Aneurysms of the basilar artery treated with circulatory arrest, hypothermia, and barbiturate cerebral protection

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Complete circulatory arrest, deep hypothermia, and barbiturate cerebral protection are efficacious adjuncts in the surgical treatment of selected giant intracranial aneurysms. These techniques were utilized in seven patients, one with a large and six with giant basilar artery aneurysms; four had excellent results, one had a good result, one had a poor outcome, and one died. The rationale for the use of complete cardiac arrest with extracorporeal circulation, hypothermia, and barbiturate cerebral protection is outlined. The surgical and anesthetic considerations are reviewed. The perioperative morbidity and long-term results support the use of these techniques in selected patients with complex intracranial vascular lesions.

KEY WORDS • basilar artery aneurysm • subarachnoid hemorrhage • cardipulmonary bypass • hypothermia • barbiturate coma • cerebral protection

Operative Techniques

Electrophysiological Monitoring

With this technique, intraoperative monitoring includes recording the spontaneous electroencephalographic (EEG) activity, somatosensory evoked potentials (SSEP's), and brain-stem auditory evoked potentials (BAEP's). The suppression of EEG activity by barbiturates is used to titrate an effective dose for cerebral protection. The preservation of SSEP's is used to confirm the integrity of sensory conduction.

The two test modalities (SSEP monitoring and evoked potential recording) complement each other. The EEG recording is a sensitive index of generalized cortical activity and a precise measure of a cerebralprotective barbiturate dose. The SSEP is a more specific response of intact sensory pathway conduction that persists despite barbiturate-induced EEG burst suppression. Spontaneous EEG activity is lost when body temperature is below 25°C and cerebral blood flow is 20 to 30 cc/100 gm/min. The SSEP's persist to hypothesia levels as low as 18° to 20°C and flows of 10 to 15 cc/100 gm/min. Together they can be monitored to achieve optimum doses of barbiturates and minimal retraction of neural structures before hypothermic arrest. During rewarmin, after the arrest period, the

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A. Initiation of Procedure

B. Burst Suppression

C. Circulatory Arrest

D. Asymmetric Post-op Recovery

E. After Hematoma Evacuation

Fig. 1. Compressed spectral electroencephalographic analysis in a patient who developed a postoperative hematoma contralateral to the operated side following hypothermia and circulatory arrest.

recovery of both the SSEP's and EEG activity can be interpreted as a reassuring measure of central nervous system (CNS) recovery. Alteration of these parameters may require reevaluation of clip placement to assure that vessels are not compromised.

The benefits of EEG monitoring were illustrated in one patient who developed a striking reduction in EEG frequency below 10 Hz on the unoperated hemisphere at the conclusion of the procedure (Fig. 1). This unexpected EEG asymmetry prompted an immediate postoperative computerized tomography scan that revealed a subdural hematoma. The hematoma was evacuated, and the patient recovered uneventfully. This lesion might not have been detected and treated effectively without the EEG change.

Both BAEP's and SSEP's are monitored simultaneously with the EEG. The BAEP's are recorded if brain-stem structures are threatened by the planned procedure. The SSEP's are recorded if thalamocortical pathways are involved. A derived parameter of the SSEP's, the central conduction time (the transit time from the cervical dorsal column to thalamocortical activation) is also used to estimate hemispheric perfusion.

Surgical Technique

The basilar artery aneurysm is exposed either through the standard transsylvian or the subtemporal approach. The specific operative approach is determined by the anatomy of the aneurysm, its relationship to the clivus and posterior clinoids, and the orientation of the aneurysm in relation to the axis of the basilar artery. When the subtemporal approach is used, the cranie-
Management of Anesthesia and Cardiopulmonary Bypass

The preoperative evaluation of neurosurgical patients who undergo a cardiopulmonary bypass procedure includes a full medical assessment and anesthesia evaluation. Patients with preexisting cardiac, pulmonary, or hematological disorders may be excluded from consideration, depending on the severity of their disease. Patients of advanced age, with a high preoperative clinical grade of subarachnoid hemorrhage (SAH), or with recent occurrence of SAH are not excluded from surgery if their general health is good. The oldest patient in our series, a 77-year-old woman with a Grade III SAH (according to the classification of Hunt and Hess), tolerated the procedure well.

Preoperatively, a large peripheral intravenous line and an arterial line are introduced under local anesthesia. Rigid blood pressure control is necessary to avoid a precipitous SAH caused by transient hypertension. The critical times of maximal stimulation occur with the induction of anesthesia, skeletal fixation, and periosteal retraction. Good management of anesthesia requires anticipation and prevention of these hypertensive events.

Induction of anesthesia is started with connection of the cardiovascular monitor and the pulse oximeter. A sleep dose of either barbiturate (thiobarbiturate at 3 mg/kg body weight) or midazolam HCl (0.1 mg/kg) is administered slowly with oxygenation. Narcotics such as sufentanil and nondepolarizing muscle relaxants such as vecuronium bromide effectively reduce any sympathetic response to anesthesia induction and prevent undesirable cardiovascular changes. After the patient is intubated, a central venous or pulmonary catheter is placed by the internal jugular route. Core temperature is recorded by a thermistor on an esophageal stethoscope. A second arterial line and a peripheral intravenous line are placed. During this time the patient is being positioned and secured by skeletal fixation for the anticipated surgical exposure.

