Decompressive Craniectomy in Children with Traumatic Brain Injury

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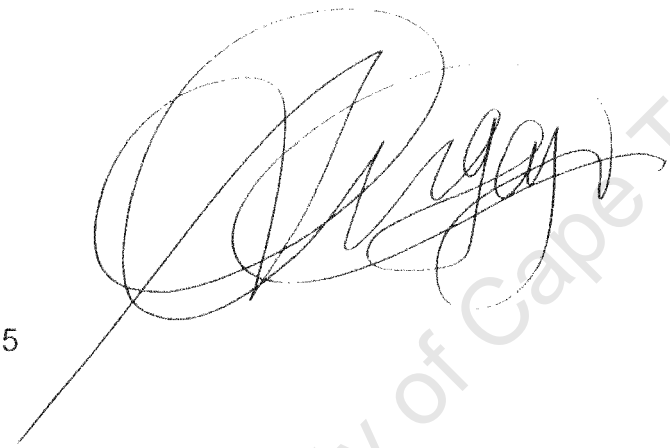

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Chapter 1: Introduction

The management of severe head injury in adults and children presents a challenge to neurosurgeons and intensivists worldwide. Despite the advances that have been made in modern medicine in the twentieth century, and the improved emergency care of head-injured patients, including prompt surgery for the evacuation of mass lesions, the mortality and morbidity associated with severe traumatic brain injury (TBI) remains high. Head trauma is one of the leading causes of death in children and young adults worldwide. In the United States, head injury is the most common cause of death and new disability in childhood (1). At Red Cross War Memorial Childrens' Hospital, mortality after severe TBI in children has been reported to be as high as 57% (2).

Although there has been progress in the understanding of some of the pathophysiological mechanisms involved in primary brain injury, novel treatment strategies have failed to produce the anticipated benefit. Despite trials involving the use of hypothermia, glutamate antagonists, free-radical scavengers and calcium-channel blockers, it is widely acknowledged that, at present, there is little that can be done to ameliorate the primary impact of the injury sustained in head trauma; therefore most of the therapeutic attention has been focussed on the prevention and treatment of the secondary brain injury that may occur.

One of the most important concepts to emerge in the management of head trauma has been that of brain swelling and raised intracranial pressure (ICP), not only as surrogate markers for the severity of injury, but also as significant contributors to secondary injury leading to poor outcome. The ability to monitor ICP continuously

has led to greater vigilance for elevated ICP after head injury, and allowed the evaluation of various therapeutic regimes that have been used to improve outcome. Hyperventilation, mannitol, and barbiturate therapy continue to be used as treatment for elevated ICP and have been investigated in numerous studies. However, there is little evidence that these treatments improve outcome after head injury and there are concerns that each of these interventions may at times be harmful to the patient. Undoubtedly, each of these treatments may lower ICP effectively, but they may also contribute further to secondary injury in ways which have only been appreciated recently.

Controversy surrounding the use of decompressive craniectomy (DC) in the management of posttraumatic raised ICP has not diminished with the passage of time, despite a century having gone by since it was first described. The operation was first reported for posttraumatic brain oedema by Kocher in 1901 (3,4), and then later by Cushing for a patient with an inoperable brain tumour in 1905 (5). For various reasons, studies since then that have investigated DC for cerebral swelling associated with infarction and trauma have failed to produce consistent findings. Proponents of the operation enthusiastically highlight the benefit it has had for individual patients, while detractors emphasize the lack of randomised trials and concerns regarding the invasiveness of the procedure. Critics also point out that DC may simply increase the proportion of survivors with severe disability, even if it does improve survival.

Although the conventional role of the operation was that of a salvage procedure when medical therapy failed in the treatment of raised ICP, two important concepts

have emerged in the recent literature that appear to challenge that approach. In addition to the lack of evidence supporting benefit from current medical forms of treatment, evidence from diverse studies that use data acquired from magnetic resonance images, cerebral oxygenation and cerebral blood flow measurements have highlighted potential adverse effects that may occur with these therapies. Also, there is a growing awareness that DC is most likely to be beneficial when the procedure is performed early and that earlier studies were hampered by its application not only as a procedure of last resort after prolonged exposure to raised ICP had already caused permanent brain injury, but also for patients in whom there was little hope of a functional outcome.

