DEEP HYPOTHERMIA IN INTRACRANIAL SURGERY*
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(Received for publication December 1, 1955)

In order to evaluate the effect of low body temperature in intracranial surgery, we have carried out 18 major brain operations under medium deep and deep† hypothermia. The series consisted of 14 cases of brain tumour and 4 cases of vascular malformation. This is a preliminary report on our experiences from a neurosurgical point of view. Problems bearing on the general effects of hypothermia lie beyond the scope of the present communication and will not be discussed in detail.

General hypothermia was introduced into practical medicine in 1939 by Smith and Fay,23,24 who used the method in the treatment of cancer. Fay11 was also the first to employ hypothermia as an adjuvant in neurosurgery. With a “cooling blanket” he lowered the body temperature of patients with head injuries and hyperthermia to about 33.0°C (91.4°F.).

In 1951 a different method for lowering the body temperature was introduced by Laborit and Huguenard14 under the name of hibernation artificielle. This method, in which a superficial hypothermia is induced mainly by means of different drugs (“lytic cocktail”), has been used in intracranial surgery by Lazorthes et al.15 and by Woringer et al.29

In 1950 Bigelow et al.4 and in 1951 Boerema et al.7 showed that at a body temperature of 20°C (68°F.) dogs can survive total occlusion of the circulation during any time up to 15 minutes without sequelae from cerebral hypoxia being demonstrable on restoration of normal body temperature. Bigelow et al.5 also found that oxygen consumption decreased almost linearly with lowering of the temperature, provided that shivering was prevented by the administration of appropriate anesthetics and arterial oxygen saturation was maintained at a high level, and that under these conditions a tissue oxygen deficit did not develop during the cooling period. It is on the basis of these fundamental experiments that hypothermia has been utilized for the last 3 years in cardiac surgery to permit intracardiac operations under visual control. Communications on these investigations have been published by Lewis et al.,16 Swan et al.,23 Bailey et al.2 and others.

Hemorrhage, increased intracranial pressure, acute brain swelling and local cerebral hypoxia still render many intracranial procedures hazardous.

† In this paper “deep” hypothermia is to be understood as 27.0°C. (80.6°F.) and below, “medium deep” as 27.1°–32.0°C. (80.8°–89.6°F.) and “superficial” as above 32.0°C. (89.6°F.).
These complications are responsible for most of the postoperative neurological sequelae and deaths, and are the main cause of most of the difficulties encountered in brain surgery.

Despite the advances made in methods of hemostasis, the prevention of hemorrhage during or after an operation is still an important problem for the neurosurgeon. The introduction of induced hypotension by ganglionic blocking agents in 1948 marked a great advance, especially in the surgery of vascular malformations. It has long been known that the blood pressure decreases with lowering of the body temperature,\textsuperscript{28} but the underlying mechanism appears to differ widely from that of hypotension induced by ganglionic blocking agents.

Studies on cerebral hemodynamics in man\textsuperscript{9,18,25} indicate that the fall in blood pressure in the cerebral arteries accompanying ganglionic block is compensated by a corresponding decrease in the peripheral resistance caused by vasodilatation, with the result that the cerebral blood flow is still sufficient for satisfactory oxygenation of the brain. Stone et al.\textsuperscript{25} found complete compensation at blood-pressure levels as low as 31 to 60 mm. Hg in 4 cases, but they pointed out that these results do not permit generalization, since many different factors, such as general anesthesia or arteriosclerosis of the cerebral arteries, might cause compensation to be incomplete. It seems reasonable to suggest that increased intracranial pressure may act similarly by deranging cerebrovascular dynamics. In hypothermia, on the other hand, the consumption of oxygen decreases simultaneously with the fall in blood pressure: oxygenation of the tissues is still satisfactory, despite low arterial pressure, peripheral vasoconstriction and diminished blood flow. In experiments on dogs Bigelow et al.\textsuperscript{5} found this to hold down to a temperature of 19.0°C. (66.2°F.) for up to 4 hours (blood pressure between 20 and 40 mm. Hg).