Anesthesia is maintained with incremental doses of narcotics and is supplemented by a mixture of nitrous oxide and oxygen or isoflurane with nitrous oxide and oxygen to maintain stable cardiovascular parameters and an adequate level of anesthesia. Baseline evoked potential recordings are made during this preparatory phase prior to the incision. Surface cooling is initiated by lowering the ambient room temperature, placing the patient on a cooling blanket, and infusing cold saline intravenously. Gradual cooling proceeds at approximately 0.2°C/min.

Hemodilution to a hematocrit level of 28% to 30% is performed by running blood from one of the arterial lines or the femoral vein during cardiopulmonary bypass into an anticoagulant solution. This blood is reintroduced after the bypass is discontinued in order to replace essential clotting factors. Circulating volume is maintained by the addition of cold intravenous saline containing KCl (4 to 6 mEq/liter). As much as 4 liters of solution may be required for adequate hemodilution and hypothermia.

Barbiturate-induced EEG burst suppression for cerebral protection is maintained intraoperatively. After the aneurysm has been exposed and hemostasis secured, cardiopulmonary bypass is begun once the patient’s core temperature reaches 34°C. Anticoagulation is ob-

A posterior approach is carried far anteriorly and a good portion of the zygomatic arch is drilled off, leaving just a rim. This allows a very anterior subtemporal approach, minimizing traction on the vein of Labbe and providing good exposure with minimal retraction. Metaculous attention to hemostasis is required to avoid any oozing during heparinization. The exposure proceeds during the early cooling stages. Prior to heparinization and actual extracorporeal pump activation, the retraction should be placed so that no further repositioning is required during aneurysm clipping. It is at this point in the procedure that the surgeon decides whether the aneurysm can be clipped primarily or whether circularly arrest is required. If significant manipulation of the aneurysm or the associated vessels is necessary, extracorporeal circulation and complete cardiac arrest are performed.

Following final clip placement, the surgical field is inspected during the rewarming phase to assure complete hemostasis. When the pump is switched off and the heparin reversed, final wound closure is completed.

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Aneurysm clipping procedure that the surgeon decides whether the aneurysm or the associated vessels is necessary, extracorporeal circulation and complete cardiac arrest are performed.

Fig. 3. Summary of the changes in somatosensory evoked potentials that occur during induced hypothermia and cardiac arrest procedures. T = body temperature.
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tained with heparin (300 to 400 IU/kg) titrated to maintain an activated clotting time of 450 to 480 seconds. Femoral-femoral cannulation is done using a No. 32 to 36 French catheter in the right femoral vein via the saphenous bulb and No. 18 to 20 French catheter in the right femoral artery (Fig. 4). Partial extracorporeal circulation is initiated at a core body temperature of 32°C. A heart-lung circulation machine with a heat-exchanger and oxygenator with in-line pump is primed with iced saline, mannitol, and autologous blood solution before initiating the bypass.* Cooling during extracorporeal circulation is continued until the desired core temperature is reached. Characteristic electrocardiographic changes occur with hypothermia and should not be confused with other cardiac arrhythmias. As the heart is cooled, the sinus rate slows, the T waves invert, and the P-R, QRS, and Q-T intervals are prolonged. The atria frequently flutter or fibrillate below 30°C, and the ventricles fibrillate continuously below 28°C. Occasionally, a secondary deflection (the J or Osborn wave) appears on the descending limb of the QRS complex. If the fibrillation persists, the heart should be stopped with the addition of 40 to 80 mEq of KCl to the heart-lung pump to prevent myocardial ischemic injury. Persistent fibrillation may be eliminated with cardioversion at 100 to 250 W/sec.

During circulatory bypass, the mean arterial blood pressure (MABP) is maintained at 40 to 80 mm Hg. Flow rates are determined by MABP, venous and arterial mixed oxygenation, and systemic pH. The desired target temperature is controlled by the bypass heat exchanger.

Circulatory arrest occurs at between 22°C and 18°C with loss of cardiac electrical activity. The pump is stopped, the patient's head is elevated to promote venous drainage into the reservoir, and circulation is suspended. The duration of circulatory arrest is timed and limited to the period of clip application. Circulation is reestablished and reperfusion is accompanied by re-warming of the patient at 0.2°C to 0.5°C/min. Too rapid re-warming exceeds the tissues' demand for oxygen; this mismatch of oxygen supply and demand can cause tissue acidosis and hypoxia. As the re-warming continues, the heart will fibrillate spontaneously. If conversion to sinus rhythm does not occur early, cardioversion may have to be repeated and supplemented with appropriate antiarrhythmic, inotropic, and vasopressor drugs to establish a normal sinus rhythm and good filling pressures. Peripheral vasodilation is achieved with sodium nitroprusside to improve re-warming.

Extracorporeal circulation is discontinued when the heart can maintain a normal cardiac output and sinus rhythm and when body temperature has risen to 34°C. The patient's whole blood with fresh platelets and clotting factors is administered after circulatory bypass to reverse any bleeding diathesis. Heparinization is reversed with protamine sulfate to reduce the activated clotting time to between 100 and 150 seconds.

