Despite these early reports, hypothermia was first cerebral metabolic rate for oxygen; SAH = subarachnoid hemorrhage.

Hypothermia has a long history as a simple and easily accessible element for neuroprotection. For example, the Hippocratic school of medicine used total body cooling for the treatment of tetanus in the fourth and fifth centuries BC. Despite these early reports, hypothermia was first systematically evaluated in the nineteenth century by James Currie in the United Kingdom. Currie assessed different cooling techniques for the treatment of several disorders and documented the effects of hypothermia on physiological and pathological parameters such as pulse or respiration. William Osler used hypothermia for the treatment of typhoid and reported a striking clinical success; the mortality rate decreased by 17% in his patients at Johns Hopkins Hospital after he implemented this procedure. In 1938 the American neurosurgeon Temple Fay started using hypothermia for the treatment of intractable pain and subsequently developed different devices for the intracranial application of cooling after traumatic brain injury and for treatment of cerebritis or brain abscesses. Fay soon contacted the cardiac surgeons Claude Beck and Charles Bailey to facilitate the pioneering work on hypothermia in their field, and these two promoted the use of deep hypothermia and the development of circulatory arrest for cardiac surgery.

Hypothermia and Neuroprotection

Hypothermia has a long history as a simple and easily accessible element for neuroprotection. For example, the Hippocratic school of medicine used total body cooling for the treatment of tetanus in the fourth and fifth centuries BC. Despite these early reports, hypothermia was first systematically evaluated in the nineteenth century by James Currie in the United Kingdom. Currie assessed different cooling techniques for the treatment of several disorders and documented the effects of hypothermia on physiological and pathological parameters such as pulse or respiration. William Osler used hypothermia for the treatment of typhoid and reported a striking clinical success; the mortality rate decreased by 17% in his patients at Johns Hopkins Hospital after he implemented this procedure. In 1938 the American neurosurgeon Temple Fay started using hypothermia for the treatment of intractable pain and subsequently developed different devices for the intracranial application of cooling after traumatic brain injury and for treatment of cerebritis or brain abscesses. Fay soon contacted the cardiac surgeons Claude Beck and Charles Bailey to facilitate the pioneering work on hypothermia in their field, and these two promoted the use of deep hypothermia and the development of circulatory arrest for cardiac surgery.

Despite these reports about the physiological actions of hypothermia, its basic mechanisms are not fully understood. The rationale for using hypothermia in intracranial surgery is based on the premise that this treatment lowers the CMRO2 of cerebral tissue. At a body core temperature of 30°C, the CMRO2 is only half the rate at the normal temperature metabolism. At a brain temperature of 25°C, the CMRO2 is reduced to 25%, and at a temperature of 20°C the CMRO2 can be lowered to 15% of the level found under normothermic conditions. Thus a tolerance to ischemia can be prolonged up to 50 to 60 minutes at a brain temperature of 18 to 20°C. At these low body core temperatures a physiological heart action is impossible. Therefore, the beneficial effects of deep hypothermia (18–20°C) could only be produced after the development of some sort of an extracorporeal circulation.

Cardiopulmonary Bypass

During the last century, several medical researchers became interested in isolated organ perfusion. One requisite for such a procedure is the extracorporeal oxygenation of blood. As detailed by Mora, et al., in their comprehensive work, as early as 1885, von Frey and Gruber described a blood pump in which gas exchange occurred as blood flowed in a thin film over the inner surface of a slanted rotating cylinder. In 1895, Jacobi passed blood through an excised animal lung that was oxygenated by artificial respiration. Brukhonenko and Tchetchuline designed a device in 1926 that used an explanted lung from an animal and two mechanical blood pumps. Initially they perfused
isolated organs and later entire animals. In 1935 Carrell and Lindbergh developed a device that perfused a cat’s thyroid gland for more than 2 weeks. Later this group kept a heart beating during artificial perfusion. Although the perfused organs showed normal physiological functions, progressive degenerative changes occurred within a few days.

Another prerequisite for cardiopulmonary bypass was anticoagulation therapy. Heparin was discovered by McLean, working with William Howell. In 1916, McLean extracted cephalin from brain specimens and reported the thromboplastic activity: in 1918 Howell and Holt confirmed that heparin was an effective anticoagulating agent by performing several animal studies.