Based on these issues, there has been a re-appraisal of the role of DC as an option in the management of refractory intracranial hypertension in cerebral ischaemia and brain trauma. Data from experimental work has provided robust data supporting an aggressive approach, and clinical evidence, although still only class III in quality, has generated growing enthusiasm for the procedure in selected cases. This thesis will explore the case for considering DC in TBI. As a background to the discussion of DC, relevant issues in the pathophysiology of head injury are discussed in chapter 2. The important factors that must be taken into consideration when evaluating the clinical problem of head injuries in children are discussed in chapter 3. Chapter 4 explores the current medical options for treating raised ICP, evaluating the theoretical basis for benefit, as well as the potential limitations. In chapter 5, the mechanical and physiological effects of craniectomy are discussed, while chapter 6 considers the experimental and clinical reports of DC in brain trauma and cerebral infarction. A case series detailing the

recent experience with this procedure at Red Cross Childrens Hospital is reported in chapter 7. Finally, suggestions are made in chapter 8 for future research involving DC.

Chapter 2: Pathophysiology of Closed Head Injury

Classification of Head Injury

The pathophysiological effects of closed head injury can be classified as primary or secondary. The primary injury is sustained at the time of impact by the force transmitted to the brain, which results in structural deformations, and it is further divided into focal and diffuse forms. Focal brain injuries include contusions, lacerations and traumatic haematomas. Diffuse injury includes cerebral concussion and diffuse axonal injury (DAI), which result from sudden acceleration/deceleration motion, with the amount of tissue disruption being proportional to the amount of energy dissipated into the brain substance (6). Patients suffering from DAI are typically unconscious from the time of impact, and exhibit a characteristic pattern of histopathological change of axons. Widespread small intraparenchymal haemorrhages due to shear injury are usually seen, classically in the corpus callosum and upper brainstem.

Secondary Brain Injury

The role of secondary injury has achieved greater prominence in clinical studies because it represents potentially avoidable or reversible insults, and attention to these factors may improve outcome after head injury. Secondary injury can be caused by systemic and local (intracranial) factors. Systemic insults include hypotension and hypoxia (7), sepsis, hyperglycemia (8), hyperthermia (9), and electrolyte abnormalities. Local factors include raised ICP and brain shifts, brain

oedema, cerebral hyperemia and ischemia, delayed haematoma formation, posttraumatic hydrocephalus, and seizures.

The concept of raised ICP occupies a central place in the thinking of the clinician treating patients with severe TBI. The brain, cerebrospinal fluid (CSF) and cerebral blood volume (CBV) are housed in a rigid, unyielding skull. The volumes occupied by these must have reciprocal relationships to maintain stable ICP (the Monroe-Kellie doctrine). The CSF and vascular spaces act as compensatory reserves to buffer increased volume within the cranium. ICP becomes elevated when this capacity is exhausted. Thereafter, smaller increments of added volume lead to exponential rises in ICP. Intracranial compliance and elastance are reciprocal measures reflecting the dynamic response of the intracranial contents to changes in volume, determining corresponding changes in pressure. Reduced compliance occurs on the steep aspect of the pressure-volume curve, signalling exhaustion of the compensatory reserves.

Intracranial hypertension has two main consequences: brain shifts due to pressure gradients between anatomical compartments (leading to subfalcine, transtentorial, and/or tonsillar herniation), and brain ischemia due to reduced CPP. The hazards of the herniation syndromes are well known. Cerebral ischaemia causes neural injury and cellular oedema, further exacerbating ICP elevation, and promoting the cycle of events that eventually culminates in irreversible neurological injury if not interrupted.

The causes and consequences of raised ICP have a significant impact on outcome in TBI (10, 11, 12, 13). ICP is elevated in 30-80% of head-injured patients without intracranial mass lesions (1, 14, 15). The majority of hospital deaths due to head injury are associated with elevated ICP (12), and this is not simply a reflection of the severity of the injury (14). Posttraumatic intracranial hypertension develops as a consequence of the primary or the secondary injury, associated with haematoma formation, brain swelling, or hydrocephalus. The management of mass effect due to focal haematoma formation or hydrocephalus is usually straightforward, but understanding the pathophysiology of brain swelling and the optimum treatment thereof, is far more challenging.