At the conclusion of the procedure, the patient is transported to the intensive care unit with the electro-physiological leads in place in order to monitor CNS activity during the slow recovery from the barbiturates administered intraoperatively. Adequate neurological assessment of gross motor function, response to painful stimuli, and pupillary reactivity may be delayed by several hours. Neither narcotic nor muscle relaxant drug effects are reversed and the patients are ventilated until they awake and are responsive. This postoperative recovery period requires critical control of cardiovascular and hemostatic parameters to ensure a good neurological outcome. The circulation volume is expanded postoperatively to enhance cerebral perfusion and minimize the potential effects of postoperative vasospasm. Extubation is attempted when the patient is responsive, airway reflexes are intact, normal blood gas values are maintained, and neuromuscular recovery is complete.

**Summary of Cases**

Seven intracranial procedures for posterior circulation aneurysms were performed under circulatory arrest
FIG. 5. Diagrammatic representation of the seven basilar artery aneurysms treated with hypothermic circulatory arrest.

FIG. 6. Case 4. Raphy scan dem.orrhage and filli and extracorp and January, basilar artery (5). Two patien SAH. Accordi Hess, one of other in Grad surgical explo following SAH weeks after SA and two were giant basilar a tally during w.

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and extracorporeal circulation between January, 1985, and January, 1987 (Table 1). All seven patients had basilar artery aneurysms, six giant and one large (Fig. 5). Two patients were operated on within 2 days of SAH. According to the SAH classification of Hunt and Hess, one of these patients was in Grade II and the other in Grade IV. One Grade I patient underwent surgical exploration and aneurysm clipping on Day 7 following SAH. Three patients were operated on 2 weeks after SAH. One of these patients was in Grade I and two were in Grade III. In one patient (Case 7), a giant basilar artery aneurysm was discovered incidentally during workup after mild head trauma.

All patients survived the neurosurgical procedure and the techniques of circulatory arrest and cardiopulmonary bypass. In every case the techniques of circulatory arrest allowed detailed dissection of the aneurysm with modest manipulation and direct clipping of the aneurysm base.

Of the patients operated on acutely, one (Case 1) had mild cognitive dysfunction, an ipsilateral third-nerve palsy, and a minimal contralateral hemiparesis after surgery. Over the next 2 months, after ventricular shunting for hydrocephalus, his motor and cognitive function returned to normal. He later developed shunt infection and ventriculitis, which was successfully treated. He had no other focal neurological deficits. He died from massive cardiopulmonary arrest 7 months after surgery. The second patient (Case 2) was in Grade IV preoperatively and underwent surgery 2 days after SAH. Postoperatively, he had an ipsilateral third-nerve palsy and a contralateral hemiparesis that improved steadily. The patient who underwent surgery on Day 7 after SAH (Case 3) had no neurological morbidity and was discharged 10 days after surgery.

Of the three patients treated 2 weeks after SAH, one (Case 4) had no neurological deficits and was discharged 1 week after surgery. Our oldest patient, a 77-year-old woman (Case 6, Figs. 6 and 7) developed a left frontal (contralateral) subdural hematoma at the conclusion of the operative procedure during a Valsalva maneuver. This was promptly evacuated. Postoperatively, she had a temporary expressive dysphasia that cleared in 2 weeks. She had no lasting neurological sequelae. The only neurological death in our series occurred in a 51-year-old woman with a severe SAH (preoperative Grade III). After awakening from surgery she was able to follow commands and move all four extremities; however, she developed sudden loss of consciousness and quadriplegia 12 hours later. She had a large brain-stem infarction despite the appearance of good clip position and elimination of the aneurysm without evidence of vessel compromise on follow-up angiography. She died 8 weeks later from severe pneumonitis. The patient with the unruptured aneurysm (Case 7) had an uncomplicated postoperative course and an excellent outcome (Fig. 8).

**Discussion**

The technical microneurosurgical advantages of employing total circulatory arrest in the treatment of giant intracranial aneurysms are many. First, the surgical field is bloodless, which improves visualization of the
vascular anatomy and pathology. Second, the danger of aneurysmal rupture during dissection is effectively eliminated. The absence of blood flow reduces both the tension in the blood vessels and the size of the aneurysm. The aneurysm may be manipulated, allowing safer dissection of the neck of the aneurysm and identification of associated vascular and neural structures. The precise application of aneurysm clips and/or end-aneurysmorrhaphy is made possible, allowing preservation of the parent artery and maintenance of the continuity of associated branches.

Not every patient with a giant or complex basilar artery aneurysm will require circulatory arrest. During the 2-year period of this report, 10 patients were taken for craniotomy and clipping of the aneurysm. In three individuals the surgical exposure allowed direct clipping of the aneurysms without undue manipulation, so complete cardiac arrest was not utilized.

In the event that circulatory arrest and extracorporeal circulation techniques are utilized, their safety has been well demonstrated. Meticulous neurosurgical and anesthetic techniques are essential for a good outcome. The following four key variables require close attention and, in large part, determine the success of neurosurgical procedures performed utilizing circulatory arrest and profound hypothermia: depth of hypothermia, duration of total circulatory arrest, barbiturate use, and hemostasis. These are examined in detail below.