Between 1935 and 1954, John Gibbon, Clarence Dennis, and others pursued the development of a mechanical device that would take over the function of the heart and lungs to permit surgery on the heart and great vessels. Gibbon used a roller pump to substitute for the heart, which remains in general practice today. As a substitute for the lung, he devised a system in which anticoagulated blood was directly exposed to O2 while dripping along the wires of a vertically mounted metal screen. This method of direct exposure of blood to O2 was successful and subsequently modified by Dennis, Morrow, Cross, DeWall, Rygg, and others, leading to the single-use, disposable, direct gas interface oxygenators that are still widely used today. Gibbon was the first to use the prosthetic heart/lung machine for a cardiac operation, pioneering the successful adoption of extracorporeal circulation for cardiac surgery.

During the 1950s, it became obvious that the life-supporting technique itself was problematic when used for more than a few hours. Thrombocytopenia, coagulopathy, hemolysis, generalized edema, and deterioration of organ function occurred, in proportion to the amount of time the patient spent on cardiopulmonary bypass. The experiments of Lee, Dobelle, and others indicated that the direct exposure of blood to O2 gas was responsible for these adverse effects on the organism. These observations led to the development of an artificial lung in which a gas-permeable membrane was interposed between the blood and the gas phase. The first successful membrane oxygenator was built by Clowes and coworkers in 1956. These researchers used sheets of a polyethylene membrane that had a low but definite permeability to O2 and CO2. The development of dimethylpolysiloxane membranes by Kamermeyer in 1957 was another major advance. This material allowed the transfer of CO2 and O2 at rates that were more than 10 times faster than those through other plastics.

During the following years several improvements were introduced, making the technique safe and widely available.

**Cardiopulmonary Bypass in Cerebrovascular Surgery**

**The Pioneer Years (1950s through 1970s).** The introduction of profound hypothermia and circulatory arrest for cerebrovascular surgery became possible after refinement of the technical advances in cardiothoracic surgery. In 1960 Woodhall, et al., described the case of a 39-year-old patient suffering from lung cancer. To allow removal of a large cerebral metastasis, deep hypothermia and car-

diopulmonary bypass were used. The cannulation for the pulmonary bypass was performed in the femoral artery and the jugular vein. Cardiac standstill time was 10 minutes. The patient recovered fully after surgery but died a few months later of the underlying disease.

The aforementioned case stimulated Uhlein and colleagues to use extracorporal circulation with profound hypothermia and circulatory arrest to repair intracranial aneurysms. These practitioners initially used simultaneous thoracotomy and craniotomy, but they experienced technical difficulties and since 1961 have used the so-called closed-chest technique. After these first reports, interest in this technique rose, and several papers were subsequently published in which extracorporal circulation was used in cerebrovascular surgery and especially in operations for large and complex aneurysms. In 1962 Patterson and Ray published a report describing a series of seven patients, of whom five recovered fully. These authors used a cannula that was advanced into the inferior and superior venae cavae through the internal jugular and femoral veins, and they placed another cannula into the femoral artery. The mean time of circulatory arrest was 24 minutes (range 9–42.5 minutes). Two years later Michenfelder, et al., reported on 15 patients undergoing aneurysm surgery. The closed-chest technique of deep hypothermia and circulatory arrest was used in their series as well. Therefore, the cannulation was performed in the femoral artery and the femoral vein. Three patients died perioperatively and the rest recovered.

In 1964 Drake and colleagues reported on 10 patients undergoing hypothermic circulatory arrest for the treatment of intracranial aneurysms. These authors attributed three deaths (30%) to the use of this technique, with postoperative coagulopathy especially responsible. Furthermore, technical problems occurred because of poor venous return when using cannulas in the superior and inferior venae cavae. This was the first report of poor results and was partly responsible for the decline in the use of this technique, as Drake recounted later. In concordance with Drake, in 1966 Uhlein, et al., reported severe procedure-related complications. In this series, 66 patients were described, 15 of whom died within the perioperative period. More than half the surgery-related deaths were attributed to intra- and postoperative coagulopathy. During the 1970s several improvements were introduced in cerebrovascular surgery; for example, microsurgical techniques, temporary aneurysm clips, and controlled systemic hypotension. Thus, surgeons at most centers abandoned the deep hypothermia and cardiopulmonary bypass technique because of the unacceptable rate of procedure-related complications.