Brain Swelling

Brain swelling is caused by cerebral oedema or cerebral hyperemia (vascular engorgement). In cerebral oedema, increased water content of the brain is caused by vasogenic or cytotoxic mechanisms. Vasogenic oedema is a consequence of the mechanical microvascular tissue disruption that occurs with trauma. This results in breakdown of the blood-brain barrier and increased vessel permeability, with accumulation of water in the interstitial spaces. The process is mediated by various compounds such as bradykinin, arachdonic acid, histamine and free radicals. Cytotoxic (or cellular) oedema on the other hand, results from ischaemic injury and the failure of cellular energy metabolism, although there is probably also a neurotoxic pathway that occurs in the absence of ischaemia as a consequence of ionic disruption (16). The extracellular-intracellular sodium gradient is disrupted, leading to the influx of water into the cells.

Cerebral hyperemia causes brain swelling due to engorgement of the vascular bed secondary to a vasoreactive event, the mechanisms for which are unclear, but which may involve injury to the vasoregulatory centres of the brain. The diagnosis is not straightforward; areas of hyperemia do not necessarily correlate with abnormal areas on MRI scans (17). In the normal state, there is functional coupling between cerebral blood flow (CBF) and cerebral metabolism (13); therefore local CBF is determined by local metabolism, and increased CBF is usually a response to increased glucose turnover or hyperglycolysis. However, vasoparalysis may cause uncoupling of cerebral metabolism and CBF, which is difficult to predict (17). Therefore, increased CBF in the setting of normal or decreased metabolism results in hyperemia, or luxury perfusion, resulting in raised ICP due to increased CBV (13).

Although hyperemia was thought to be the most common pattern of CBF in diffuse brain swelling in severe paediatric TBI, more recent studies have challenged this (18). Normal CBF and even ischaemia may be seen in children with brain swelling with a higher frequency than previously thought. Ischaemic injury is a consequence of the primary injury or secondary factors (local or systemic). It is associated with poor outcome after head injury and is a common finding at post-mortem after severe TBI (19). Ischaemia may result from systemic hypotension, decreased cerebral perfusion pressure (CPP) due to raised ICP and/or impaired pressure autoregulation. It causes the failure of energy metabolism and cytotoxic oedema, and is therefore both a cause and consequence of the vicious cycle of

injury that is associated with elevated ICP. Recent evidence suggests that cellular oedema is more prominent after head injury than vasogenic oedema or vascular engorgement (16, 20).

Pressure Regulation

Autoregulation refers to the ability of cerebral blood vessels to maintain a constant supply of blood to brain tissue while the cerebral perfusion pressure is between 40-150 mmHg (13, 21). Cerebral perfusion pressure above or below these limits may lead to cerebral hyperemia or cerebral ischaemia respectively. There is mounting evidence that, in head injury, there may be disturbances of regulation that are local, hemispheric or global. Impaired pressure regulation may be seen in as much as 42% of children with severe head injury (21). If cerebral autoregulation is deficient, not only does ICP fluctuate with mean arterial pressure (1,19), the interpretation of CBF patterns also becomes more complex. The topic is further explored in chapter 4 as part of the discussion on cerebral perfusion pressure-directed therapy.

The various contributions of cellular oedema, vasogenic oedema and cerebral hyperemia, combined with the changing patterns over time and the potential for focal, rather than global, occurrence of these phenomena, as well as the uncertain state of autoregulation, create a complex set of parameters in an individual patient with the problem of raised ICP. This impacts upon the strategies chosen for ICP treatment as most options, including hyperventilation, mannitol, and barbiturates, have an influence on one or more of the above factors. Depending on the

prevailing dynamics, these treatments may be beneficial or hazardous to the outcome of the patient.

Chapter 3: Severe Traumatic Brain Injury and Brain Swelling - Scope of the Problem and Factors Influencing Outcome

Severe TBI is usually defined as a Glasgow Coma Score (GCS) of 8 or less in a patient with a head injury (13, 22). A host of factors associated with outcome have been reported, some in a causal relationship, such as type of injury, and others as predictors of likely outcome, such as pupillary responses to light. Some of the relevant issues which impact on decision-making in the management of patients with severe head injuries without focal mass lesions will be explored, in preparation for a discussion of ICP treatment strategies.

Age

The influence of the age of a patient on outcome after severe TBI has been the subject of much debate over the years. While there is general consensus that patients at the extremes of life fare worse, there is less certainty about the rest. Although most would agree that older patients (over 40) fare less well after head injury, determining the difference in outcome in the younger age groups is much more difficult. Even the definition of childhood varies in different reports and becomes a potential confounding factor.