**Depth of Hypothermia**

The major clinical value of hypothermia is offered by the decrease in the rate of cellular oxygen-requiring enzymatic reactions and the subsequent reduction in the cerebral metabolic rate of oxygen consumption (CMRO₂). A number of investigators have demonstrated the protective potential of hypothermia with experimental cerebral anoxia and during circulatory arrest with extracorporeal circulation. Oxygen consumption as a function of body temperature differs from species to species, and the safe limits of the depth of hypothermia vary accordingly. Rats have survived after cooling to a core temperature of 5°C, dogs have survived with minimal morbidity at temperatures down to 8.5°C, and monkeys have tolerated hypothermic circulatory arrest at temperatures of 15° to 20°C. Humans have been cooled to core temperatures as low as 10°C without permanent cerebral injury, however, most surgical procedures utilizing circulatory arrest and hypothermia are performed at core temperatures between 13° and 21°C.

The safe period of cerebral ischemia can be increased significantly by markedly reducing body temperature. Investigators in the early 1960's considered that, while the benefits of hypothermia were promising, the incidence of cerebral injury increased with core temperatures below 15°C. More recently, however, several large clinical series have demonstrated that cooling human patients to core temperatures of 13° to 14°C has few deleterious complications. Laboratory work further supports the notion that lower core temperatures may be more efficacious. Haneda, et al., found that dogs cooled below 10°C had a better neurological outcome than their counterparts cooled to only 12° or 18°C. These lower temperatures may be tolerated because of the nonlinear reduction in oxygen consumption with decreasing temperature. Peirce documented that oxygen consumption in humans drops to 50% of normal values with hypothermia to 30°C, 25% of normal at 25°C, 15% of normal at 20°C, and 10% of normal at temperatures as low as 15°C.

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Hypothermia has other effects besides reduced CMRO$_2$. These include increased blood viscosity, a 40% to 50% increase in the blood-gas partition coefficient that alters anesthetic transport, an increase in the serum glucose level secondary to reduced glucose utilization, a 30% to 50% reduction in blood flow rates during cardiopulmonary bypass, a left shift of the oxyhemoglobin dissociation curve with reduced oxygen availability, and a reduction in capacitance vessel diameter with subsequent alterations in the size and distribution of the circulating blood volume. The rate of heparin inactivation is also slowed with hypothermia. These complexities require knowledgeable neuroanesthetic management, close attention to heparinization and hemodilution, ventilation with an increased fraction of inspired oxygen (and less anesthesia), and frequent measurement of cardiac filling volumes and serum glucose values.

**Duration of Total Circulatory Arrest**

For practical surgical considerations, useful circulatory arrest has not been performed without also employing hypothermia for its cerebral protective effects. While the safe limit of total circulatory arrest for any given species is variable, the safe duration of complete arrest time is increased by reductions in body temperature. Lundar, et al., reported reduced mortality and neurological morbidity rates with arrest times below 50 minutes—a duration they described as the “safe period.” Rittenhouse, et al., limited cardiac arrest to 60 minutes at core temperatures of 17°C to 20°C in infants undergoing cardiac surgery. Barratt-Boyes and coworkers described safe limits of circulatory arrest up to 75 minutes at 20°C. Bland, et al., used profound hypothermia of 18°C and 20°C together with circulatory-arrest times of 60 to 90 minutes for pediatric cardiovascular procedures with good results.

Laboratory results obtained with animal models have been conflicting. Molina, et al., noted microscopic cellular damage and clinical neurological impairment in dogs treated with 60 minutes of circulatory arrest at 18°C. Haneda and associates reported the safe extension of total circulatory arrest to 90 minutes in their dog model, but noted that the incidence of neurological deficits was inversely proportional to the animal’s core temperature. Animals with the greatest reduction in body temperature had the lowest incidence of postoperative neurological compromise.

The median duration of complete arrest in our series was 11 minutes; the range was 7 to 53 minutes. This is consistent with reports from other neurological surgeons who have employed extracorporeal circulation for intracranial vascular surgery (Table 2).

**Role of Barbiturates**

Barbiturate administration has been used in conjunction with hypothermia during total circulatory arrest. Barbiturates reduce the metabolic requirements of neural tissue and may be responsible for extending the tolerance of the brain for the reduction in substrate supply that occurs during ischemia. Other neurochemical mechanisms may play a contributory role in barbiturate-induced cerebral protection. Regardless of the mechanism, barbiturates (in particular, thiopental and pentobarbital) clearly have the capacity to modify or prevent cerebral injury due to focal ische-
Barbiturate therapy is most effective when the agent is administered before a period of temporary ischemia. Laboratory experience with a primate model has established that preemptive administration of barbiturates provides cerebral protection even during 6 hours of middle cerebral artery (MCA) occlusion. The degree of protection provided by barbiturates far surpasses that of other general anesthetic agents.

Barbiturates offer less protection when administered after the onset of ischemia and appear to convey no protection when given more than 3 hours after the onset of temporary 6-hour MCA occlusion. Barbiturate administration may be deleterious when given in the presence of permanent vascular occlusion.

The role of barbiturates is less well established in the setting of temporary global ischemia. Laboratory studies with the hypoxic mouse model indicate that barbiturates offer global neuroprotective benefits. This protection was enhanced with the addition of hypothermia. Goldstein, et al., found that barbiturate anesthesia administered before the onset of global brain ischemia was protective in dogs; in contrast, Steen, et al., found no such benefit.

