THERAPEUTIC HYPOTHERMIA IN CASES OF HEAD INJURY*

C. B. SEDZIMIR, M.D.

Regional Neurosurgical Centre, Walton Hospital, Liverpool, England

(Received for publication February 24, 1958)

The combination of a safe hypothermic technique and general anaesthesia during neurological operations is now an established procedure and its advantages have already been discussed.\textsuperscript{1, 2, 5, 11} Following its evolution, our attention was turned to the possible use of hypothermia as a therapeutic measure in cases of severe head injury and of spontaneous intracranial haemorrhage. This communication discusses and evaluates its use in a series of severe head injuries, from December 1953 to October 1957.

It is not necessary to enlarge upon the clinical manifestations and poor prognosis of a primary brain-stem injury, nor upon the pathology and mechanism of the shifts of the brain which may lead to a secondary brain-stem lesion. Once extradural and acute subdural haematoma are excluded, or dealt with surgically, we are left with the problems associated with diffuse neuronal paralysis or destruction, contusion of the brain, laceration and cerebral haemorrhage, giving rise to progressive swelling of the brain. This leads to an ever increasing cerebral circulatory embarrassment. The tendency to pyrexia is pronounced and oxygen requirements of the tissues rise steeply.

Hypothermia reduces the cerebral metabolism and oxygen consumption, thus protecting the endangered neural elements.\textsuperscript{4, 8} Survival and function at a lower metabolic level may still continue within areas rendered anoxic or ischemic by oedema or by vascular insufficiency.\textsuperscript{7, 15} Time is gained for the oedema to subside or the circulation to become re-established, and the neural tissues can survive to resume their activity at more customary metabolic levels. Furthermore, as the intracranial pressure is considerably lowered under hypothermia, this may help to avert the serious consequences of foraminal herniations. Rosomoff\textsuperscript{8} in an experimental study stated:

"The use of hypothermia aborts the development of brain swelling following experimental brain trauma at 25°C. The pathology of the lesions is also affected in that there is less widespread destruction of neural elements, less hemorrhagic diathesis, and diminished host reaction to injury during hypothermia. Animals kept hypothermic 18 hours and then rewarmed survive 5 times longer than their normothermic control equivalents."

Sponging with iced water in cases of hyperthermia is a valuable and long-

\* Based on the communication read to the Society of British Neurological Surgeons at a meeting in Stockholm, May 1956.
recognised measure, but frequently the temperature can be reduced only insignificantly or is entirely refractory to the sponging, because of cutaneous vasoconstriction and shivering in response to the cold. If it does fall, it rarely approaches normal, let alone below. For persistent brain oedema, dehydration therapy has only a limited application. Major neurosurgical procedures of splitting the tentorium or resection of the herniated uncus are rarely practicable.

The administration of chlorpromazine and an analgesic increases the efficacy of exposure to cold air and sponging with iced water by inducing cutaneous vasodilatation and reducing the shivering. This we call the "exposure therapy," and using this method only, the temperature may drop from 40–41°C. (105°F.) to the region of 34°C. (95°F.). When this simple exposure therapy fails, a more effective technique of surface cooling must be employed. The patient is covered with ice-bags, more drugs are given if shivering occurs, and the temperature is gradually reduced to 34°C. (95°F.) before the ice is removed. It should not be allowed to drop below 30°C. (90°F.), which we consider to be the limit of safety in cases of head injuries. The hypothermia should be maintained, if at all possible, until there is no clinical deterioration, when the temperature is tentatively allowed to rise.

The improvement gained during the period of hypothermia may be maintained subsequently, even when the temperature has risen to about 38°C. (100°F.). The exposure therapy is then continued until the danger to life has passed, usually coinciding with recovery of consciousness. Should deterioration be evident at any time, cooling with ice must be re-employed after further surgical exploration, if the latter is judged to be necessary.

Lazorthes et al. gave a warning that hypothermia may mask the usual signs of massive intracranial haemorrhage. This observation is important, particularly during the indiscriminate use of hypothermia by clinicians unfamiliar with this method or with the supervision of cases of cranial trauma. In these cases there must be very strict vigilance, and with the moderate degree of hypothermia here advocated, the experienced eye will detect signs of deterioration without difficulty. If deterioration ensues, appropriate surgery should be performed immediately, as illustrated by a number of our cases.

MATERIAL AND RESULTS

In the following group of 30 patients to whom this treatment was given, the only selection lay in the severity of the condition. Only the most serious head injuries qualified and no one was too ill if alive on admission to hospital. The patients have been divided into two groups:

1. Those, apparently moribund on admission, with signs of primary brain-stem damage.
2. Those rapidly deteriorating despite surgical and conservative treatment.

