The Use of Extracorporeal Circulation and Profound Hypothermia in the Treatment of Ruptured Intracranial Aneurysm

C. G. Drake, M.D., H. W. K. Barr, M.D., J. C. Coles, M.D., and N. F. Gergely, M.D.
Divisions of Neurosurgery and Cardiovascular Surgery, University of Western Ontario, London, Canada

The aim of direct surgical treatment in cases of ruptured intracranial aneurysm is the prevention of recurrent hemorrhage by obliteration or reinforcement of the sac. The results of treatment are in large part predicated on the pre-operative condition of the patient, particularly in relation to the state of the arterial tree (age, hypertension, local spasm) and the presence of cerebral edema, infarction or clot. The deep exposure required adds further insult to the brain damaged through retraction, injury to small perforating arteries or the parent vessels, and the production of arterial spasm. To increase the safety of operation various adjuncts have been favored, such as hypotension, urea and hypothermia.

Conventional hypothermia introduced by Botterell et al. has become used widely in the protection of the brain during craniotomy in these cases. Experimentally at 28°C cerebral metabolism is reduced below 50 per cent and the effects of hypoxia have been avoided in patients during intervals of 5 to 10 min. of occlusion of the carotid and/or vertebral artery. Early favorable impressions are now under scrutiny, and Hamby has stated recently that in his cases the use of hypothermia has not increased useful survival materially. From experience in this unit conventional hypothermia, with or without urea, has not prevented the development of postoperative arterial spasm and ischemic brain damage which, in our opinion, are chief causes of morbidity and mortality resulting from early direct surgical attack.

Cardiovascular surgeons introduced profound hypothermia to protect the brain during longer periods of circulatory arrest in open-heart surgery employing a cardiovascular by-pass pump and heat exchanger. Core temperatures were reduced to 10°–15°C and periods of total circulatory arrest amounting to 45 min. have been accomplished safely. Woodhall et al. and Guiot et al. explored the use of deep hypothermia during craniotomy for ruptured aneurysm. Patterson and Ray described their laboratory work and the use of closed-chest perfusion with 2 deaths in 7 clinical cases. Uihlein reported on 36 cases with 8 deaths. These reports aroused considerable interest, for the method seemed to provide the means of approaching an aneurysm with the minimum of injury to the brain through an excellent exposure in a completely dry field.

The cardiovascular unit at this University has been interested in deep hypothermia for several years. A method had been developed and studied in over 50 experiments on dogs in the laboratory, followed by 40 operations on humans. In view of this experience it was decided to use the technique in a series of especially selected cases of ruptured intracranial aneurysm. This report is based on 10 patients with ruptured intracranial aneurysms deemed to be particularly hazardous in view of their size or position. Direct surgical attack was carried out during hypothermia of 10°–15°C., exsanguination and circulatory arrest. Because of the complicated nature of the procedure it has not been used in cases when the aneurysm could be obliterated by more standard means.

Technique
The craniotomy and preparation for cardiopulmonary by-pass were performed simultaneously by the two teams. The bone flap was turned down

Received for publication October 10, 1963.
with meticulous hemostasis in anticipation of the exasperating bleeding to be faced during the re-warming phase. After the dura mater was opened, the route to the aneurysm was inspected gently and, when necessary, division of a dural partition was completed before heparinization. During the cooling phase the temperature gradient between the cortex and room air was minimized by cold saline packs. Core temperature was monitored through esophageal and rectal leads.

Cardiopulmonary by-pass was established in 8 cases by an atrial cannula inserted directly through a small right thoracotomy or sternal split, together with the standard femoral arterial cannula. In 2 cases the closed-chest method was used whereby the right atrium was cannulated indirectly via the femoral vein.

A gradient of not more than 13° C. was maintained between the perfusing blood and core temperature. The average time for cooling was 58 min. (Table 1).

When the core temperature approached 18°–15° C., the exposure of the aneurysm was initiated under low rates of flow of 500–1000 cc. per min. This period averaged 16 min. with a range from 8 to 25 min. The final dissection of the sac was completed after exsanguination of 2500 cc. and total circulatory arrest. The wide exposure and dry field allowed precise delineation of the origin of the aneurysm and accurate placement of a suitable clip or ligature. Since most of the dissection was done under low rates of flow, the periods of total circulatory arrest were short, varying from 2 to 18 min., while the esophageal temperature varied between 9.6° and 16.8° C.

With the re-establishment of circulation, re-warming was begun and the 19° gradient was maintained until the esophageal temperature reached 35.5° C., with a rectal temperature of at least 38° C. This period averaged 75 min. No difficulty was encountered in restoring sustained cardiac action. Spontaneous rhythm occurred in 2 cases; in the remainder only minimal defibrillation was necessary.