Nussmeier, et al., recently demonstrated a definitive improvement in the outcome of patients who received randomized barbiturate therapy during cardiopulmonary bypass procedures. This followed earlier work by Slogoff, et al., in which the benefits of thiopental administered during procedures employing cardiac arrest were suggested. Nussmeier, et al., used high-dose thiopental therapy (average patient dose 39.5 mg/kg) to maintain constant EEG burst suppression throughout the circulatory bypass period. They found a statistically significant reduction (p < 0.025) in postoperative neuropsychiatric dysfunction among patients randomized to the thiopental group.

Our experience with profound hypothermia and circulatory arrest indicates that prearrest, precircling administration of barbiturates (thiopental) in quantities sufficient to maintain burst suppression of EEG activity has not been deleterious and probably has improved cerebral protection. The average thiopental dose in this series was 21 mg/kg. After an initial loading dose of 3 mg/kg, patients received between 0.1 and 0.2 mg/kg/min (mean 0.17 mg/kg/min) to maintain EEG burst suppression throughout the operative procedure.

**Hemostasis and Clotting Mechanisms**

Complete circulatory arrest with extracorporeal circulation disrupts the coagulation cascade and normal hemostatic mechanisms in several ways. The most direct effect is due to the use of heparin, an essential component of cardiopulmonary bypass procedures. Heparin acts instantaneously to produce thrombin-antithrombin complexes that deactivate thrombin and factor X and inhibit the coagulation cascade. Protein-bound heparin is distributed throughout the plasma volume and is eliminated by first-order biodegradation and sequestration in the liver via the reticuloendothelial system. The half-life of heparin is approximately 100 minutes; however, this varies with dose and body temperature. There is also marked individual variability in the initial effect of heparin, its clearance, and its subsequent half-life.

Heparinization must be controlled by measuring the activated clotting time. The test, described by Hattersley, may be used as early as 3 minutes after heparin administration to control the extent of heparinization and the reversal of its effects with protamine sulfate. Normal activated clotting time values are between 140 and 160 seconds measured via a Hemachron device.

Other mechanisms that affect normal hemostasis are hypothermia, hemodilution, and the use of the heart-lung circulation pump. The heart-lung pump and plastic or gas oxygenator and the subsequent red blood cell (RBC)-foreign surface interface results in RBC and platelet trauma that contributes to their fragility, consumption, and consumption. The high oxygen tension, violent turbulence, negative pressure, and shear forces generated by the use of suction during extracorporeal circulation lowers hematocrit and platelet counts postoperatively. Heparin contributes to RBC dysfunction and platelet sequestration and slows the enzyme-mediated steps of the coagulation cascade. Hemodilution dilutes essential coagulation factors and enzymes, further contributing to the hypoaggregable state. Fibrinolysis and hypofibrinogenemia add to the hemostatic defects known to occur after cardiopulmonary bypass.

The major complication associated with the neurosurgical application of cardiopulmonary bypass procedures has been postoperative hemorrhage. Several mechanisms to combat perioperative hemorrhagic complications have been identified. First, most of the intracranial dissection should be performed before initiating circulatory arrest. Microneurosurgical techniques must be employed, and absolute hemostasis is mandatory. Close attention to anticoagulation with heparin during the operative procedure is required.

### TABLE 2

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Cases</th>
<th>Body Temperature (°C)</th>
<th>Duration of Arrest</th>
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<tr>
<td>Woodhall, et al., 1963</td>
<td>1</td>
<td>12</td>
<td>30 min</td>
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<tr>
<td>Patterson &amp; Ray, 1962</td>
<td>7</td>
<td>14-17</td>
<td>25 min - 94.5 min</td>
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<td>15</td>
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<td>Drake, et al., 1964</td>
<td>10</td>
<td>13-17</td>
<td>14 min - 2-18 min</td>
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<td>Uihlein, et al., 1966</td>
<td>67</td>
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<td>NA</td>
</tr>
<tr>
<td>Sundt, et al., 1972</td>
<td>1</td>
<td>13</td>
<td>30 min</td>
</tr>
<tr>
<td>Beugmattner, et al., 1983</td>
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<td>16-21.5</td>
<td>19 min - 0-51 min</td>
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<td>Spetzler, et al., 1988</td>
<td>7</td>
<td>17.5-21</td>
<td>11 min - 7-53 min</td>
</tr>
</tbody>
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*NA = data not available.

† Hemachron manufactured by International Technic Co., Metuchen, New Jersey.
Aneurysms of the basilar artery

nimed a heparin infusion (after an initial loading dose of 3 d 0.2 mg/kg/ in EEG burst procedure.

Corporal circulation and normal factors. We

of heparin, an bypass procedure thrombin thrombosis. Protamine sulfate, which binds milligram for milligram with heparin, is used as a heparin antagonist at the conclusion of the procedure. In the absence of heparin, protamine sulfate can produce a consumption coagulopathy and hypotension. For these reasons, heparin reversal with protamine sulfate requires titration by measuring the half-life. 11 Measuring the initial effect 17 half-life. 21 measuring the between 140 min.

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Hemocyanin is used as a heparin antagonist at the conclusion of the procedure. After discontinuation of circulatory arrest, the rewarming-recirculation period (mean approximately 90 minutes) is initiated. During rewarming, shivering should be avoided because of the compensatory increase in oxygen consumption (reportedly between 135% and 486% of normal) associated with it; if the cardiac output cannot keep pace with this accelerated oxygen demand, serious oxygen desaturation and tissue ischemia can occur.