Clinical investigations of the side effects of induced hypotension show that this method involves certain risks of damage to the brain and other organs by hypoxia. By means of questionnaires to British anesthetists, Hampton and Little\textsuperscript{12} collected information about 21,000 cases in which hypotension had been induced by ganglionic blocking agents. There were 42 deaths (0.2 per cent), probably ascribable to the hypotension. Statistical evaluation suggested that 80 mm. Hg is a critical level, above which complications are infrequent. The incidence of cerebral hypoxia cannot be estimated from these series. Berg\textsuperscript{3} and Nilsson,\textsuperscript{19} using flicker fusion after administration of Evipan as a test of cerebral function, found values supposed to indicate diffuse cerebral injury in 12 of 29 patients operated upon extracranially under induced hypotension with blood pressures between 60 and 80 mm. Hg. As to deep hypothermia, no comparable investigations are available, but, as far as we know, no experimental or clinical data available show that hypothermia involves a risk of cerebral hypoxia (provided that ventilation is sufficient and shivering is prevented). Smith\textsuperscript{22} reviewed a number of patients with cancer treated with hypothermia. He found no signs of mental dis-
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inchurbances, and at 50 autopsies he could not detect any evidence of injury from cerebral hypoxia. Callaghan et al.\(^8\) induced hypothermia (20° C., 68° F.) in monkeys. After rewarming they could not find any signs of mental disorder or electroencephalographic abnormalities.

The above-mentioned investigations suggest the following conclusion: In hypotension induced by ganglioplegic agents hemodynamic mechanisms try to maintain cerebral blood flow at a normal level by means of vasodilatation. Under certain circumstances, however, these mechanisms fail and thereby create the risk of cerebral hypoxia, this risk being increased below a critical level of 80 mm. Hg. In hypothermia the low blood pressure is accompanied by a decrease in cerebral blood flow. Nevertheless the risks of cere-

![Diagram](https://via.placeholder.com/150)

**FIG. 1.** Diagram illustrating the interplay of different factors suggested as possibly producing increased intracranial pressure and brain swelling.

bral hypoxia seem to be less than at normal body temperature, even if the blood-pressure level is far below 80 mm. Hg.

*Increased intracranial pressure and swelling of the brain* are complex phenomena correlated with many factors, several of which are themselves correlated. This explains the tendency to the development of a frequently fatal vicious cycle. We have tried to depict the interplay of these factors diagrammatically in Fig. 1, which is based on well known clinical and experimental observations.

The interrelationships apparent from the diagram suggest that hypothermia might be able to diminish or counteract swelling of the brain by diminishing the risk of general hypoxia and decreasing the cerebral blood pressure and blood flow. The above-mentioned studies on cerebral blood flow in hypotension induced by ganglioplegic agents indicate that these agents do not produce any decrease in the volume of the brain. This is in line with our clinical experience that induced hypotension has only a slight
effect, if any, on the persistent increase in intracranial pressure in cases of brain tumours. Obrador et al.\textsuperscript{20} made similar observations in an experimental and clinical investigation. In contrast therewith they found a clear effect of ganglioplegic agents on sudden increase of intracranial pressure and brain volume produced in dogs by lesions of the floor of the fourth ventricle as well as on the acute swelling of the brain that sometimes occurs in humans during intracranial operations. In the present investigation special interest was focused on the effect of hypothermia on increased intracranial pressure and acute swelling of the brain.

Local cerebral hypoxia with consequent functional disorders must always be taken into consideration when manipulation of large arteries or veins is necessary during an intracranial procedure. Functional disturbances after direct traumatisation of the brain tissue during an operation can probably also be at least partly ascribed to disturbance of the circulation with consequent local hypoxia. It is known from Bigelow et al.\textsuperscript{4} that the risk of general hypoxia and its sequelae after temporary occlusion of the blood supply to the brain decreases with lowering of the body temperature. It does not sound unreasonable to suppose that this might also hold for lesions from local hypoxia, especially if the lesions are caused by reversible circulatory disturbances such as ligation of parasagittal veins, spastic arterial constriction, temporary clamping of a cerebral artery or pressure on the brain. Judging by the experiments of Ralston et al.\textsuperscript{21} and Thompson and Smith\textsuperscript{27} on dogs, hypotension produced by loss of blood or ganglionic blocking agents enhances the cerebral injury following ligation of the middle cerebral artery. These investigations suggest that, as far as local hypoxia is concerned, deep hypothermia implies better surgical conditions than those prevalent in normothermic patients with or without hypotension induced by means of ganglionic blocking.