There were 10 patients in the first group: 8 of these were children aged between 3 and 10 years; 2 were male adults aged 18 and 20.
Four patients died. One, a boy aged 7, died after 24 hours of continuous hypothermia without showing any substantial improvement. In this case tracheotomy was performed immediately after admission. Postmortem examination was refused. The second was a boy aged 5, death taking place 96 hours after the induction of hypothermia and operation on an extensive compound fracture. There was slight initial improvement but this was not progressive. Autopsy showed extensive laceration of the right hemisphere involving the basal ganglia and right thalamus. There were also areas of contusion in the left hemisphere and a fracture across the pituitary fossa. The third, a boy aged 4, died 6 days after hypothermia was commenced, without showing any improvement after the first few hours. Autopsy was refused. The fourth (Fig. 1), a boy aged 3, lived for 3 days under continuous hypothermia and was respirated artificially. At autopsy massive haemorrhagic destruction of the cerebellum was found.

Six patients recovered. Four of them, including 2 adults, became mentally and physically normal; 2 are attending a school for disabled children.

Fig. 1. A small boy under hypothermia. He is intubated and attached to an automatic respirator as the spontaneous respirations ceased on his admission. Head surgery has been performed. He is hypothermic, ice-bags were removed, skin was dried and he is lying in a dry bed. A sucker is ready for use. A slow intravenous drip is maintained. Chart is kept half hourly, temperature being recorded in rectum.
A detailed description of one of them has already been published.10 Recently another case of this type was reported by Rowbotham et al.9

In the second group, there were 20 patients. Of these, 13 exhibited decerebrate posture which occurred from a few hours to a few days after the injury. This group is shown in Table 1. Nine patients died and 11 survived.

Of those who died, 1 (Case 1) survived 8 days, 4 of these under continuous hypothermia, and at autopsy there was a thrombosis of the lateral sinus extending into the sagittal sinus, with massive swelling of both hemispheres. Another (Case 2) died 4 days after the accident and 58 hours after the induction of hypothermia. Autopsy showed extensive contusion of the right hemisphere and bilateral petechial haemorrhages. Case 3 was complicated by extradural, acute subdural and massive intracerebral haematomata. He was originally operated upon in a remote cottage hospital, transferred to us 12 hours later and re-operated upon. A tracheotomy was performed and he lived under hypothermia for 3 days