Protamine sulfate is given before femoral deification once the heart is capable of sustaining systemic blood pressure and a normal sinus rhythm. The patient's initial whole blood and additional platelets (approximately 1 U/10 kg) are transfused. In addition to restoring normothermia, these maneuvers usually correct the aforementioned deficits in the coagulation cascade. Close attention to the patient's clotting parameters is required in the postoperative period. Calcium chloride and fresh frozen plasma are often administered to hasten normal hemostasis. The postoperative use of autologous blood has resulted in an 18% reduction in blood-bank requirements for patients undergoing cardiological bypass procedures. 21 Patients who received fresh frozen plasma and platelets as replacement in lieu of autologous whole blood showed slightly better results in postoperative clotting studies; however, this placed a tremendous drain on banked blood products and resulted in a 2.3% incidence of symptomatic hepatitis. 22 Combined use of the patient's autologous whole blood and supplemental banked blood products as required probably represents the most efficacious way to restore normal hemostasis after cardiological bypass procedures.

Baumgartner, et al. 3 reported a high incidence of associated deep venous thrombosis and/or pulmonary embolization, and attributed it to catheterization of the femoral vein. We did not encounter problems with deep venous thrombosis in our limited series. The routine cannulation of the saphenous bulb with the femoral venous catheter devised by Baumgartner and coworkers may have reduced the likelihood of this complication.

Table 3 outlines the morbidity, mortality, and outcome associated with treating patients undergoing surgery for giant basilar artery aneurysms with circulatory arrest. Ours is the largest reported series treated in this fashion, including one large and six giant basilar artery aneurysms. As with conventional surgical techniques, the relatively high associated morbidity reflects the difficulty of the surgical dissection of these complex basilar artery lesions. The five patients with excellent outcomes showed no evidence of neurological sequelae; the patient with a good outcome was minimally compromised neurologically; the four with fair results were functional, three despite an ipsilateral third nerve palsy and contralateral hemiparesis. Two patients had major neurological deficits and poor outcomes, and two patients died: one 5 hours postsurgery and one (our Case 5), a patient with poor outcome who had a brain-stem stroke, died 8 weeks after surgery from severe pneumonia. Ten (71%) of the 14 total patients (six of seven in our series) had functional outcomes or better.

There was no association between a patient's clinical SAH grade and the operative outcome. Similarly, we identified no contraindication to early surgery after SAH when using the techniques of circulatory arrest. Two patients in our series made functional recoveries despite having preoperative grades of III or IV (an excellent and a fair outcome, respectively). Drake, et al., 4 reported a patient who was in Grade III preoperatively and who had a fair operative result. Conversely, among the 14 patients outlined in Table 3, the two poor results and two deaths occurred in the three Grade II and one Grade III patient. Three of the 14 patients underwent early surgery (within 48 hours of aneurysm rupture); one had good and two had fair results. Three patients underwent surgery 6 to 7 days after hemorrhage; two had an excellent outcome, and the other died. Seven patients were operated on between 2 and 5

<table>
<thead>
<tr>
<th>Authors</th>
<th>Total Cases</th>
<th>Excellent</th>
<th>Good</th>
<th>Fair</th>
<th>Poor</th>
<th>Death</th>
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<td>1</td>
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<td>0</td>
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<tr>
<td>Morgan, et al., 1973</td>
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<td>Baumgartner, et al., 1983</td>
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<tr>
<td>Spetzler, et al., 1988</td>
<td>7</td>
<td>4</td>
<td>1</td>
<td>1</td>
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</tr>
<tr>
<td><strong>total cases</strong></td>
<td><strong>14</strong></td>
<td><strong>5</strong></td>
<td><strong>1</strong></td>
<td><strong>4</strong></td>
<td><strong>2</strong></td>
<td><strong>2</strong></td>
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</tbody>
</table>
years after SAH; two had excellent results, two had a fair result, two had poor outcomes, and one died. The single patient who was treated without prior SAH had an excellent result. The morbidity from these procedures appears to be related to the patient's general health and to the ability of the neurosurgeon to dissect and expose the aneurysm without undue retraction and manipulation rather than to the preoperative SAH grade or the length of time from aneurysm rupture to surgery. In an otherwise healthy patient, we advocate an early operation after SAH regardless of the clinical grade. We have restricted the use of circulatory arrest to complex lesions of the basilar artery because we believe that other vascular lesions are managed adequately with conventional techniques.

Conclusions

The inherent risks associated with the direct surgical treatment of giant basilar artery aneurysms can be reduced with the use of extracorporeal circulation, cardiac arrest, deep hypothermia, and barbiturate cerebral protection. The practice of gradual cooling and rewarming, the use of barbiturates for cerebral protection, adequate with conventional techniques.

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Aneurysms of the basilar artery

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50. Steen PA, Milde JH, Michenfelder JD: No barbiturate protection in a dog model of complete cerebral ischemia. Ann Neurol 5:343-349, 1979

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FIG. 6. Case 6. Contrast-enhanced computerized tomography scan demonstrating the significant subarachnoid hemorrhage and filling of the basilar artery aneurysm.

and extracorporeal circulation between January, 1985, and January, 1987 (Table I). All seven patients had basilar artery aneurysms, six giant and one large (Fig. 5). Two patients were operated on within 2 days of SAH. According to the SAH classification of Hunt and Hess,24 one of these patients was in Grade II and the other in Grade IV. One Grade I patient underwent surgical exploration and aneurysm clipping on Day 7 following SAH. Three patients were operated on 2 weeks after SAH. One of these patients was in Grade I and two were in Grade III. In one patient (Case 7), a giant basilar artery aneurysm was discovered incidentally during workup after mild head trauma.