When planning the present investigation there were thus ample experimental and clinical data available suggesting that deep hypothermia might imply certain advantages in intracranial surgery, especially with regard to hemorrhage, increased intracranial pressure, brain swelling and lesions from local hypoxia. Our decision to try deep hypothermia in brain operations was preceded by experimental work with special reference to the effect of hypothermia on different kinds of brain lesions (unpublished). It was the experience gained thereby that guided our choice of technique for the induction of hypothermia in the clinical trial.

The risks of deep hypothermia were known beforehand from experimental studies on animals and from clinical reports of surgery on the open heart. In the clinical series ventricular fibrillation was responsible for most of the postoperative deaths. In the 3 largest series,\textsuperscript{2,16,26} including 34 cases in all, ventricular fibrillation occurred in 13 cases with 6 fatalities. In only 3 cases did fibrillation start before the heart had been exposed, apparently at body temperatures between 27.0\degree C., and 30.0\degree C. (80.6\degree F.–86.0\degree F.). It sounds reasonable to suppose that the risk of ventricular fibrillation is less in pa-
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Patients without severe organic heart disease and operated upon without manipulation of the exposed heart. On the other hand, in cases of emergency, countermeasures can be taken with less loss of time if the thorax is open. It was mainly because of the risk of cardiac complications that the first 6 operations in the present series were carried out on patients with gliomata or metastases in the brain. No patients with serious organic heart disease were accepted for hypothermia. Apart from this, the patients were not selected according to any standardized criteria.

METHOD

Hypothermia was induced and body temperature was restored by means of circulating air in an apparatus described by Lundberg and Nielsen. The design and mode of action of the apparatus are apparent from Fig. 2.

The anesthetic procedure was as follows. The usual premedication was given: to patients with symptoms or signs of increased intracranial pressure phenobarbital and atropine; to the remainder phenobarbital, morphine and scopolamine. Anesthesia was induced with a basic dose of Evipan (200–400 mg.), after which the patient was intubated with a cuff-tube, relaxation being secured by succinylcholinechloride. Anesthesia was maintained by inhalation of nitrous oxide and ether. In order to get the shivering under control from the very beginning of the cooling procedure, we aimed at securing moderately deep anesthesia (third stage, plane 2) before it was started.

As soon as the anesthesia was considered deep enough, the patient was placed in the cold box and connected to the anesthesia machine and the equipment for recording blood pressure and body temperature as well as to the electrocardiograph. In order to insure adequate ventilation throughout the procedure of hypothermia, the respiration of the patient was taken over by a respirator during the period of active cooling, i.e., before the body temperature reached 30°C (86°F.). In the beginning the patient’s hands, feet and external genital organs were protected, but later this practice was found unnecessary. The temperature in the box was maintained at a fairly constant level between −5°C. and −10°C. (23°–14°F.). In all cases except 3, active cooling was interrupted at a rectal temperature of about

* Manufactured by Atlas, Copenhagen.
30°C. (86°F.), which was reached after an average of 2 hours, 20 minutes (range: 3 hours, 20 minutes–1 hour, 25 minutes).

As soon as the patient was removed from the box, he was laid on the operating table, and the operation was started after catheterization of the radial artery and a subcutaneous vein. The rectal temperature continued to fall after active cooling had been stopped: at the beginning of the operation it varied between 28.0°C and 29.0°C. (82.4–84.2°F.); 1–1½ hours after the end of active cooling the fall in temperature ceased at between 24.8°C and 27.0°C. (76.6°–80.6°F.). The rectal temperature persisted at this low level until rewarming was started, in one case as long as 8 hours (see Fig. 3).