This task is made more complex by a number of variables that one must take into account. Often comparative studies between adults and children include elderly patients in the adult data which leads to a bias in their results, as this group of patients fares particularly poorly after head injury. In young children, the use of the

same scoring system as adults (Glasgow Coma Score) may not be ideal; yet using a different scoring system makes it difficult to compare outcomes. In adults, outcome evaluation is more straightforward, because there are basic criteria involving activities of daily living and a premorbid level of functioning that can be used for comparison. Children, however, are very different depending on their age-related development; they are on a steep curve of acquiring knowledge. Therefore, their capacity for further acquiring knowledge and skills should also be taken into account. Brain plasticity also potentially affects recovery from severe brain injury and is a function of age (1). Lastly, there must be control for the type of injury. Children are more likely to be involved as pedestrians in motor vehicle accidents, while adults are more likely than children to be victims of assault, sustaining focal injury. Children with severe TBI are more likely to have diffuse cerebral swelling than adults, who tend to have a higher incidence of traumatic mass lesions (1, 23, 24, 25).

Mortality figures reported following severe TBI show significant variation. There are numerous confounding variables. Selection bias may be significant in single-centre studies, influenced by regional ethnic and socioeconomic factors, as well as mechanisms of injury sustained. Due to local referral patterns, the most severely injured patients may not be reflected in intensive care unit statistics, dying either prior to hospital admission, at a referring hospital, or in the resuscitation area. A large outcome study published in 1988 found a significantly lower mortality rate in a cohort of 1906 children compared with adults in a prospective evaluation of head-injured patients (26). And Bruce et al (27) reported a very low mortality rate

of 6% in their series of 53 children with severe TBI, although other centres have been unable to match this figure.

However, in the largest series yet reported, Johnson and Krishnamurthy (28) surveyed 5 Level 1 trauma centres and compared the outcomes after severe TBI of 4041 children to that of 14 789 adults. The overall mortality rate in the study was 36.5%, with none of the hospitals reporting a mortality rate less than 30%. For patients referred indirectly, i.e. via a local hospital, this figure rose to 50%. When comparing outcomes between children and adults with injuries sustained in motor-vehicle accidents, they found no significant difference. Their contention was that mortality rates between adults and children are similar if selection bias and confounding factors, such as the mechanism of injury, are removed. Other studies report death or unfavourable outcome in 15-65% of severely head-injured children (2, 23, 25, 29, 30, 31, 32).

GCS and Raised ICP

Elevated ICP is common in patients with severe head injury. Low GCS post-resuscitation and persistently raised ICP are strongly associated with increased mortality and poor neurological outcome in survivors (1, 6, 10, 32, 33, 34, 35). Patients who exhibit decerebrate or decorticate posturing after head injury fare particularly poorly. Initial GCS is a reflection of the severity of the primary injury, while elevated ICP is a secondary phenomenon causing delayed neurological deterioration. The outcome in the patients who undergo this secondary deterioration due to raised ICP also tends to be poorer (34).

CT Evidence of Brain Swelling

There is a strong relationship between brain swelling, usually reflected in the state of the mesencephalic cisterns, and poor outcome (24, 36, 37, 38, 39). Marshall and colleagues (36) recognised this relationship and proposed a computed tomography (CT) - based classification system that contained 4 grades of severity in diffuse injury (Table 1).

Grade	CT features
I	no visible intracranial pathology
II	cisterns present with midline shift of 0 to 5 mm and/or there is no high- or mixed-density lesion greater than 25 cc
III	cisterns compressed or absent with midline shift of 0 to 5mm
IV	midline shift greater than 5mm
evacuated mass lesion	any lesion surgically evacuated
non-evacuated mass lesion	high- or mixed-density lesion greater than 25cc, not surgically evacuated

Table 1: Grading of severity in diffuse injury, according to Marshall et al (36).

The same authors then looked at the data from 746 patients with severe TBI from the Traumatic Coma Data Bank (TCDB) using this classification (22). Overall mortality was 36%. Of the patients classified as grade III, 34% died, 23% were vegetative, and 27% had a severe disability. Only *16%* had a favourable outcome. In grade IV, 56% of the patients died, 18 % were vegetative, 18% were left with a severe disability, and only *6%* had a favourable outcome. Of the patients that died, 90% did so in the first 2 weeks after sustaining the injury. Van Dongen et al (39) found that the state of the cisterns was the most powerful predictor of

outcome after head injury. Aldrich and colleagues (24) reviewed data from 753 patients (111 children and 642 adults), showing a mortality rate of 53% in patients with diffuse brain swelling compared with 16% of those without brain swelling. Ropper described the significance of the state of the mesencephalic cisterns as one of the CT features of transtentorial herniation (38).