### TABLE 1

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Name</th>
<th>Age</th>
<th>Unconscious</th>
<th>Decerebrate</th>
<th>Tracheotomy</th>
<th>Other Operations</th>
<th>Other Operations</th>
<th>Outcome</th>
<th>Hypothermia</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>P.H.</td>
<td>2</td>
<td>8 days</td>
<td>Yes</td>
<td>Yes</td>
<td>Exploratory burr holes</td>
<td>Died 8 days</td>
<td>Continuous 4 days</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>M.T.</td>
<td>39</td>
<td>4 days</td>
<td>No</td>
<td>No</td>
<td>Exploratory burr holes</td>
<td>Died 4 days</td>
<td>Continuous 4 hrs</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>A.W.</td>
<td>39</td>
<td>4 days</td>
<td>Yes</td>
<td>Yes</td>
<td>Evacuation extradural, subdural &amp; cerebral haematomata</td>
<td>Died 4 days</td>
<td>Continuous 3 days</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>O.H.</td>
<td>44</td>
<td>6 wks.</td>
<td>Yes</td>
<td>Yes</td>
<td>Exploratory burr holes</td>
<td>Died 7 wks.</td>
<td>Intermittent; exposure therapy 8 wks.</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>E.S.</td>
<td>56</td>
<td>4 wks.</td>
<td>Yes</td>
<td>Yes</td>
<td>Evacuation acute subdural &amp; cerebral haematomata</td>
<td>Died 5 wks.</td>
<td>Continuous 2 days; exposure therapy 36 days</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>R.R.</td>
<td>48</td>
<td>4 wks.</td>
<td>Yes</td>
<td>No</td>
<td>Evacuation acute subdural haematoma</td>
<td>Died 9 wks.</td>
<td>Intermittent; exposure therapy 4 wks.</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>F.A.</td>
<td>35</td>
<td>13 days</td>
<td>No</td>
<td>Yes</td>
<td>Evacuation extradural &amp; acute subdural haematomata</td>
<td>Died 2 wks.</td>
<td>Continuous 2 days; exposure therapy 11 days</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>A.W.</td>
<td>25</td>
<td>15 days</td>
<td>Yes</td>
<td>No</td>
<td>Evacuation acute subdural &amp; cerebral haematomata</td>
<td>Died #2 days</td>
<td>Continuous 2 days; exposure therapy 13 days</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>J.F.</td>
<td>33</td>
<td>3 wks.</td>
<td>Yes</td>
<td>Yes</td>
<td>Exploratory burr holes</td>
<td>Male nurse</td>
<td>Intermittent; exposure therapy 9 wks.</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>P.Mc.</td>
<td>15</td>
<td>20 days</td>
<td>Yes</td>
<td>Yes</td>
<td>Exploratory burr holes</td>
<td>Office boy</td>
<td>Intermittent; exposure therapy 3 wks.</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>P.F.</td>
<td>38</td>
<td>10 days</td>
<td>No</td>
<td>Yes</td>
<td>Exploratory burr holes</td>
<td>Clerk</td>
<td>Intermittent; exposure therapy 8 wks.</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>N.E.</td>
<td>25</td>
<td>3 wks.</td>
<td>Yes</td>
<td>No</td>
<td>Evacuation bilateral acute subdural haematomata</td>
<td>Riveter</td>
<td>Intermittent; exposure therapy 2 wks.</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>F.J.</td>
<td>29</td>
<td>1 wk.</td>
<td>No</td>
<td>No</td>
<td>Evacuation subdural hygroma</td>
<td>Salesman</td>
<td>Intermittent; exposure therapy 2 wks.</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>J.F.</td>
<td>34</td>
<td>4 wks.</td>
<td>Yes</td>
<td>Yes</td>
<td>Excision compound fracture</td>
<td>Chronic invalid at home</td>
<td>Intermittent; exposure therapy 4 wks.</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>I.S.</td>
<td>37</td>
<td>10 days</td>
<td>Yes</td>
<td>No</td>
<td>Evacuation acute subdural haematomata</td>
<td>Receptionist</td>
<td>Continuous 4 days; exposure therapy 6 days</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>M.W.</td>
<td>9</td>
<td>24 days</td>
<td>Yes</td>
<td>Yes</td>
<td>Evacuation extradural haematomata</td>
<td>Special school</td>
<td>Continuous 2 days; exposure therapy #2 days</td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>D.K.</td>
<td>4</td>
<td>9 days</td>
<td>No</td>
<td>Yes</td>
<td>Excision compound fracture</td>
<td>Normal, at home</td>
<td>Continuous 2 days; exposure therapy 7 days</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>R.O.</td>
<td>12</td>
<td>30 days</td>
<td>Yes</td>
<td>Yes</td>
<td>Excision comminuted depressed fracture</td>
<td>Normal, school</td>
<td>Continuous 4 days; exposure therapy 25 days</td>
<td></td>
</tr>
<tr>
<td>20 (Fig. 2)</td>
<td>S.B.</td>
<td>30</td>
<td>33 days</td>
<td>Yes</td>
<td>Yes</td>
<td>Exploratory burr hole; subtemporal decompression</td>
<td>In hospital; mutes &amp; paralysis 9 mos.</td>
<td>Continuous 5 days; exposure therapy 4 wks.</td>
<td></td>
</tr>
</tbody>
</table>
In Case 4, the patient regained consciousness after 24 hours of exposure therapy, only to lapse into a sudden coma with hemiplegia. A subdural or extradural haematoma was excluded surgically, a tracheotomy was performed and hypothermia was induced. She recovered consciousness after 6 weeks, but died 1 week later. The pathologist reported that death was from toxaemia caused by extensive bedsores and terminal bronchopneumonia. In the right hemisphere there was a cyst with a deposit of haemosiderin in the walls, which was the residuum of a haemorrhage that had resulted in her sudden deterioration. The progress made from the cerebral point of view was very impressive.

Case 5, a female aged 56, had bilateral acute subdural haematomata evacuated a few hours after her injury. Her temperature was then reduced to 96°F, and the following day a tracheotomy was performed. Two days later she deteriorated and was re-explored surgically. A small amount of subdural blood was re-aspirated and exploration with a brain cannula revealed a large intracerebral haematoma which was evacuated from the temporal lobe. Hypothermia to a level of 92°F was induced. Four weeks after the injury she regained consciousness but she later deteriorated rather suddenly and pus was found on re-opening the wounds. She died 3 days after this and post-mortem examination was refused.