All patients survived the neurosurgical procedure and the techniques of circulatory arrest and cardiopulmonary bypass. In every case the techniques of circulatory arrest allowed detailed dissection of the aneurysm with modest manipulation and direct clipping of the aneurysm base.

Of the patients operated on acutely, one (Case 1) had mild cognitive dysfunction, an ipsilateral third-nerve palsy, and a minimal contralateral hemiparesis after surgery. Over the next 2 months, after ventricular shunting for hydrocephalus, his motor and cognitive function returned to normal. He later developed shunt infection and ventriculitis, which was successfully treated. He had no other focal neurological deficits. He died from massive cardiopulmonary arrest 7 months after surgery. The second patient (Case 2) was in Grade IV preoperatively and underwent surgery 2 days after SAH. Postoperatively, he had an ipsilateral third-nerve palsy and a contralateral hemiparesis that improved steadily. The patient who underwent surgery on Day 7 after SAH (Case 3) had no neurological morbidity and was discharged 10 days after surgery.

Of the three patients treated 2 weeks after SAH, one (Case 4) had no neurological deficits and was discharged 1 week after surgery. Our oldest patient, a 77-year-old woman (Case 6, Figs. 6 and 7) developed a left frontal (contralateral) subdural hematoma at the conclusion of the operative procedure during a Valsalva maneuver. This was promptly evacuated. Postoperatively, she had a temporary expressive dysphasia that cleared in 2 weeks. She had no lasting neurological sequelae. The only neurological death in our series occurred in a 51-year-old woman with a severe SAH (preoperative Grade III). After awakening from surgery she was able to follow commands and move all four extremities; however, she developed sudden loss of consciousness and quadriaparesis 12 hours later. She had a large brain-stem infarction despite the appearance of good clip position and elimination of the aneurysm without evidence of vessel compromise on follow-up angiography. She died 8 weeks later from severe pneumonitis. The patient with the unruptured aneurysm (Case 7) had an uncomplicated postoperative course and an excellent outcome (Fig. 8).

Discussion

The technical microneurosurgical advantages of employing total circulatory arrest in the treatment of giant intracranial aneurysms are many. First, the surgical field is bloodless, which improves visualization of the

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age (yrs), Sex</th>
<th>Preop Grade*</th>
<th>Timing of Surgery</th>
<th>Postop Morbidity</th>
<th>Outcome</th>
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<tbody>
<tr>
<td>1</td>
<td>66, M II</td>
<td>Day 2</td>
<td>3rd nerve palsy, minimal contralateral hemiparesis; shunt infection</td>
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<td>2</td>
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<td>Day 2</td>
<td>3rd nerve palsy, contralateral hemiparesis</td>
<td>fair</td>
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<tr>
<td>3</td>
<td>41, M I</td>
<td>Day 7</td>
<td>none</td>
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<tr>
<td>4</td>
<td>58, M I</td>
<td>Day 14</td>
<td>none</td>
<td>excellent</td>
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<tr>
<td>5</td>
<td>51, F III</td>
<td>Day 12</td>
<td>brain-stem infarct, quadriaparesis; pneumonia</td>
<td>poor; died 8 wks postop</td>
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<tr>
<td>6</td>
<td>77, F III</td>
<td>Day 14</td>
<td>temporary dysphasia</td>
<td>excellent</td>
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<tr>
<td>7</td>
<td>62, F 0</td>
<td>Day 0</td>
<td>none</td>
<td>excellent</td>
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* Grade according to Hunt and Hess.24

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vascular anatomy and pathology. Second, the danger of aneurysmal rupture during dissection is effectively eliminated. The absence of blood flow reduces both the tension in the blood vessels and the size of the aneurysm. The aneurysm may be manipulated, allowing safer dissection of the neck of the aneurysm and identification of associated vascular and neural structures. The precise application of aneurysm clips and/or end-aneurysmorrhaphy is made possible, allowing preservation of the parent artery and maintenance of the continuity of associated branches.

Not every patient with a giant or complex basilar artery aneurysm will require circulatory arrest. During the 2-year period of this report, 10 patients were taken to the operating room with the anticipation that circulatory arrest would be employed to facilitate clipping of their basilar artery aneurysms. In three individuals the surgical exposure allowed direct clipping of the aneurysms without undue manipulation, so complete cardiac arrest was not utilized.

In the event that circulatory arrest and extracorporeal circulation techniques are utilized, their safety has been well demonstrated. 2,3,7,38 Meticulous neurosurgical and anesthetic techniques are essential for a good outcome. The following four key variables require close attention and, in large part, determine the success of neurosurgical procedures performed utilizing circulatory arrest and profound hypothermia: depth of hypothermia, duration of total circulatory arrest, barbiturate use, and hemostasis. These are examined in detail below.