Pupillary Abnormalities

Abnormalities of the pupillary response to light are also strongly associated with poor outcome in head-injured patients (22, 39, 40). From the TCDB data (22), 47% of patients with a unilateral unreactive pupil, and 82% of those with bilaterally unreactive pupils were dead or in a vegetative state at discharge. The association between pupillary abnormalities and compression of the mesencephalic cisterns on CT has also been made. In a series of 121 head injured patients, Van Dongen et al (39) showed that 75% of patients with complete obliteration of the cisterns also had unilateral or bilateral pupillary abnormalities. They found that a combination of criteria which included CT findings (state of cisterns and brain parenchymal lesions) and clinical findings (motor score, pupil abnormalities and age) could be used to correctly predict outcome in 96% of their cases.

Chapter 4: Treatment Strategies for Raised ICP

It is recommended that ICP monitoring is indicated for head-injured patients with a GCS of 8 or less, particularly if the CT scan is abnormal (10). Although there are no good randomised trials evaluating the benefit of ICP monitoring and treatment, it is generally accepted that elevated ICP after severe TBI is associated with increased mortality and poor neurological outcome in survivors (10, 11, 12, 13, 35), and that monitoring and aggressive treatment of elevated ICP has historically produced the best outcomes (41). Although it is difficult to establish from scientific evidence what ICP threshold should be accepted in children, most clinicians agree that, as in adults, ICP above 20mmHg should be treated (42). Although this threshold is probably lower for younger children, agreement on the age-related levels is yet to be reached (1, 43). ICP of 2-10 mmHg may be normal for younger children (1, 33).

Attempts have been made to collate the available evidence supporting the various forms of medical and surgical treatment of severe head injury to establish standards of care, guidelines, or at least options (44, 45). In a recent review investigating severe paediatric TBI, the authors suggested a critical pathway for the treatment of established intracranial hypertension, grouping strategies as first- and second-tier therapies (45). First-tier therapies included sedation and analgesia (46), CSF drainage via ventriculostomy, neuromuscular blockade, hyperosmolar therapy (47) and mild hyperventilation (45). Should these methods fail to control ICP, second-tier therapies may be employed as options. These include decompressive craniectomy, barbiturate therapy, hypothermia, moderate

hyperventilation, and controlled lumbar CSF drainage. Because there is no Class I evidence supporting clinical benefit for any of these therapies, the authors could only recommend options rather than guidelines. It is important to note that, while some methods are relatively innocuous, such as head elevation and sedation, the benefits of the others may be offset by associated adverse effects.

Mannitol

Mannitol is commonly used to reduce ICP, which it does by inducing water transfer along an osmotic gradient. It initially increases CBF by volume expansion and decreased blood viscosity, which permits vasoconstriction, thereby reducing CBF and lowering ICP (20). Mannitol has been investigated in numerous trials, including a systematic review by the Cochrane database (48), both as a sole agent, as well as in comparison with other ICP-lowering agents. Although mannitol usually decreases ICP the effect is time-limited, generally persisting for 45-90 minutes (49). In addition to renal injury that can complicate mannitol therapy due to increased serum osmolarity, intracranial adverse effects may occur due to extravasation of mannitol through the damaged blood-brain barrier, causing a reversal of the osmotic gradient that results in net inflow of water, thereby exacerbating vasogenic oedema. In an experimental study by Kaufmann et al (50), 23 cats were subjected to a cold lesion-induced injury. They were divided into a control group, a group that received a single dose of mannitol for raised ICP, and a group that received 5 doses. They found a progressive increase of mannitol in oedematous white matter, and that multiple doses caused an increase in brain water. Loss of pressure autoregulation, and the unreliable vasoconstrictor

response to increased CBF, may lead to unpredictable effects of mannitol in the injured brain. Mannitol-induced vasoconstriction may be harmful in the presence of cerebral ischaemia (51).

Barbiturates

Barbiturate treatment lowers ICP by suppressing cerebral metabolism and altering vascular tone to reduce CBF (52). However, if the reduction in CBF is greater than the decrease in the cerebral metabolic rate for oxygen, this results in cerebral ischemia. Benefit from barbiturate treatment may not be seen when metabolism and CBF are uncoupled in TBI, as reduced CBF does not necessarily follow any reduction achieved in cerebral metabolism. The lack of certainty regarding the specific cerebrovascular haemodynamics in an individual head-injured patient compounds the unpredictability of the effects of barbiturates.