Continuous infusion of 5 per cent glucose by intravenous drip and one or two infusions of 500 ml. citrated blood were routine measures. In 2 cases Arfonad* in a 0.1 per cent solution was administered by intravenous drip.

The rewarming procedure was varied. After the operation the patients were usually placed in the box in which the temperature was maintained at 35°–40°C. (95°–104°F.) with the fan running. Rewarming to 34.0°C. (93.2°F.) usually required 3–4 hours. During this period shivering could usually be controlled with nitrous oxide only. In some cases the patients also received chlorpromazine in one or more doses of 50 mg. After the rectal temperature had increased to about 34.0°C. (93.2°F.) the patient was put to bed and transported to the ward. In some cases rewarming was intentionally retarded: on conclusion of the operation the patient was immediately placed in bed and removed to a room with a thermostatically controlled temperature of 30°C–35°C. (86°–95°F.). In one instance (Case 7) recovery of body temperature to 34.0°C. (93.2°F.) required 11 hours (see Fig. 3). The respirator was disconnected during the rewarming period at varying levels of temperature from 26.0°C–34.0°C. (78.8°–93.2°F.).

The rectal temperature was measured with a thermocouple and a mirror galvanometer,† and the blood pressure by sphygmomanometer and palpation of the radial pulse. (All blood-pressure values in this paper are therefore only approximate and are given to the nearest degree.) The electrocardiograms were recorded by a direct writing apparatus‡ and could also be followed continuously on the screen of a cathode-ray oscillograph.§ This equipment also permitted continuous recording of the muscle activity in association with shivering.

RESULTS

Mortality. Two deaths (Cases 10 and 11) occurred in this series (operative mortality 11 per cent). In Case 10 postmortem examination revealed diffuse purulent meningo-encephalitis, the origin of which could not be explained. In Case 11 the cause of death was increased intracranial pressure from multiple metastatic tumours in the brain and possibly accentuated by the operative trauma. In neither of the 2 fatal cases did the postoperative course or the postmortem examination reveal anything suggesting that the hypothermia per se had played a contributory rôle as a cause of death. This possibility, however, cannot be excluded with certainty.

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* Manufactured by Hoffmann-La Roche, Inc., Basel, Switzerland.
† "Electric Universal Thermometer" type TE 3, Elektrolaboratoriet, Copenhagen.
‡ "Mingograf," type 28, Elema, Stockholm.
§ "Cardioscope," Elema, Stockholm.
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Fig. 8. Diagrams illustrating the fluctuations of rectal temperature, blood pressure and pulse during hypothermia in two different cases. (I) Cooling in the box. (II) Operation. (III) Rewarming. (IV) Patient back in the ward. ↓ indicates transfusion.


(Below) Case 7. Female. Aged 48 years. Partial removal of meningioma from clivus and left petrous bone.

Extracerebral Complications. Ventricular fibrillation did not occur in any of the patients.* Electrocardiographic abnormalities (arrhythmia, extrasystole, deformation of the auricular and ventricular complexes) were re-