This phase is trying for the neurosurgeon. Bleeding seems to well from everywhere, particularly from the dura mater and beneath the edges of the bone. This bleeding can be stemmed by adding more tacking sutures and Gelfoam. Hemorrhage from the depths of the brain exposure, although persistent and not easily defined, was never severe except in 1 case. In this instance, re-exposure of the large aneurysm showed it to be leaking from the fundus and it was necessary to place a clip beyond the ligature.

The artificial circulation was discontinued when the patient maintained adequate cardiac action and body temperature. Patience and restraint on the part of the surgeon are now rewarded for the bleeding gradually comes under control as the heparin is neutralized with Polybrene. Considerable drift may occur (down 2°–5° C.) when the pump is stopped. After the field is dry, the wound is closed in the usual manner.

Case Reports

The cases are summarized in Figs. 1–3 under tracings of the angiograms.

Aneurysms of the Anterior Communicating Artery (Fig. 1). The aneurysms in Cases 1 and 2 were bilobed so that each sac had to be clipped sepa-

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Total Pump Run (hrs., min.)</th>
<th>Low Flow (min.)</th>
<th>Total Arrest (min.)</th>
<th>Cooling Time (hrs., min.)</th>
<th>Rewarming Time (hrs., min.)</th>
<th>Lowest Esophageal Temp. °C.</th>
<th>Pump*</th>
<th>Method</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. P.C.</td>
<td>F</td>
<td>33</td>
<td>1:54</td>
<td>20</td>
<td>5</td>
<td>0:20</td>
<td>1:00</td>
<td>12.0</td>
<td>Disc</td>
<td>Open</td>
</tr>
<tr>
<td>2. H.G.</td>
<td>M</td>
<td>57</td>
<td>2:35</td>
<td>10</td>
<td>14</td>
<td>1:00</td>
<td>1:10</td>
<td>14.0</td>
<td>Disc</td>
<td>Open</td>
</tr>
<tr>
<td>3. L.M.</td>
<td>F</td>
<td>51</td>
<td>3:16</td>
<td>22</td>
<td>16</td>
<td>1:55</td>
<td>2:00</td>
<td>16.8</td>
<td>Disc</td>
<td>Open</td>
</tr>
<tr>
<td>4. B.G.</td>
<td>M</td>
<td>34</td>
<td>2:21</td>
<td>12</td>
<td>14</td>
<td>0:58</td>
<td>0:59</td>
<td>12.0</td>
<td>Disc</td>
<td>Open</td>
</tr>
<tr>
<td>6. G.M.</td>
<td>F</td>
<td>36</td>
<td>3:00</td>
<td>8</td>
<td>6</td>
<td>1:05</td>
<td>1:30</td>
<td>9.6</td>
<td>Disc</td>
<td>Closed</td>
</tr>
<tr>
<td>7. M.T.</td>
<td>F</td>
<td>49</td>
<td>2:42</td>
<td>12</td>
<td>8</td>
<td>1:13</td>
<td>1:17</td>
<td>12.0</td>
<td>Disc</td>
<td>Open</td>
</tr>
<tr>
<td>8. J.E.</td>
<td>M</td>
<td>23</td>
<td>1:51</td>
<td>20</td>
<td>15</td>
<td>0:40</td>
<td>1:00</td>
<td>12.0</td>
<td>Disc</td>
<td>Open</td>
</tr>
<tr>
<td>9. H.R.</td>
<td>M</td>
<td>63</td>
<td>2:28</td>
<td>25</td>
<td>18</td>
<td>0:48</td>
<td>1:17</td>
<td>12.5</td>
<td>Disc</td>
<td>Open</td>
</tr>
<tr>
<td>10. J.S.</td>
<td>M</td>
<td>66</td>
<td>2:55</td>
<td>8</td>
<td>2</td>
<td>0:50</td>
<td>1:00</td>
<td>14.2</td>
<td>Disc</td>
<td>Open</td>
</tr>
</tbody>
</table>

* The disc oxygenator was used with Mark pumps and the Mayo screen was used with the Mayo-Gibbon pump. The Ivan-Brown heat exchanger was used with the disc and the Mayo heat exchanger was used with the Mayo screen apparatus.
Surgical Treatment of Ruptured Aneurysm

May have been performed the operative angiogram. However, this patient has shown remarkable improvement in mentation and her chief disability is a spastic quadriaparesis. In Case 2 death occurred from a deep left frontal hemorrhage 18 hours after operation. The bleeding, which was difficult to control even after the heparin was neutralized,* seemed to come from a small vessel behind the aneurysm. In Case 3 the aneurysm proved to be much larger than the angiogram suggested, probably because of intramural clot. It was not possible to ligate the sessile neck without kinking the parent trunks. This sac was dissected free and then enveloped totally in a gauze filigree, and the patient has remained well for over a year.