**Depth of Hypothermia**

The major clinical value of hypothermia is offered by the decrease in the rate of cellular oxygen-requiring enzymatic reactions and the subsequent reduction in the cerebral metabolic rate of oxygen consumption (CMRO₂). 7,37,38 A number of investigators have demonstrated the protective potential of hypothermia with experimental cerebral anoxia 49 and during circulatory arrest with extracorporeal circulation. 16,20,31,38,38 Oxygen consumption as a function of body temperature differs from species to species, 37 and the safe limits of the depth of hypothermia vary accordingly. Rats have survived after cooling to a core temperature of 5°C, 7,37; dogs have survived with minimal morbidity at temperatures down to 8.5°C, 37 and monkeys have tolerated hypothermic circulatory arrest at temperatures of 15°C to 20°C. 31 Humans have been cooled to core temperatures as low as 10°C without permanent cerebral injury, however, most surgical procedures utilizing circulatory arrest and hypothermia are performed at core temperatures between 13°C and 21°C. 2,19,23,28,35,42,52,54

The safe period of cerebral ischemia can be increased significantly by markedly reducing body temperature. 7,17,20,35 Investigators in the early 1960's considered that, while the benefits of hypothermia were promising, the incidence of cerebral injury increased with core temperatures below 15°C. 12,26 More recently, however, several large clinical series have demonstrated that cooling human patients to core temperatures of 13°C to 14°C has few deleterious complications. 3,38 Laboratory work further supports the notion that lower core temperatures may be more efficacious. Haneda, et al., 20 found that dogs cooled below 10°C had a better neurological outcome than their counterparts cooled to only 12°C or 18°C. These lower temperatures may be tolerated because of the nonlinear reduction in oxygen consumption with decreasing temperature. Peirce 36 documented that oxygen consumption in humans drops to 50% of normal values with hypothermia to 30°C, 25% of normal at 25°C, 15% of normal at 20°C, and 10% of normal at temperatures as low as 15°C.

**Hypothermic CMRO₂.** The 40% to 50% decrease that alters the serum glucose utilization, 30; rates during cerebral anoxia; oxygen availability and distribution rate of heparinization and anticoagulation, and filtered volumes and

**Duration of Hypothermia**

For practical purposes, temperature was considered that, while the benefits of hypothermia were promising, the incidence of cerebral injury increased with core temperatures below 15°C. 12,26 More recently, however, several large clinical series have demonstrated that cooling human patients to core temperatures of 13°C to 14°C has few deleterious complications. 3,38 Laboratory work further supports the notion that lower core temperatures may be more efficacious. Haneda, et al., 20 found that dogs cooled below 10°C had a better neurological outcome than their counterparts cooled to only 12°C or 18°C. These lower temperatures may be tolerated because of the nonlinear reduction in oxygen consumption with decreasing temperature. Peirce 36 documented that oxygen consumption in humans drops to 50% of normal values with hypothermia to 30°C, 25% of normal at 25°C, 15% of normal at 20°C, and 10% of normal at temperatures as low as 15°C.
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Hypothermia has other effects besides reduced CMRO₂. These include increased blood viscosity, a 40% to 50% increase in the blood-gas partition coefficient that alters anesthetic transport, an increase in the serum glucose level secondary to reduced glucose utilization, a 30% to 50% reduction in blood flow rates during cardiopulmonary bypass, a left shift of the oxyhemoglobin dissociation curve with reduced oxygen availability, and a reduction in capacitance vessel diameter with subsequent alterations in the size and distribution of the circulating blood volume. The rate of heparin inactivation is also slowed with hypothermia. These complexities require knowledgeable neuroanesthetic management, close attention to heparinization and hemodilution, ventilation with an increased fraction of inspired oxygen (and less anesthesia), and frequent measurement of cardiac filling volumes and serum glucose values.

Duration of Total Circulatory Arrest

For practical surgical considerations, useful circulatory arrest has not been performed without also employing hypothermia for its cerebral protective effects. While the safe limit of total circulatory arrest for any given species is variable, the safe duration of complete arrest time is increased by reductions in body temperature. Lundar et al. found neurological only 12° or tolerated be- documented s to 50% of 25% of normal 10% of arrest up to 75 minutes at 20°C. Bland et al. used profound hypothermia of 18° and 20°C together with circulatory-arrest times of 60 to 90 minutes for pediatric cardiovascular procedures with good results.

Laboratory results obtained with animal models have been conflicting. Molina et al. noted microscopic cellular damage and clinical neurological impairment in dogs treated with 60 minutes of circulatory arrest at 18°C. Haneda and associates reported the safe extension of total circulatory arrest to 90 minutes in their dog model, but noted that the incidence of neurological deficits was inversely proportional to the animal's core temperature. Animals with the greatest reduction in body temperature had the lowest incidence of postoperative neurological compromise.

The median duration of complete arrest in our series was 11 minutes; the range was 7 to 53 minutes. This is consistent with reports from other neurological surgeons who have employed extracorporeal circulation for intracranial vascular surgery (Table 2).

Role of Barbiturates

Barbiturate administration has been used in conjunction with hypothermia during total circulatory arrest. Barbiturates reduce the metabolic requirements of neural tissue and may be responsible for extending the tolerance of the brain for the reduction in substrate supply that occurs during ischemia. Other neurochemical mechanisms may play a contributory role in barbiturate-induced cerebral protection. Regardless of the mechanism, barbiturates (in particular, thiopental and pentobarbital) clearly have the capacity to modify or prevent cerebral injury due to focal ische-