the rubber had been placed. There was a suggestion of a slight degree of bony resorption of the edge of the craniectomy along which rubber had been placed in the 313-day specimen.

**Condom Rubber.** Thin, white, translucent condom rubber was placed around the saw cuts in 6 cats with survivals of 1, 2, 7, 183, 306, and 365 days. In each experiment the rubber was found to be intact. It had changed color and was an opaque, faintly yellowish-white. The rubber appeared to have lost a slight degree of its normal resiliency. There were no wound infections in this group. At 1, 2 and 7 days, a thin grayish-white fibrinous material was noted on the surface of the rubber. It was loosely adherent and readily wiped away.

At 138, 306 and 365 days (Fig. 7), tough, grayish-white, slightly shiny fibrous capsule was completely enclosing each piece of rubber. The capsules were judged to be of similar...
thickness as those enclosing the Penrose rubber. The capsules were intimately attached to the underlying dura mater and to the overlying soft tissues. It was noted that there was a very slight thickening of the underlying dura mater in the 306- and 365-day animals. In each experiment there was complete prevention of bony union across the saw cuts.

Histological examination revealed a fibrous capsule similar to that enclosing the Penrose rubber. At 183 days the capsule appeared definitely thinner than the capsules enclosing the latex surgical tubing at 92 and 369 days and enclosing Penrose drains at 313 and 368 days. The histological preparations noted after 306 and 365 days, in which condom rubber had been embedded, did not present a clear-cut distinction between the fibrous capsule and the adjacent soft tissues. There was no invasion of the fibrous capsules by bone formation. However, small fingers of bone were projecting beneath the capsules along the outer layer of the dura mater (Fig. 8).

The underlying brain was normal except for friable meningocerebral adhesions noted at 7 days and at 306 days in instances in which the dura mater and underlying brain had been inadvertently lacerated.

Roentgenograms at 183 (Fig. 9), 306
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(Fig. 10), and 365 days (Fig. 11), revealed no evidence of bony fusion across the saw cuts around which the rubber had been placed. In the 306- and 365-day specimens there was a suggestion of a slight degree of bony resorption of the edges of the craniectomy along which the rubber had been placed.

DISCUSSION

The gross inspection and radiological examinations of these chronic animal preparations revealed that the rubber material tested was effective in the prevention of bony union in linear craniectomies in every case up to 369 days. Excluding one operative infection, there were no untoward gross reactions to the rubber. Histological examinations did reveal a slight foreign-body reaction and/or capsular formation around the rubber in every specimen. This reaction was not considered severe enough in any case to contraindicate the use of rubber material. The presence of the shiny fibrous capsule in every animal with a survival of longer than 19 days is in agreement with the work of Cone et al. and of Pudenz and Odom on dural substitutes. They found that a capsule formed around every type of material used as a dural prosthesis, no matter what material. It was interesting to note the degree of variability of bony fusion across the control craniectomies, as revealed roentgenographically. The cranial vault of the animal surviving 183 days (Fig. 3) had a greater degree of bony fusion than the animal surviving 369 days (Fig. 4).

The suggestive bony resorption in the linear craniectomies wrapped with rubber as noted in the roentgenograms of several of the animals with survivals longer than 300 days is a noteworthy observation. It may indicate that the rubber not only prevents bony union but that it also produces in
FIG. 8. Cat P55-259. Cross section through linear craniectomy at 365 days in which condom rubber had been interposed. The rubber enclosed the edge of the bone on the right. There is a well formed fibrous capsule without evidence of bony fusion. However, small fingers of bone are seen projecting beneath the capsule along the surface of the dura mater on the right. Hematoxylin van Gieson, X15.

some unknown manner a slight degree of bony erosion. This characteristic may possibly be considered as a desirable factor in favor of the use of rubber in the treatment of craniosynostosis. The absence of underlying brain damage (excluding the inadvertent operative woundings) indicates that rubber is a safe material for embedding in tissues in close proximity to cerebral tissue.