Aneurysms of the Carotid Artery (Fig. 3). These aneurysms were unusually large with necks that were equal to or greater than the caliber of the parent artery. Occlusion with a ligature (reinforced with a clip in 3) was possible without encroaching on the lumen of the carotid artery. As a group the results were poor, but in Cases 4 and 6 the patients were critically ill prior to operation. There were 3 deaths. Case 4 died from pneumonia 4 months later in a convalescent hospital although the patient remained unchanged from his preoperative state. In Case 5 death occurred 6 days postoperatively, the patient having remained decorticate and oliguric. Inadequate perfusion was blamed because the closed-chest method was used and satisfactory venous return could not be maintained. In Case 6 removal of the bone flap was required on the second day because of cerebral swelling. Three weeks later a lumboperitoneal shunt was performed for communicating hydrocephalus and for 3 months thereafter improvement was slow but progressive until unexpected death occurred from status epilepticus and pneumonia. The sole survivor in this group, Case 7, was well for 18 hours but then she became stuporous with arterial spasm and cerebral swelling. Following decompression she gradually improved, became ambulatory and 9 months later was considered an excellent result, although the oculomotor palsy had not disappeared completely.

Aneurysms of the Basilar Artery (Fig. 3). In Case 8 there was mild postoperative confusion but the patient recovered completely and remains actively engaged in farming. Case 9† was more stuporous after operation and removal of the bone flap was required. However, over a 10-month period he has shown remarkable recovery and is now self-sufficient but moderately disabled by an expressive dysphasia, undoubtedly the sequel to a left subtemporal approach.

The aneurysm in Case 10 was clipped without difficulty but only the surface of the angioma was seen and packed gently with muscle. The patient, although drowsy, appeared to be improving when he died suddenly 5½ hours later from a massive

* Following this case a titration test with Polybrene has been performed to avoid paradoxical bleeding which may occur in an excess of Polybrene.

† The patient was operated upon in conjunction with Dr. T. Speakman and Dr. J. Callaghan at the University Hospital, Edmonton, Alberta.

---

Fig. 1. Anterior communicating aneurysms.
Internal carotid aneurysms.

Results

The unparalleled exposure and lack of concern over inadvertent rupture made it relatively simple to obliterate all but 1 of the aneurysms. All patients survived the opera-
tion. Of the 7 patients conscious before operation (Grades I and II), only 3 regained consciousness immediately, but 1 deteriorated with postoperative arterial spasm and swelling. Ultimately, however, she improved remarkably and is now considered an excellent result. Five patients were worse and the 3 postoperative deaths occurred in this group, 2 from hemorrhage and the other from poor perfusion. The 2 patients classified as Grade IV remained unchanged and died subsequently 4 and 5 months later.

Three patients required re-exploration following deterioration and angiographic demonstration of a shift. Despite heparinization there were no significant clots on the surface. In each case the shift resulted from massive cerebral swelling, clearly related to arterial spasm in 2 instances. In all, 7 postoperative angiograms were done. Each aneurysm had been obliterated, but the arterial spasm was present in 5 cases. The clinical course correlated with the site and degree of spasm.

In summary, only 3 patients can be classified as excellent results. Another is considered to be fair in that he is self-sufficient and socially acceptable but moderately disabled by lingering dysphasia. One patient is more severely disabled by a spastic quadriparesis. Three patients died following the procedure and 2 other deaths occurred months later.

Discussion

The use of deep hypothermia in these 10 cases was not rewarding, even though exsanguination and circulatory arrest facilitated superb exposure of the aneurysm and its connections and accurate placement of a ligature or clip. The 3 postoperative deaths resulted directly from the use of extracorporeal circulation. Both patients in Grade IV category were operated upon early in the series in the hope that the brain would not be injured further by this technique despite the size of the aneurysm. Both were unchanged basically after operation until their deaths from pneumonia several months later. The operative mortality was 30 per cent but the case mortality then became 50 per cent.

The high morbidity as compared to that of Patterson and Ray\(^6\) and Uihlein\(^1\) resulted in part from the special selection of patients. Each aneurysm was considered to be particularly hazardous because of size and position necessitating more retraction and dissection than in the average case. Eight patients were operated upon within a week of the last hemorrhage before arterial spasm and brain swelling had subsided. The majority of Uihlein’s patients were operated upon more than 3 weeks after the last hemorrhage. This is very important factor, but early operation was used to ascertain whether deep hypothermia lessened the danger of operation within the first week. It was disappointing to learn that in spite of the facility with which the aneurysm could be obliterated this technique did not prevent the dreaded complications of postoperative arterial spasm and ischemic brain damage which have been a chief cause of morbidity and mortality with other methods after early operation.\(^3\)

It is interesting that the 2 late cases had uncomplicated postoperative courses (Cases 3 and 4).