Maximal reduction of metabolism occurs only when burst suppression on the electroencephalogram is achieved, which requires a significant dose. A common problem with the use of thiopentone and the other barbiturates is the occurrence of haemodynamic instability compromising CPP, especially at higher doses of the drug. Often treatment must be stopped or positive inotropes must be commenced to support the cardiovascular system. In a review by the Cochrane database (53), no evidence was found that barbiturates improved outcome, and in 1 in 4 cases the potential benefit was offset by hypotension. Ward and colleagues (54) found that as many as 54% of their barbiturate-treated subjects developed significant hypotension (systolic blood pressure below *80mmHg*) compared with 7% of

controls. Cruz (55) prospectively evaluated 151 comatose patients with jugular oxygen saturation monitoring who received intravenous boluses of pentobarbital. Of these, 32% had episodes in which saturation dropped to less than 45% after the pentobarbital bolus. Follow-up in this group demonstrated worse outcomes at 6 months. They recommended that pentobarbital should be avoided if there was no jugular bulb saturation or tissue oxygenation monitoring. And lastly, because barbiturates have a long half-life, it takes a long time to be eliminated from the patient's system, to the point where the clinical examination is reliable again and the patient can be extubated.

Propofol

Although not as established in the treatment protocols for raised ICP as the other therapies considered here, propofol is worth separate consideration because it is being used more often for this purpose. Propofol is also used for metabolic suppression, its ease of administration and short half-life making it an attractive alternative to conventional barbiturates. Unlike thiopentone, the effects are relatively rapidly reversed. However, there are concerns that propofol may cause a deterioration of cerebrovascular pressure regulation and increase the brain's vulnerability to secondary insults (56), and its overall usefulness in reducing the level of ischaemic burden has been called into question (57). Severe, intractable metabolic acidosis has also been linked to prolonged propofol infusion (58).

Hyperventilation

Treatment of raised ICP with moderate-severe hyperventilation has largely ceased due to concerns about the ensuing cerebral vasoconstriction (59), although some centres use controlled hyperventilation under transcranial Doppler guidance where CBF can be monitored. Most centres aim for controlled ventilation only. Again, lack of knowledge of the status of CBF and CBV make the impact of controlled hyperventilation too unpredictable for it to be used routinely.

Hypothermia

Hypothermia has been employed in the treatment of head-injured patients for the amelioration of the primary injury sustained. Although promising in concept, numerous studies have failed to produce convincing evidence of benefit (9, 60, 61). A recent landmark study was halted prematurely after the enrolment of 392 of the planned 500 patients because, not only was the treatment ineffective, patients older than 45 years of age had a higher incidence of poor outcomes (60). Although the benefit of hypothermia has not been confirmed in clinical trials, it is commonly agreed that *hyper*thermia should be avoided.

Ventriculostomy

Placement of an external ventricular drain for the monitoring and control of raised ICP is favoured by many centres in the initial treatment of patients with severe TBI (45). Apart from allowing accurate monitoring of ICP, the catheter also serves to

vent CSF from the ventricular system for ICP reduction. Although the procedure is often effective, there are a few potential problems. In head trauma with brain swelling, the ventricles are characteristically slit-like, making accurate placement of the catheter challenging. Repeated attempts at passing the catheter into the lateral ventricle are not recommended in a brain which is already severely injured. Even once a catheter has been successfully placed, the usefulness may be compromised by collapse of the ventricles, with apposition of the ependymal surface onto the catheter, limiting effective drainage of CSF. Finally, there are the risks of intracranial sepsis that must be considered. One study reported a 10% incidence of ventriculitis, with a 2.5% associated mortality despite the use of prophylactic antibiotics, in a series of head-injured patients in which most of the ICP monitoring was conducted with a ventricular catheter (62).

CPP-targeted Therapy

The need to maintain adequate CPP to avoid cerebral ischemia is intuitive. It is recognised that ischaemic episodes after head injury are associated with increased mortality and poor neurological outcome (7, 19). However, determining what constitutes an adequate CPP is difficult, and an optimum level is not universally accepted (1, 43, 63). A rational argument is made that CPP augmentation may reduce cerebral ischemia by improving tissue perfusion (64). CPP is also an important physiological stimulus for autoregulation. Optimising CPP in patients with intact autoregulation indirectly controls ICP by the cerebral vasoconstrictor response to elevated CPP, which reduces CBV (19, 65, 66). Conversely, decreased CPP causes cerebral vasodilation in an attempt to

preserve CBF, which may exacerbate intracranial hypertension as a result of the increase in cerebral blood volume.