**The Recent Years (1980s to present).** Advances in the management of anesthesia in the 1980s, especially with regard to post- and intraoperative coagulopathy, combined with refinements in extracorporeal circulation techniques, encouraged surgeons at several centers to reevaluate the use of deep hypothermia and circulatory arrest for complex cerebrovascular lesions. A summary of the most recent studies is given in Table 1. In 1983 Baumgartner, et al., reported on 14 patients who underwent 15 operations. The surgical technique in these cases consisted of peripheral cannulation with two femoral vein cannulas for venous return and a single femoral arterial cannula. The
Deep hypothermia and circulatory arrest in cerebrovascular surgery

TABLE 1
Literature review of recent studies of intracranial aneurysm surgery in which cardiopulmonary bypass was used

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Patients</th>
<th>Mortality Rate (%)</th>
<th>Morbidity Rate (%)</th>
<th>Favorable Outcome (%)</th>
<th>Duration of Circulatory Arrest (mins)</th>
<th>Temp During Arrest (˚C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sundt, 1982</td>
<td>8</td>
<td>50</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Baumgartner, et al., 1983</td>
<td>14</td>
<td>0</td>
<td>21</td>
<td>13</td>
<td>21</td>
<td>16–20</td>
</tr>
<tr>
<td>Gonski, et al., 1986</td>
<td>40</td>
<td>25</td>
<td>23</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Richards, et al., 1987</td>
<td>11</td>
<td>27</td>
<td>9</td>
<td>64</td>
<td>5–39</td>
<td>14–22</td>
</tr>
<tr>
<td>Solomon, et al., 1991</td>
<td>14</td>
<td>0</td>
<td>14</td>
<td>71</td>
<td>8–51</td>
<td>15–18</td>
</tr>
<tr>
<td>Williams, et al., 1991</td>
<td>10 (4)</td>
<td>10</td>
<td>20</td>
<td>80</td>
<td>1–60</td>
<td>8–14</td>
</tr>
<tr>
<td>Ausman, et al., 1993</td>
<td>9</td>
<td>22</td>
<td>22</td>
<td>44</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Aeber, et al., 1998</td>
<td>24</td>
<td>12.5</td>
<td>12.5</td>
<td>70.3</td>
<td>22.5</td>
<td>18.2</td>
</tr>
<tr>
<td>Lawton, et al., 1998</td>
<td>60 (58)</td>
<td>8</td>
<td>13</td>
<td>76</td>
<td>22.9</td>
<td>12–19.6</td>
</tr>
<tr>
<td>Sullivan, et al., 1999</td>
<td>7</td>
<td>NR</td>
<td>0</td>
<td>100</td>
<td>22</td>
<td>12.7</td>
</tr>
</tbody>
</table>

* Numbers in parentheses represent the number of patients with aneurysms who were treated with cardiopulmonary bypass. Abbreviations: NR = not reported; temp = temperature.

Deep hypothermia bypass flows ranged from 1 to 3.5 L/minute, and the total bypass time averaged 146 minutes. Circulatory arrest times averaged 21 minutes. The lowest core temperature ranged from 16 to 20°C. One patient sustained a hemorrhagic infarction of the cerebellum andpons.

In 1986 Gonski, et al.,10 reviewed the outcomes in 40 patients with intracranial aneurysms, 10 (25%) of whom died within the perioperative period. Four (10%) of the 40 patients died due to intractable postoperative hemorrhage. In 1987, Richards, et al.,21 published a series of 11 patients, seven (64%) of whom suffered from giant aneurysms. Three aneurysms were located in the posterior circulation, and seven patients (64%) reached a favorable outcome. Sundt26 reported a series of eight patients who underwent surgery with this technique. All patients suffered from giant aneurysms in the posterior circulation. In four of these eight patients, symptoms developed after surgery and a combined mortality and morbidity rate of 50% was reported. Williams, et al.,12 described 10 patients in their series published in 1991. Four patients were treated for aneurysms, three were treated for glomus jugulare tumors, two for recurrent arteriovenous malformations, and one for a hemangioblastoma. Of the four patients suffering from aneurysms, two had anterior circulation and two had posterior circulation lesions. One patient died and two others experienced Symptoms after surgery.