Case 6, a male aged 48, was kicked on the head by a camel (in the streets of Liverpool). Acute subdural haematoma was drained. Tracheotomy was performed and hypothermia was induced to a level of 93°F. Three weeks later he was again explored by burr holes. Only a small subdural hygroma was found but the brain was atrophic. He regained consciousness 4 weeks after the injury but 5 weeks later he suddenly collapsed and died. At autopsy a thrombosis of the intracranial segment of the left internal carotid artery was found with evidence of old and recent softenings of the brain in both hemispheres.

In Case 7 the patient was admitted to the Neurosurgical Unit 14 hours after an injury and was operated upon immediately. Extradural and acute subdural haematomata were evacuated but diffuse congestion of both lungs was already present. Tracheotomy and suction were instituted and the patient regained consciousness 13 days after injury. Chest condition worsened and he died 2 days later. At autopsy bilateral bronchopneumonia was found and also an extensive and deep contusion of left parietal and temporal lobes.

In Case 8 death occurred within 6 hours of injury. A compound fracture of skull was excised and acute subdural haematoma was evacuated. Tracheotomy and hypothermia were instituted and with the aid of these he lived for another 4 hours. There was no postmortem examination.

The last patient in this group (Case 9) was referred to us 7 days after injury. He was operated upon immediately and subdural and intracerebral haematomata were removed. Hypothermia was induced; he improved and then deteriorated and surgical re-exploration was performed. Chest infection
was evident and he was looked after by chest physicians. Further deterioration in chest condition led to death 22 days after the injury. At autopsy multiple small lung abscesses and purulent pleural effusion were found. Brain showed extensive temporoparieto-occipital contusions and temporal laceration.

Of the 11 patients that survived, 7 showed no mental or physical disabilities and returned to their previous occupations or school. One child under school age is at home, well and normal. One boy is in a special school and 1 adult is a chronic invalid at home. Finally, 1 adult patient is still in hospital 9 months after the injury. She is mute and paralysed.

**DISCUSSION**

Of a total of 30 consecutive patients with head injuries of the severest kind, only 13 died. One death was caused by intracranial infection and the 2 deaths caused by major chest complications should have been avoidable. It is not suggested that treatment by cooling is entirely responsible for these results; the care of respiratory passages (including more frequent tracheotomies), maintenance of fluid requirements followed by artificial feeding and the timely performance of any essential surgery, all play their respective important roles. *It is stressed that any degree of CO₂ accumulation in blood which appears instantly whenever there is an obstruction to respiratory passages or inadequate ventilation because of failure of respirations, will nullify the beneficial effects of hypothermia* (Fig. 1).

Following the institution of hypothermia, the impression gained was that if there was no response in the patient’s condition during the first 24–48 hours the prognosis was poor. Most of the patients who survived showed some response as soon as the temperature was brought within the limits of safe hypothermia.

It is noteworthy that the initial severity of the head injury or the patient’s condition could give no reliable guide as to the subsequent mental state. Some of these patients belonging to the group showing secondary mid-brain signs did exhibit definite mental change, but patients in an equally
critical condition and showing similar injuries have returned to normal both with regard to their personality and their previous mental capacity. All the important data relating to surgical and hypothermic management of the second group of our cases together with the final outcome are compiled in Table 1.

With regard to the technique of induction of hypothermia, we are still lacking a drug which would more effectively suppress muscular shivering in the unconscious but unanaesthetised patient than does a combination of chlorpromazine, Pethidine and Dromoran, at present time in use. Such a drug would be ideal if it reduced shivering or the appreciation of cold without influencing the level of consciousness and respiratory rate. More recently we have found that a combination of Dromoran and levallorphan is effective in that levallorphan counteracts the respiratory depressant action of Dromoran, but the control of shivering is probably in direct proportion to the sedative action of Dromoran and observations upon the conscious level of the patient might be hampered by using an effective dose. We have injected on several occasions 4–6 mg. of Dromoran in combination with 1 mg. of levallorphan with safety.

In one case, in order to induce a satisfactory hypothermia when shivering was a predominant and exhausting feature, it was considered that a light general anaesthesia, intubation and a gas/O\textsubscript{2} mixture with very short periods of ether and maintained for 24 hours, might be safer than effective sedation. This produced very satisfactory results and has recently been reported in full.\textsuperscript{6} The trial, as always, continues.

Some 50 patients with head injury judged to be less severe than in the series presented were treated by "exposure therapy" alone, described at the beginning of this communication. This group is not yet analysed.

SUMMARY

Thirty consecutive cases of the severest types of head injuries are described, in which hypothermia was induced as a therapeutic measure. It is suggested that hypothermia, as a part of the treatment, is of great value in cases of serious head injury with signs of primary or secondary mid-brain involvement.

REFERENCES