CPP-directed protocols therefore, strive to maintain an elevated CPP by using aggressive fluid resuscitation (to supranormal levels) and inotropic support. This approach has potential drawbacks though, including the potential contribution of aggressive fluid resuscitation to brain oedema and the increase in cerebral metabolism that may occur with norepinephrine (64). Moreover, the relationship between CPP and CBF is altered in patients with disturbed cerebrovascular reactivity after head injury; therefore the effects of elevated CPP are difficult to predict. In the presence of impaired autoregulation, elevated CPP may lead to cerebral hyperemia, thus exacerbating intracranial hypertension (63, 67).

Making the situation even more unpredictable is the recognition that there may be a striking *asymmetry* of pressure autoregulation after brain injury. One study showed that the left-to-right difference in pressure autoregulation was significantly associated with a fatal outcome, and that the hemisphere containing the predominant lesion demonstrated the greater disturbance of vasoreactivity (66). Therefore, it is theoretically possible that this could cause one hemisphere to respond to therapy better than the other. The beneficial effects of elevated CPP in the less-affected hemisphere may not be evident in the hemisphere with the greater autoregulation disturbance, favouring the development of interhemispheric pressure gradients, and exacerbating shift. It is uncertain whether similar principles are relevant for other strategies where medical treatment is globally applied to an injured brain in which there are unpredictable regional variations.

Finally, the extracranial effects of aggressive fluid resuscitation and catacholamines must be considered. When CPP values above 60 are targeted with active support, the extracranial complications of this approach largely determine the outcome (14). Therefore, published guidelines in adults (44) recommended a lower CPP (60 versus 70mmHg). It is not yet clear to what extent the same targets can be set in paediatrics, or how optimum CPP should be calculated in younger children (1, 43, 68).

Controlled Lumbar CSF Drainage

Lumbar CSF drainage has been recommended as a second-tier therapy for the management of refractory intracranial hypertension (69). This should only be instituted in the presence of a functioning ventriculostomy. Wider use of this technique is probably limited by the concern of developing tonsillar herniation, which may not be offset by the concurrent drainage of ventricular CSF.

Decompressive Craniectomy

At present, DC is recommended only as a second-tier option in the guidelines for treatment of severe TBI (45). However, it seems that there is less negativism about the procedure than was the case a decade ago. Although the weight of the evidence is still only Class III, there is a gradually increasing optimism for using the procedure in selected patients, particularly as early intervention for intracranial hypertension (within 48 hours) and for patients who develop secondary

neurological deterioration (4, 41, 68, 70) The evidence for and against the procedure in the current literature will be explored in the following two chapters.

Chapter 5: Mechanical and Physiologic Effects of Decompressive Craniectomy

Most clinicians would agree that removing a bone flap and opening the dura of a patient with severe brain swelling has an effect on various dynamics of the underlying brain. In theory, the procedure should allow increased volume for brain expansion and protect brain function by reducing ICP and improving cerebral tissue perfusion. There is a concern however, that, in addition to not achieving these goals, the operation may have negative consequences that further endanger the already compromised brain.

ICP Reduction

The majority of published experimental and clinical reports support the contention that DC is effective in the treatment of raised ICP (3, 4, 68, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80). The benefit is intuitive. The rise in ICP that is seen with brain swelling is a consequence of the brain being housed in a rigid, non-compliant cranium when the compensatory reserves have been exhausted (Monroe-Kellie doctrine). Lifting a bone flap immediately changes the compliance of the system by creating greater volume and allowing dissipation of pressure. The larger the craniectomy, the greater the effect this is likely to achieve. Wide opening and grafting of the dura further reduces the ICP. Studies that have measured the ICP while removing the bone flap and opening the dura support this contention. In 20 patients with brain swelling, Yoo et al (80) noted an average of 85% immediate reduction of ICP with a bifrontal DC. Of this, 50% percent was achieved with bone

removal alone, while dural opening contributed a further 35%. Jaeger and co-workers (81) as well as Hieu and colleagues (73) also noted a 2-step drop in ICP with bone removal followed by dural augmentation, with the addition of the latter producing almost double the benefit.