* Since this series was presented we have had one case of ventricular fibrillation with fatal outcome.
<table>
<thead>
<tr>
<th>Case No.</th>
<th>Age</th>
<th>Sex</th>
<th>Diagnosis</th>
<th>Operation</th>
<th>Cooling Time</th>
<th>Rectal Temp. at End of Cooling °F</th>
<th>Rectal Temp. °C</th>
<th>Lowest Rectal Pressure (mm Hg)</th>
<th>Operating Time</th>
<th>Rewarming Time (to 34° C.)</th>
<th>Postoperative Complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>48</td>
<td>M</td>
<td>Metastatic carcinoma, lt. occipital, Bronchial carcinoma</td>
<td>Extirpation</td>
<td>3 hrs</td>
<td>99.6 (85.3)</td>
<td>29.9 (84.6)</td>
<td>90</td>
<td>3 hrs</td>
<td>5 hrs</td>
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<tr>
<td>2</td>
<td>31</td>
<td>F</td>
<td>Astrocytoma, rt. frontal</td>
<td>Resection of frontal lobe</td>
<td>2 hrs</td>
<td>30.0 (86.0)</td>
<td>28.6 (83.3)</td>
<td>90</td>
<td>2 hrs, 50 min</td>
<td>2 hrs</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>02</td>
<td>M</td>
<td>Glioblastoma, rt. parietal</td>
<td>Partial extirpation</td>
<td>2 hrs, 45 min</td>
<td>29.4 (84.9)</td>
<td>25.1 (77.8)</td>
<td>50</td>
<td>3 hrs</td>
<td>7 hrs</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>57</td>
<td>M</td>
<td>Glioblastoma, rt. parieto-occipital</td>
<td>Extirpation</td>
<td>3 hrs, 20 min</td>
<td>29.9 (85.8)</td>
<td>24.8 (76.7)</td>
<td>&lt;50</td>
<td>3 hrs, 45 min</td>
<td>4 hrs, 40 min</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>47</td>
<td>F</td>
<td>Glioblastoma, lt. parietal</td>
<td>Extirpation</td>
<td>2 hrs, 15 min</td>
<td>31.3 (88.4)</td>
<td>27.0 (80.4)</td>
<td>75</td>
<td>3 hrs</td>
<td>4 hrs, 15 min</td>
<td></td>
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<tr>
<td>6</td>
<td>61</td>
<td>F</td>
<td>Glioblastoma, rt. frontal</td>
<td>Resection of frontal lobe</td>
<td>1 hr, 45 min</td>
<td>31.8 (88.4)</td>
<td>27.2 (81.0)</td>
<td>65</td>
<td>2 hrs, 40 min</td>
<td>3 hrs, 15 min</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>43</td>
<td>F</td>
<td>Meningioma, clivus and lt. pyramid</td>
<td>Partial extirpation</td>
<td>2 hrs</td>
<td>29.9 (85.8)</td>
<td>25.7 (78.3)</td>
<td>50</td>
<td>7 hrs, 30 min</td>
<td>10 hrs</td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>47</td>
<td>M</td>
<td>Aneurysm, ant. communicating artery</td>
<td>Intracranial ligation</td>
<td>3 hrs, 15 min</td>
<td>30.7 (87.3)</td>
<td>26.6 (79.9)</td>
<td>40</td>
<td>4 hrs, 30 min</td>
<td>3 hrs, 10 min</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>22</td>
<td>F</td>
<td>Arteriovenous aneurysm, rt. parietal</td>
<td>Extirpation</td>
<td>2 hrs, 15 min</td>
<td>30.0 (86.0)</td>
<td>24.8 (76.7)</td>
<td>45</td>
<td>4 hrs</td>
<td>3 hrs, 50 min</td>
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</tr>
<tr>
<td>10</td>
<td>58</td>
<td>M</td>
<td>Aneurysm, ant. communicating artery</td>
<td>Intracranial ligation</td>
<td>3 hrs</td>
<td>30.0 (86.0)</td>
<td>25.6 (78.0)</td>
<td>45</td>
<td>4 hrs, 10 min</td>
<td>4 hrs</td>
<td>Diffuse purulent hemorrhagic encephalitis, Died 7th postop. day</td>
</tr>
<tr>
<td>11</td>
<td>51</td>
<td>M</td>
<td>Multiple cancer metastases to brain, Bronchial carcinoma</td>
<td>Extirpation of temporal metastasis</td>
<td>1 hr, 45 min</td>
<td>30.3 (86.5)</td>
<td>24.9 (76.8)</td>
<td>50</td>
<td>3 hrs, 15 min</td>
<td>3 hrs, 30 min</td>
<td>Brain swelling and extradural hematoma, Died 8th postop. day</td>
</tr>
<tr>
<td>12</td>
<td>57</td>
<td>F</td>
<td>Glioblastoma, lt. parietal</td>
<td>Extirpation</td>
<td>1 hr, 25 min</td>
<td>30.3 (86.4)</td>
<td>27.0 (80.6)</td>
<td>65</td>
<td>3 hrs, 5 min</td>
<td>5 hrs</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>88</td>
<td>M</td>
<td>Astrocytoma, lt. parietal</td>
<td>Extirpation</td>
<td>2 hrs, 45 min</td>
<td>29.9 (85.8)</td>
<td>25.0 (77.0)</td>
<td>65</td>
<td>2 hrs, 30 min</td>
<td>7 hrs</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>65</td>
<td>F</td>
<td>Convexity meningioma, lt. parietal</td>
<td>Extirpation</td>
<td>2 hrs</td>
<td>30.0 (86.0)</td>
<td>25.8 (78.4)</td>
<td>90</td>
<td>3 hrs</td>
<td>3 hrs, 40 min</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>44</td>
<td>M</td>
<td>Glioblastoma, lt. temporal</td>
<td>Partial extirpation</td>
<td>2 hrs</td>
<td>30.0 (86.0)</td>
<td>25.2 (77.4)</td>
<td>60</td>
<td>3 hrs</td>
<td>4 hrs</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>49</td>
<td>F</td>
<td>Acoustic neurinoma, rt. side</td>
<td>Radical extirpation; preservation facial nerve</td>
<td>2 hrs</td>
<td>30.0 (86.0)</td>
<td>25.2 (77.4)</td>
<td>70</td>
<td>5 hrs, 3 min</td>
<td>7 hrs, 15 min</td>
<td>Bronchopneumonia</td>
</tr>
<tr>
<td>17</td>
<td>53</td>
<td>M</td>
<td>Arteriovenous aneurysm, rt. parietal</td>
<td>Extirpation</td>
<td>3 hrs, 15 min</td>
<td>30.0 (86.0)</td>
<td>26.0 (78.8)</td>
<td>65</td>
<td>4 hrs, 3 min</td>
<td>7 hrs</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>40</td>
<td>F</td>
<td>Glioblastoma, rt. frontal</td>
<td>Extirpation</td>
<td>2 hrs</td>
<td>30.0 (86.0)</td>
<td>25.7 (78.3)</td>
<td>65</td>
<td>4 hrs, 15 min</td>
<td>2 hrs, 30 min</td>
<td>Postop. intracerebral hematoma (evacuated), Probably damage to brain stem</td>
</tr>
</tbody>
</table>
corded in most cases. These abnormalities regularly disappeared during rewarming.

