Treatment of Intracranial Vascular Disorders with the Aid of Profound Hypothermia and Total Circulatory Arrest: Three Years’ Experience

Collin S. MacCarty, M.D., John D. Michenfelder, M.D., and Alfred Uihlein, M.D.
Sections of Neurologic Surgery and Anesthesiology, Mayo Clinic and Mayo Foundation, Rochester, Minnesota

Our interest in the application of deep hypothermia to neurologic surgery was stimulated by the success of this procedure in cardiovascular surgery. The method of Drew and associates was suggested to us by Kirklin. The Drew technic was introduced in the Section of Neurologic Surgery of the Mayo Clinic on March 2, 1960. From that date until December, 1961 the Drew technic was used in 18 cases. In January, 1962, we adopted a modification of the “closed-chest technic” described by Woodhall et al. and Patterson and Ray. Between January, 1962, until March, 1963, we employed the closed-chest technic of hypothermia in 26 cases. We have not, however, used these methods exclusively during the period under consideration. For instance, 45 intracranial aneurysms were treated by intracranial surgical procedures without the use of profound hypothermia, and some form of extracranial carotid ligation was used in 22 cases.

In brief, 111 operations were carried out during this 3-year period, 44 with the adjunct of profound hypothermia and 67 by other methods. It is of further interest that 69 patients were seen in our institution who died without having undergone a definitive surgical procedure, and necropsy in these instances revealed intracranial aneurysms, most of which had ruptured, causing the patient’s death.

Methods

Open-Chest (Drew). The responsibility for application of either of the two methods used has rested among the neurologic surgeon, the cardiovascular surgeon and the neuroanesthesiologist.

When the Drew technic is used the heart is exposed by way of median sternotomy. Three cannulae are emplaced in the heart and 1 is emplaced in the left femoral artery. Initially, the left side of the heart is by-passed by means of a cannula in the left atrium in a circuit which goes to a reservoir, a pump, a heat exchanger, a bubble trap and then into the left femoral artery. The blood is cooled by maintenance of the temperature of the blood in the heat exchanger at a value 12°C cooler than the patient’s esophageal temperature. The right side of the heart is by-passed by emplacement of a cannula in the right atrium in a circuit which leads to a reservoir; then the blood is pumped back into a cannula inserted by way of the right ventricle into the pulmonary artery. As the patient is cooled, his heart becomes ineffective at about 28° to 30°C. Then the right-heart by-pass is instituted. The patient’s lungs are used as an oxygenator. Manual or mechanical respiration is maintained until circulatory arrest is desired.

The extracorporeal unit is primed with 3500 cc. of fresh heparinized blood. The degree of heparinization achieved is based on the calculation of 90 mg. per sq. m. of body surface, the agent being administered prior to cannulation. Rates of flow can be maintained at 2.0 to 2.5 l. per min. per sq. m. of body surface. During cooling, blood must be administered repeatedly to maintain these rates, apparently because of the vasodilatation which takes place at temperatures less than 28°C. During circulatory arrest or at low rates of flow, blood can be withdrawn from the patient, if the neurologic surgeon so desires, to improve exposure and to reduce bleeding of stasis. More blood can be administered for replacement during the rewarming process.

Rewarming is accomplished by reversing the process and maintaining the temperature at a value about 12°C. warmer than the patient’s esophageal temperature. When the patient’s temperature increases to about 28° to 30°C., the heart is defibrillated and use of the by-pass of the right side of the heart is discontinued. Rewarming is continued by means of the left system until a temperature of 35° to 37°C. has been reached. The cannulae are then removed and the effects of heparin are combatted by the administration of

Received for publication August 12, 1963.
hexadimethrine (Polybrene) at the rate of 185 mg. per sq. m. of body surface. Other adjuncts we have used are protamine, antihemophilic plasma and epsilon aminocaproic acid.

Closed Chest. In December, 1961, we visited Patterson and Ray, who suggested a technic for cooling of the whole body by means of peripheral cannulation, thus obviating the necessity for thoracotomy. This simple method is incapable of producing the high flows obtained with the Drew technic, but it was noted that if "precooling" of the patient with surface methods is done, some of this disadvantage is eliminated. On the other hand, elimination of thoracotomy and cardiac cannulation gives the procedure certain obvious advantages. Three cannulae are used: 1 in each femoral vein and 1 in a femoral artery. A right venous cannula is passed to the level of the diaphragm by way of the common femoral vein. The blood is collected from both venous cannulae in a reservoir, is pumped to a heat exchanger (Brown-Emmons), to a Mayo-Gibbon sheet oxygenator, to a bubble trap and finally into the left femoral artery. Cannulation is performed by a separate surgical team after craniotomy has been completed and the patient has been heparinized. Prior to cannulation the patient is cooled to a value of 30° to 32°C. by surface methods by means of a Thermo-O-Rite blanket.