Abbe\textsuperscript{1,2} in 1895 and in 1897 reported 2 cases in which he placed a sheet of rubber on the human brain in an attempt to prevent the reformation of meningocephalochorial cicatrices. He noted no untoward reactions, even with a 3-year follow-up on one of the cases. The only known experimental study of rubber material applied to the surface of the brain was carried out by Giangrasso\textsuperscript{8} in 1940. He implanted sheets of rubber material as dural prosthesis in 6 dogs, with survivals from 15 days to 2 years. He noted no un-

FIG. 9. Cat P55-280. Roentgenogram of cranial vault at 183 days in which condom rubber had been interposed in a linear craniectomy on the right. It has completely prevented bony fusion across the gap. The control craniectomy on the left shows several points of bony fusion.

FIG. 10. Cat P55-281. Roentgenogram of cranial cap at 306 days in which condom rubber had been interposed in a linear craniectomy on the left. Note the strongly suggestive bony resorption. The control craniectomy on the right shows bony fusion.

FIG. 11. Cat P55-259. Roentgenogram of cranial cap at 365 days in which condom rubber had been interposed in a linear craniectomy on the left side. Note absence of bony union. The control craniectomy on the right side shows obvious bony fusion.
toward effects of the rubber. Neither Abbe\textsuperscript{1,2} nor Giangrasso\textsuperscript{8} specified the type of rubber that they used.

Three types of rubber were used in the present experiment: latex surgical tubing, Penrose rubber drains, and condom rubber. As previously noted the Penrose rubber is free from lead but contains a 2 per cent chemical content. The Schmidt condom is similarly a latex rubber but prepared by a method that gives a film of pure rubber with only a trace of sulphur. The latex surgical tubing is 95 per cent latex rubber. Rubber may be sterilized either by boiling or by autoclaving and thus has an advantage over such materials as polyethylene which cannot be autoclaved.

In a review of the literature I have found no report of a clinical or experimental case in which embedded rubber has produced a true neoplastic growth.

In view of the one operative infection and the usual slight foreign-body reaction to the rubber, it is suggested that clinical application of this experimental study be carried out with the utmost care in asepsis and surgical technique, and that local antibiotics should be instilled in the operative wound. A word should be said regarding the technique of interposing the rubber between the linear craniectomies. The latex surgical tubing, when split longitudinally, molded very readily around the edge of the bony wall. Unfortunately, it is probably too thick for clinical use. However, no untoward behavioral or pathological reactions were noted from its use in this experiment. The condom rubber was found to be very easily manipulated and was readily wrapped around the bony edges and held in place with fine No. 40 stainless steel wire sutures passed through small 1-mm. dental drill holes. The combined qualities of thinness, durability, minimal foreign-body reaction, and ease of use of the condom rubber have led us to consider that it is probably the most satisfactory material to recommend for clinical use. The absence of the 2 per cent chemical content which is present in the Penrose rubber is in favor of the use of the condom rubber over the Penrose rubber.

**SUMMARY AND CONCLUSIONS**

1. Experimental observations were made on the use of latex surgical tubing, Penrose rubber drains, and condom rubber interposed in linear craniectomies in 14 mature cats with survival times from 1 to 369 days.

2. The rubber material tested was effective in preventing bony union across the linear craniectomies in every case.

3. Gross and histological studies revealed that rubber is well tolerated by the tissues of the cat. A slight insignificant foreign-body reaction and/or capsular formation was noted in every case. (There was 1 animal with an operative infection which was excluded in the final analysis of these data.)

4. Control linear craniectomies in the 7 cats with survivals of 92 days or longer all showed bony fusion.
5. This study indicates that condom rubber would be a satisfactory and desirable material for interposition in artificial cranial sutures in the treatment of clinical cases of craniosynostosis.

I wish to thank Dr. W. V. Cone for his criticisms and suggestions in the preparation of this study.

REFERENCES