In Case 16 bronchopneumonia and fever developed on the 3rd day after operation and persisted for 3 days. This complication was probably ascribable in part to the lateral position of the patient during a fairly time-consuming operation (radical removal of an acoustic neurinoma with preservation of the facial nerve).

No symptoms or signs of prolonged renal complications were observed (only the nonprotein nitrogen and the daily urinary output were determined routinely). In analogy with what was observed by Andersen and Nielsen in rabbits, the excretion of urine decreased considerably or almost ceased during hypothermia, to increase again during restoration of body temperature. In 1 patient (Case 10) urinary excretion was almost or completely suppressed for about 12 hours after the end of the operation, but without any accompanying increase in the nonprotein nitrogen. In this case the blood pressure had been lowered with Arfonad from 80 mm. Hg to 30–40 mm. Hg for about 45 minutes.

Though measures were usually not taken to protect the peripheral parts of the body, none of the patients showed any signs of superficial frostbite or pressure gangrene. The healing of the scalp wounds was uncomplicated in all cases.

Cerebral Complications. In 2 cases a postoperative hematoma was evacuated. In one of these (Case 11) the hematoma was caused by a silver clip having slipped off a dural artery; in the other (Case 18) it was not possible to ascertain the source of hemorrhage. Apart from these 2 cases and Case 10, we had the impression that, as far as cerebral symptoms in general are concerned, the postoperative course was usually smoother than what might have been expected without the use of hypothermia. No statistical data are available in support of this impression, but the following observations might be mentioned. As a rule, the patients were mentally clear the day after the operation. Three patients were out of bed sitting in a chair on the 2nd day after operation, 5 on the 3rd, and 4 on the 4th. On the average the patients were out of bed on the 4th postoperative day. The early postoperative rise in temperature was moderate, and no late fever reactions with or without signs of meningeal irritation were seen during the later postoperative course.