The volume of perfusate is 1500 ml. of citrated blood, 45 mg. of heparin, 1500 ml. of a 10 per cent solution of calcium chloride, 1500 ml. of 5 per cent dextrose in a 0.2 per cent solution of sodium chloride and 240 ml. of serum albumin. Rates of flow obtained with this method have ranged from 1.1 to 1.81 l. per min. per sq. m. of body surface.

Cooling is accomplished by maintenance of a 12°C. gradient between the temperature of the blood leaving the heat exchanger and the temperature of the esophagus. Initially, the heart contributes to the rates of flow, but when cardiac function becomes ineffective as the patient is cooled, the entire rate of flow is maintained by the extracorporeal system. The lower rates of flow are safe because of the lowered body temperature. It is our opinion that rates of 1.4 l. per min. per sq. m. of body surface would be inadequate at temperatures more than 28°C. Ventilation of the lungs is discontinued as soon as the heart rate becomes ineffective. Cooling is continued until the temperature of the esophagus is 15°C. or lower, at which point either low rates of flow or circulatory arrest may be established, depending upon the neurologic surgeon's wishes. Rewarming is accomplished with the same rates of flow and a 12°C. temperature gradient. When the esophageal temperature reaches 26° to 28°C., the heart is defibrillated with a Morris external defibrillator. Rewarming is then continued until a body temperature of 32° to 34°C. is reached, at which stage the cannulae are removed and Polybrenel is administered. Further rewarming is carried out by surface methods.

Comment on Methods

The open-chest or Drew method produces higher rates of flow. The cooling and rewarming times are therefore more rapid than those achieved when the peripheral or closed-chest method is used. However, the open-chest method is a more formidable surgical procedure. Loss of blood is greater. Defibrillation has not been the problem we anticipated in use of the closed-chest method. In fact, of the 26 patients operated upon by this method, 3 did not require defibrillation and in only 1 was defibrillation difficult. The patient required multiple shocks of 750 V.

In the use of the closed-chest method we had anticipated left auricular distention as a result of bronchial flow, since there is no means of decompressing the left side of the heart with this method. But thus far there has been no clinical evidence of left auricular distention. In the application of both methods a competent aortic valve is an absolute necessity to prevent the left cardiac distention as a consequence of retrograde flow into the left side of the heart which occurs if the valve is incompetent, with resultant cardiac dilatation. In only 1 instance have we had to debar a patient from this type of operation because of the complication mentioned.

Indications

In 1961 one of us (MacCarty) defined his ideas regarding the use of profound hypothermia for the treatment of intracranial aneurysms. These conclusions were based on his experience with the Drew technic. There were four indications. Subsequent experience with the closed-chest technic has produced little reason to alter these conclusions.

The first indication embraces multiple aneurysms, particularly of both carotid arteries. Repair of one aneurysm should be accomplished without sacrifice of the carotid vessel; if this can be done, the flow of blood will not be increased in the other carotid artery associated with the un repaired or re-
maining aneurysm. In our opinion, repair of an aneurysm under such circumstances can be achieved best with the aid of circulatory arrest to lessen the possibility of sacrifice of the vessel.

The second indication is any large, broad-based aneurysm which cannot be repaired easily except by collapsing the lesion, reducing its size and obliterating it but preserving the parent vessel. This procedure can be accomplished under conditions of circulatory arrest, but is often impossible to carry out if the aneurysm remains full of blood under normotensive or near-normotensive conditions.

The third indication is an aneurysm which is difficult to expose without resort to considerable manipulation, thereby increasing the danger of rupture of the aneurysm, with the end result of sacrifice of the parent vessel. An aneurysm of this type is best manipulated and repaired under conditions of circulatory arrest.

The fourth indication is an anomalous vascular configuration in which sacrifice of a parent vessel, such as a carotid artery, in all likelihood would produce irreparable neurologic damage or death, as opposed to the outcome in the presence of normal vascula-
tion, in which sacrifice of the vessel might not produce damage or death. If there is an incomplete circle of Willis without communication between a carotid artery and the anterior cerebral arteries, so that occlusion of the carotid artery would result in no flow or a markedly reduced flow to the corresponding middle cerebral artery, infarction in this system would result. When a carotid aneurysm is on the vessel that does not communicate with the other carotid system, we believe that the aneurysm is repaired best with the aid of circulatory arrest and profound hypothermia.

**Contraindications**

In our entire series of cases in which operation was done with the aid of one of the two methods of profound hypothermia, 1 case can be mentioned in which the patient died of a pulmonary pathologic process which probably was related to the open-chest procedure.