In the ensuing years three studies were published: Solomon, et al.,25 reported on 14 patients in 1991; Ausman, et al.,9 on nine patients in 1993; and the largest study, published in 1998 by Lawton, et al.,16 included 60 patients. All these studies have in common the fact that circulatory arrest and deep hypothermia treatments were used mostly in patients suffering from posterior circulation aneurysms. (In the Solomon series 64% of the patients were treated for posterior circulation aneurysms, in the Ausman series 78%, and in the Lawton series it was 90%). In this selected population the morbidity rate is reported to be between 13 and 22%, and the mortality rate ranges from 0 to 22%. These papers show the tendency to limit the use of hypothermic circulatory arrest to cerebrovascular lesions of the posterior circulation. Lawton and colleagues16 conclude that currently, hypothermic circulatory arrest is reserved for lesions that either cannot be treated by conventional techniques or for which such techniques carry significant risks to the patient. In these authors’ experience the use of hypothermic circulatory arrest has been limited to complex and giant aneurysms of the basilar artery.

The most recent series was published by Sullivan, et al.,27 in 1999. They report a series of seven patients suffering from aneurysms of the posterior circulation. Five patients attained an excellent outcome and the other two were classified as having a good outcome. Indications for the use of deep hypothermia and circulatory arrest were as follows: 1) a complex aneurysm arising from the posterior circulation; 2) a large or giant aneurysm, often with significant intraaneurysmal thrombosis or a broad neck; 3) an aneurysm whose projection endangers safe dissection and preservation of perforating arteries; or 4) a fusiform aneurysm without a neck, in which an artery exists distal to the lesion that is not suitable for arterial bypass. All aneurysms were explored before the final decision was made about use of the circulatory arrest and deep hypothermia technique. Prompted by these results, deep hypothermia and circulatory arrest is now used in several centers throughout the world.7,11,12,17,23,24,26

Our own experience involves 24 patients who were treated using hypothermic cerebral circulatory arrest and cardiopulmonary bypass (eight of these cases have already been reported).2 There were 12 female and 12 male patients, whose mean age was 41.2 years (range 17–63 years at the time of surgery). Six of our patients underwent surgery in which deep hypothermia and cardiopulmonary bypass was used for aneurysms of the posterior circulation. One patient was treated for a vertebral artery aneurysm and five others for lesions of the basilar artery; nine lesions were giant aneurysms. The mean total bypass time was 142.33 minutes (range 82–240 minutes), and the mean circulatory arrest time was 22.55 minutes (range 3–68 minutes) at a mean brain temperature of 18.2°C (range 18–19°C). Three patients died during the perioperative period. One patient who was admitted for SAH suffered a malignant infarction in the middle cerebral artery territory postoperatively and died of brain herniation. This neurological deficit was attributed to the initial SAH. One patient experienced septicemia and multiple organ failure. Another individual suffered infarction of the perforating vessel after surgery for a basilar artery aneurysm and died within the perioperative timeframe.
Current Situation

At present it seems clear from our own experience, from the aforementioned recent articles, and the experience with deep hypothermia and circulatory arrest in cardiothoracic surgery, that this technique has low procedure-related morbidity and mortality rates (general morbidity is 13%). Although morbidity and mortality rates seem to be relatively high, one has to keep in mind that the series reported here reflect a high-risk population. Furthermore, the complication rates in the recent series are relatively low compared with historical groups. In our series three patients died after surgery. In one case severe vasospasm occurred after acute SAH, in another the neurological deficit could be attributed to problems with perforating vessels after surgery for a giant basilar artery aneurysm, and in the third the patient died of multiple organ failure due to septicemia after pneumonia. None of these complications can be attributed to the use of deep hypothermia and cardiac arrest. Furthermore, “alternative techniques” for surgery of these highly challenging neurovascular lesions, like bypass surgery or improved skull base approaches are not without risk for the patient. Complication rates for bypass surgery are reported to range from 7 to 33%, with a neurological deterioration rate of up to 80% after bypass occlusion in long saphenous vein bypasses. Therefore, we think that deep hypothermia and circulatory arrest is a safe tool for surgery of complex cerebrovascular lesions, even in the acute stage, to prevent the high risk of early rebleeding.

Conclusions

Indications for surgery using this technique are evaluated on an individual basis. Important criteria are the aneurysm neck, proximal and distal vessel anatomy, collateral vasculatization, localization, wall condition (calcification, thrombosis, and so on), and concomitant brain edema in the case of an acute SAH. Keeping these criteria in mind, deep hypothermia and circulatory arrest seems to be a safe and valuable method for the treatment of complex and giant aneurysms, even in the acute stage of SAH. Nevertheless, indications for the use of this technique are extremely limited, but according to our experience it may not need to be reserved solely for lesions of the posterior circulation.

References


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