Blood Pressure and Bleeding. The fall and rise of the blood pressure followed a fairly uniform pattern during the different phases of the procedure of hypothermia (Fig. 3). In all 12 cases, where the lowest rectal temperature was 26.0°C. (78.8°F.) or less, a drop in blood pressure of about 50 per cent was recorded, and in 6 of these cases the blood-pressure level lay below 60 mm. Hg. In the remaining 6 cases there was a 50 per cent decrease in 3 and a level under 60 mm. Hg in only 1. In 2 cases (Nos. 8 and 10) the blood pressure was lowered further by the administration of Arfonad (Fig. 3): in Case 8 from 80–90 mm. Hg to 40–50 mm. Hg; in Case 10 from 70–80 mm. Hg to 30–40 mm. Hg. Apart from the aforementioned transient anuria, the administration of Arfonad was not followed by any demonstrable side effects.
At all operations except 1 (Case 7) bleeding was only slight and hardly disturbing. The operative field could easily be kept entirely visible, and in most cases hemostasis presented no difficulties. The effect of the low blood pressure and decreased blood flow was particularly favourable in cases of intracranial aneurysms and richly vascularized gliomata. In 4 cases the control of venous bleeding from the dura mater was somewhat more troublesome than usual. This was obviously caused by a decrease of the coagulability and not by any high pressure in the cerebral veins.

*Increased Intracranial Pressure and Swelling of the Brain.* No measurements were made of the intracranial pressure during hypothermia. Of the 14 patients with cerebral tumour, 8 had papilledema, which was advanced in 5 and moderate in 3. Of these patients with papilledema, 3 were profoundly somnolent and 3 moderately so. At all operations for tumours, the gyri were found to be flattened, suggesting that the intracranial pressure had been raised for some time before the operation. When the dura mater was exposed at a rectal temperature of about 28.0°C. (82.4°F.) it regularly appeared to be less tense than what is generally seen in the presence of brain tumour with increased intracranial pressure. In 3 cases the dura mater was slightly tense; in the remainder it was, if anything, flaccid. The dura mater was always opened without previous ventricular puncture and neither immediately nor later during the operation did the brain bulge out through the defect. In those cases in which a glioma or a metastatic tumour was removed from the depth of a cerebral hemisphere, the wound in the brain was open and could be visually inspected until the very end of the operation. In all cases the dura mater was sutured without disturbing tension, and the rest of the wound was closed without decompressive measures. Thus, on no occasion did acute swelling of the brain occur during the operation.

**DISCUSSION**

Though no measurements were made of the intracranial pressure in these series, our observations at the operating table might be regarded as sufficiently conclusive to establish that lowering of the body temperature to 25°–27°C. (77°–80.6°F.) appreciably diminishes the increased intracranial pressure caused by brain tumours and mitigates the risk of acute swelling of the brain during intracranial operations. This implies a better approach to, and view of, the operative field as well as less traumatisation of the brain, and it also facilitates adequate closing of the wound. We offer no explanation for the underlying mechanism of this effect of hypothermia, but we suppose that it is the combined result of several factors including decreased blood pressure and blood flow, better oxygenation of the brain tissue, and possibly also a decreased production of cerebrospinal fluid. Neither do we know the minimum decrease in body temperature necessary to secure these surgical advantages, but even at 29.0°C. (84.2°F.) we observed a marked effect in 1 case.

Diminution of the bleeding at operation on richly vascularized tumours
proved valuable, but the greatest direct advantage of the low blood pressure and blood flow was observed in operations on vascular malformations, for the treatment of which deep hypothermia might open new surgical possibilities. Judging by observations made in our cases, this favourable effect of hypothermia is generally not optimal until the blood pressure has dropped below 60 mm. Hg, a level usually not reached until the temperature has fallen to below 27.0°C. (80.6°F.). Hypothermia in combination with ganglionic block was tried in 2 cases of intracranial arterial aneurysms. The fall in blood pressure obtained thereby (down to 30–50 mm. Hg) produced unusually favourable conditions for dissection of the aneurysm and neighbouring arteries. From what is known about oxygen transport and utilization at low body temperatures, it seems probable that lowering the blood pressure from 80 to 40 mm. Hg at 25°C. (77°F.) involves less risk than does lowering it from 120 to 60 mm. Hg at a normal body temperature, above all if cerebrovascular dynamics are deranged by increased intracranial pressure. Dundee et al.¹⁰ have reported good results of a combination of medium deep hypothermia (30°–32°C.) and the administration of Arfonad by which method they obtained blood-pressure levels between 60 and 70 mm. Hg.