A 64-year-old man who had bilateral arteriosclerotic carotid aneurysms underwent repair of the left one on June 19, 1961. The open-chest technic was used. The total time of circulatory arrest was 16 min. at 18°C, which was reached in 19 min. He awakened neurologically intact and remained so until he died on June 25 of bronchial pneumonia and staphylococccic septicemia.

This complication apparently was the result of bronchial secretions retained since the patient was reluctant to cough because of the thoracic pain induced by coughing. As a consequence of this event, it might be concluded that the intensive surgical measures required in open-chest surgery increase the risk of pulmonary complications, and that they must be weighed carefully against the advantages of circulatory arrest in the repair of intracerebral aneurysms.

Both technics present the problem of hemorrhage after decannulation. The tendency toward hemorrhage is aggravated by the hypothermic state and by perfusion. In our series of patients operated upon with the open-chest technic, 2 of the 5 died of postoperative hemorrhage, and in a third patient postoperative hemorrhage played a dominant role in the patient’s death. Another died from sacrifice of the parent vessel. In the series in which the closed-chest technic was used there were also 5 deaths. One patient died of infarction of the basal ganglia and internal capsule, a state which antedated the operation and consequently made operation impossible of success. One died of complications of postoperative bleeding from an ulcer and gastrectomy. One patient died of infarctions secondary to sacrifice of the parent vessel. Another, operated upon with the aid of the closed-chest procedure, died of postoperative hemorrhage and edema. Another died of infarction and intracerebral hemorrhage associated with sacrifice of the parent vessel.

Thus, the complication of postoperative hemorrhage must be kept in mind. It seems redundant to say that if a parent vessel is to be sacrificed permanently, profound hypo-
hydrothermia offers no protection to the brain.

In consideration of use of either technic it is important to rule out preoperatively the presence of such cardiac abnormalities as aortic insufficiency, patent ductus arteriosus and coarctation of the aorta. Such abnormalities would contraindicate perfusion achieved by either method. Impaired hepatic function or renal function are two other possible contraindications to performance of these technics.

Of course, profound hypothermia and circulatory arrest should not be applied when it is clear that aneurysms in the area under consideration can be repaired safely without such aid.

Arrest and Periods of Low Flow

Open-Chest Technic. In 18 cases in which operation was performed by the open-chest technic the periods of total circulatory arrest and low flows varied from 5 min. and 20 sec. to 90 min. In 2 cases circulatory arrest was not employed. In 1 the period of low flow was 17 min. and in the other it was 90 min. The patients concerned probably needed profound hypothermia because of the long periods of low flow. In 3 other cases circulatory arrest was of sufficiently short duration to allow the estimate that the procedure might have been done under moderate hypothermia of 29°C. In 1 the total duration of multiple periods of arrest was only 9 min. and 20 sec. In another the duration of circulatory arrest was 8 min., and in the third it was only 5 min. and 20 sec. In the remaining 13 cases the duration of circulatory arrest exceeded periods which would be considered safe under circumstances other than profound hypothermia; the longest successful period of arrest was 44 min. Thus, of the 18 patients for whom profound hypothermia was induced, 15 probably required it.

Closed-Chest Technic. Twenty-six patients were operated upon by the closed-chest technic. In 3 of the patients circulatory arrest was not used. However, in these 3 the duration of low rates of flow was prolonged: in 1 it was 15 min., in 1 it was 26 min., and in 1 it was 87 min. Among 23 patients the duration of circulatory arrest varied from 2 min. and 30 sec. to 43 min. The latter patient (circulatory arrest of 43 min.) died after sacrifice of the anterior cerebral arteries. However, 1 patient whose circulation was arrested for 39 min. survived with no neurologic deficit. In the patient whose circulation was arrested for 2 min. and 30 sec. the duration of low flows was 20 min., and thus it is questionable whether his aneurysm could have been managed as well under conditions of moderate hypothermia. In each of 2 other cases, however, circulation was arrested for 7 min. without periods of low flows. Two patients, then, might have been operated upon with the aid of more conventional conditions of hypothermia.

In conclusion, we suspect that of the 26 patients, the 3 whose circulation was not arrested required sufficiently long periods of low flows to make it questionable whether moderate hypothermia would have been adequate. In 1 instance in which circulatory arrest was of short duration the period of low flows was of sufficient magnitude to warrant the use of profound hypothermia. In 2 cases of the total series the neurosurgical procedures might have been done under moderate conditions of hypothermia. Therefore, in 24 of the 26 patients operated upon profound hypothermia probably was needed.

In the total series of 44 cases, the evidence suggests that in 39 cases (15+24) the circulatory arrest or the low flows required were of sufficient magnitude to make profound hypothermia necessary.