Craniotomy under deep hypothermia is a considerable undertaking involving two teams and a maze of equipment and technical help. However, the pump runs went smoothly except in Case 5 where, with the closed-chest method, venous return through two femoral cannulae was poor and perfusion was probably inadequate. The average operating time was 8 hours with a mean cooling phase of 58 min. and average rewarming period of 75 min. The final core temperatures ranged from 9.6° to 16.8°C. with an average total arrest period of 10 min. (2 min. to 18 min.). Temperature gradients occur not only between other parts of the body and the brain, but also within the brain itself. In cooled experimental animals a gradient of several degrees exists between cortex and base, the base being cooler in the majority of cases.\(^5\)

However, the temperature of the cortex in 1 case was 10°C, as compared to an esophageal temperature of 11°C., while
in the other recorded case it was the same (12.5°C.). It is possible that the use of 7 per cent CO₂ in the oxygenator induced cortical vasodilation, increased flow and decreased surface temperatures.

There were no difficulties with the 8 thoracotomies for direct right atrial cannulation.

The closed-chest method of Patterson and Ray is favored by Uhlein et al., and has been used in their last 26 cases. The last 2 patients in this series were operated upon by this method. Although atrial cannulation was simplified, poor venous return resulted in inadequate perfusion in one, while in the other a severe deep thrombophlebitis developed. While experience with only 2 patients does not justify conclusion, it is our impression that the small right thoracotomy is satisfactory and avoids these serious complications.

The problems with perfusion and deep hypothermia have been discussed elsewhere. Of particular concern to the neurosurgeon was the danger of bleeding. Although troublesome, bleeding during the period of heparinization came under control after administration of Polybrene and there were no postoperative clots on the surface. However, 2 of the 3 postoperative deaths occurred from deep intracerebral bleeding quite possibly related to heparin as discussed under the case reports. Tiny arterial channels are collapsed and not seen easily. Disregard of these vessels may lead to serious consequences and it is considered that the deep fatal bleeding in Case 2 resulted from injury to such a vessel.

A 12°C. gradient was carefully maintained between the temperatures of the core and perfusing blood to minimize the risk of gaseous micro-emboli. Bjork and Hulquist have commented on the dangers of emboli of fibrin and platelets as a cause of dementia following deep hypothermia. Zingg, in preliminary studies in dogs, felt that this degree of cold may injure the nerve cells directly. Our cases were not studied in this regard as hemorrhage or arterial spasm and edema seemed to account clearly for the ensuing neurological difficulties. The experience of the pump team in cardiac cases made it extremely unlikely that these mechanisms played a major role at these temperatures.

The periods of total arrest were brief, but it must be remembered that most of the exposure and dissection of the aneurysm was done under low flow (500-1000 cc./min.) during periods varying from 8–25 min. Low rates of flow were used in an attempt to avoid hypoxic acidosis which can occur at 10º–15ºC. Experimentally the mean intake of oxygen at this low temperature was less than 1 cc. per kg. per min., but the tissues can incur an oxygen debt if they are not perfused adequately or if the circulation is interrupted for long periods of time. Acidosis, which becomes evident in the rewarming phase, was not a problem. In this series the arterial pH following the pump run ranged from 7.28 to 7.41.

Summary

Ten patients with ruptured intracranial aneurysms, deemed to be particularly hazardous for direct surgical attack under conventional means because of size or position, were subjected to profound hypothermia (10º–15ºC.), exsanguination and complete circulatory arrest during the dissection and obliteration of the sac. The dissection and ligation of the aneurysmal sac were greatly facilitated by this technique, although bleeding in the rewarming phase was troublesome.

Three patients are well but 1 is only a fair result and the other survivor is poor. There were 3 postoperative deaths all attributable to the use of extracorporeal circulation (inadequate perfusion 1; bleeding 2). The 2 Grade IV patients died unchanged several months after operation.

The use of cardiopulmonary by-pass and deep hypothermia in the surgical treatment of ruptured intracranial aneurysms creates enough additional hazards so that it is probably not warranted in cases in which the aneurysm can be obliterated by more conventional means. It is considered that the superb exposure created by this technique may still favor its use in difficult cases of
aneurysms of the region of the anterior communicating artery and middle cerebral bifurcation in which precise delineation of the sac and its neck is essential.

The results even in these special cases were not encouraging, although the size and position of the sac, the poor pre-operative condition of 3 patients, early operation, and postoperative spasm were contributing factors. The complication of postoperative arterial spasm and ischemic brain damage has not been avoided by this technique and remains a major problem in the early surgery of aneurysms.

References
2. Baker, A. S. Personal communication.
6. Guzon, G., Rougerie, J., Arfel, G., Dubost, C., and Blondeau, P. Le “grand froid” en neuro-chirurgie. Possibilités et perspectives d’avenir. Réflexions à propos de la 1re observation de malforma-

14. Zingg, W. Personal communication.