The suggested rôle of hypothermia in diminishing the frequency of lesions caused by local hypoxia cannot be evaluated on the basis of the present investigations. Transient occlusion of a major brain artery under hypothermia is an expedient to facilitate surgical treatment of intracranial vascular malformations. In none of our cases was this procedure indicated.

Our experience with the method for inducing hypothermia used in the present study was promising. We cannot confirm the opinion of Bailey et al.² that the use of cold circulating air is unsuitable because of the risk of cold injuries to the skin. Our decision to use inhalation anesthesia was based on the assumption that the diffusion processes dominating the transport of gaseous anesthetics are influenced less by low temperature than the processes responsible for breaking down anesthetics administered parenterally. Several of our patients still breathed spontaneously at rectal temperatures of 25.0°–26.0°C. (77.0°–78.8°F.). This observation is not in accordance with the opinion of Keown et al.¹¹ and others that respiration ceases below 28°C.

The induction of deep hypothermia is a major undertaking, which still involves certain risks. Is it nevertheless justifiable to use deep hypothermia in neurosurgery? Our experience suggests that the risks are not so great as to contraindicate its use in selected cases in which control of hemorrhage and brain swelling are imperative for the success of a hazardous operative procedure such as the extirpation of certain less readily accessible or highly vascularized tumours and very large arteriovenous aneurysms. But as yet we know too little about the untoward side effects of hypothermia, especially about ventricular fibrillation and how to prevent it, to advocate a more general use of deep hypothermia in intracranial surgery. If, however, future investigation can show that the risks are not significantly greater than those involved by the anesthetic methods now used in neurosurgery, deep hypo-
hypothermia might prove a valuable adjuvant in many intracranial operations: it will improve the results and decrease the strain on the neurosurgeon and perhaps permit operations now usually regarded as too risky, such as intracranial ligature of ruptured aneurysms in the acute stage.

SUMMARY

1. Eighteen major intracranial operations were done under general hypothermia with a lowest rectal temperature of between 24.8°C. (76.6°F.) and 29.2°C. (84.6°F.). The series included 14 cases of brain tumour and 4 cases of vascular malformation.

2. Hypothermia was induced and body temperature was restored by means of circulating air in a specially constructed apparatus.

3. There were 2 deaths, 1 caused by multiple cerebral metastases from a generally metastasizing bronchial cancer and 1 caused by a diffuse purulent meningo-encephalitis of unknown origin. Apart from bronchopneumonia of moderate severity in 1 case there were no extracerebral complications of any significance. Two postoperative hematomas were evacuated. There were no signs of cerebral complication ascribable to hypothermia.

4. Blood-pressure levels between 40 and 60 mm. Hg were recorded in 8 cases and between 60 and 90 mm. Hg in 10 cases. In 2 cases of arterial aneurysm an additional decrease in blood pressure to between 30 and 50 mm. Hg was induced by means of Arfonad. At these blood-pressure levels the conditions with regard to bleeding, hemostasis and dissection of aneurysms were highly favourable.

5. In the cases of brain tumour, observations during the operations showed that the preoperatively increased intracranial pressure was considerably reduced during the state of deep hypothermia. In none of these cases was a tendency to acute swelling of the brain observed during operation.

6. It is concluded that deep hypothermia produces certain favourable effects in intracranial surgery for brain tumours and vascular malformations, and that it should be used in selected cases in which these effects are of special importance.

We are indebted to the manufacturer of the cooling device, A/S Atlas, Copenhagen, and its representative in Sweden, Disponent G. Ekblad, Malmö, for valuable technical and economic help.

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