Results

All patients who underwent operation had intracranial aneurysms, except for 1 patient who had a large arteriovenous anomaly. The locations of the aneurysms were as follows: 18 arose from the anterior cerebral or anterior communicating arteries, 12 from the posterior communicating arteries, 5 from the middle cerebral arteries, 7 from the internal carotid artery, proximal to the bifurcation, and 1 from an ophthalmic artery. Nine patients had 2 or more aneurysms; in
such cases the aneurysm that had ruptured was the 1 selected for repair.

In 5 instances definitive repair of the aneurysm was judged to be inadvisable. In these instances the aneurysms were simply wrapped. In the remaining 38 patients the aneurysms were obliterated by the use of clips or ligation. Of the 43 patients who had aneurysms, 38 had experienced one or more episodes of bleeding before operation, and of these, 14 were operated upon within 14 days of the last hemorrhage.

The over-all mortality rate was 22.7 per cent: 10 deaths in 44 cases. The mortality rate accompanying the open-chest technic was 27.8 per cent (5 of 18), and the mortality rate associated with the closed-chest technic was 19.2 per cent (5 of 26). During this same 3-year period 45 patients underwent operations for intracranial aneurysms without the use of profound hypothermia. For these operations the mortality rate was 22.2 per cent (10 deaths). Twenty-two patients underwent some form of extracranial carotid ligation and 1 died (a mortality rate of 4.5 per cent). The total number of patients operated upon was 111, of whom 21 died in the hospital, producing an over-all hospital mortality rate of 18.9 per cent.

Any attempt to evaluate postoperative complications among these patients is difficult. However, one of us (Michenfelder) devised a classification which differs somewhat from the classification proposed by Botterell and associates. This consists of dividing the patients into 5 preoperative categories comprising (1) those who have no neurologic deficit, (2) those who have a minimal neurologic deficit, (3) those who have a significant neurologic deficit, (4) those who have mental alteration, and (5) those who are in coma. By assigning arbitrary points for each type of complication noted, an attempt is made to compare the preoperative and postoperative complications associated with each technic (Drew method and the closed-chest technic) in an effort to ascertain which produces the fewest postoperative complications. The comment was:

"The results suggest that the closed-chest technic carries with it a smaller risk than does the open-chest method, although the difference in mortality and morbidity are not statistically significant because of the relatively small number of cases."

**Physiologic Effects.** Rehder and associates have reported on physiologic data concerning 5 of our patients operated upon with the aid of the open-chest technic. Michenfelder et al. have duplicated these studies in respect to several patients who were operated upon by the closed-chest technic. These data disclose no significant disturbance in hemodynamics. There has been no indication of pulmonary vascular damage as a result of the perfusion technic. When the open-chest technic was employed metabolic acidosis was not observed. When the closed-chest technic was used because of the borderline rates of flow (1.41 l per min. per sq. m.), we have seen minimal but consistent metabolic acidosis in the patients studied. This state reverted to normal in each instance within 48 hrs. after operation, and did not require specific therapy.

**Summary**

We have reviewed our experience from March, 1960, to March, 1963, in the treatment of intracranial aneurysms. Particular emphasis has been given to the two methods of producing circulatory arrest under conditions of deep hypothermia as produced by the open-chest and the closed-chest technic. During this 3-year period 111 patients were operated upon: 18 by the open-chest technic, 26 by the closed-chest technic, 45 by other intracranial procedures in which profound hypothermia was not induced and 22 by some form of extracranial carotid ligation (Table 1). In our institution during this same period 69 patients came to necropsy who had had intracranial aneurysms without having undergone definitive neurosurgical attempts at repair of the lesions.

The mortality rate for the entire group of 111 patients was 18.9 per cent. For the open-chest technic the mortality rate was 27.8 per cent and for the closed-chest technic this rate was 19.2 per cent. The mortality rate
for the entire group of patients who underwent operation with the adjunct of profound hypothermia was 22.7 per cent. Among the 45 patients operated upon by craniotomy or craniectomy without profound hypothermia, the mortality rate was 22.2 per cent. Extracranial carotid ligation produced a mortality rate of 4.5 per cent. We have arrived at no conclusions on the basis of these data because of the numerous and variegated circumstances involved in the selection of patients and the type of operation performed.

References

<table>
<thead>
<tr>
<th>Operation</th>
<th>Patients</th>
<th>Hospital Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Repair</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With profound hypothermia</td>
<td>44</td>
<td>10</td>
</tr>
<tr>
<td>Open chest*</td>
<td>18</td>
<td>5</td>
</tr>
<tr>
<td>Closed chest</td>
<td>26</td>
<td>5</td>
</tr>
<tr>
<td>Without profound hypothermia†</td>
<td>45</td>
<td>10</td>
</tr>
<tr>
<td>Extracranial carotid ligation</td>
<td>22</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>111</td>
<td>21</td>
</tr>
</tbody>
</table>

*1 arteriovenous anomaly.
†1 ventriculostomy, 1 ventriculocisternostomy, 1 burr hole.