Intracranial Compliance

Some investigators have specifically considered the impact of DC on intracranial compliance in experimental and clinical studies. Intracranial compliance is a measure of the pressure-volume relationship of the intracranial contents. A system with high compliance demonstrates smaller elevations in pressure when discrete boluses are added to the volume of the system. Conversely, compliance is reduced at higher intracranial volumes; therefore small volume changes result in greater changes in pressure. This can be measured in clinical and experimental studies.

Shapiro and Marmarou (15) studied intracranial compliance in children with severe head injuries and raised ICP. In each patient a ventricular catheter had been placed to monitor ICP and compliance was calculated by measuring the changes in ICP that occurred when bolus withdrawal or injection of fluid to the system was performed. Because the pressure-volume curve is exponential and compliance is influenced by ICP, they used a pressure-volume index (PVI), which is a linear plot achieved by graphing pressure on a logarithmic scale against volume. This provides a measure of compliance independent of ICP. They found that decreased neural axis compliance was associated with raised ICP, as one would expect, but

also that decreased compliance was predictive of later rises in ICP in patients who at the time demonstrated normal ICP.

Shapiro et al. (82) then studied pressure-volume relationships in 28 cats in the intact state (control group), after bilateral craniectomy (bone removal only), and after craniectomy plus dural expansion. In addition to ICP, they also measured superior sagittal sinus venous pressure, pressure-volume index and resistance to cerebrospinal fluid absorption. They found a sequential increase in the volume-buffering capacity of the system after surgery, which was maximal when craniectomy was accompanied by dural expansion. Hatashita and Hoff (83) investigated 32 normal cats, 16 of which formed the control group, and 16 of which were subjected to DC, also finding an increase in the volumetric compensatory capacity of the intracranial cavity, with ICP reduction and increased compliance demonstrated in the treatment group.

In another clinical series, Hase and co-workers (84) measured compliance in 47 patients with raised ICP after trauma. DC was performed in 33 patients and the results were compared with 14 controls. After DC compliance was increased and the pressure-volume curve was shifted to the right, i.e. the patients reacted to volume loading with a much lower rise in ICP. These patients were less sensitive to sustained increases in volume as well as to short-term variations in CBF, arterial carbon dioxide concentrations and venous outflow obstruction.

Exacerbation of Cerebral Oedema

One of the concerns regarding DC is that it may enhance underlying cerebral oedema. It is suggested that this may occur due to the reduced tissue pressure achieved by decompression, which in turn leads to a reduced transmural hydrostatic pressure gradient that may promote local vasogenic oedema, particularly if the blood-brain barrier has been compromised (85). However, with the purpose of investigating this possibility, Hatashita et al (86) studied 4 groups of cats - 1 control group, and 3 treatment groups which were subjected to: craniectomy alone, hypertension alone, and craniectomy plus induced hypertension. They found that cerebral oedema occurred only when the mean arterial pressure was elevated. There was no evidence of enhanced oedema in the animals which underwent craniectomy only, without induced hypertension. In a subsequent report, Hatashita and Hoff (83) considered the theoretical case for increased oedema secondary to decreased tissue pressure after craniectomy, but found no evidence of increased brain water content in 16 normal cats that underwent DC compared with 16 controls.

Rinaldi and colleagues (76) used Evans blue histological staining to examine the brains of 7 rabbits with cold lesion-induced cerebral oedema, 3 of which acted as controls, and 4 that underwent DC with dural opening. They found no difference in fluid extravasation between the 2 groups. The effect that DC has on CBF in the underlying brain is unclear; both increased CBF as well as decreased CBF have been reported after craniectomy (87, 88). In absence of measurements of metabolism, the significance of this is uncertain. Finally, there is evidence that

cellular oedema rather than vasogenic oedema predominates in head injury (16, 20).

Although these studies do not provide a definitive analysis of the risk of enhanced brain oedema after DC, it is reasonable to expect that this risk is reduced by the avoidance of hypertension and the performance of DC early rather than as a last resort in patients with malignant intracranial hypertension. In recent studies in which DC is performed earlier, and targets for cerebral perfusion pressure are set, enhanced oedema is not reported as a common finding (4, 68, 70, 72, 78, 81, 89).

Brain Entrapment

There is a concern that brain entrapment and venous drainage obstruction occurs at the edges of the craniectomy site, resulting in localised venous hypertension, again favouring oedema. Whitfield et al (79) performed angiography on one of their patients to investigate this concern, but found no evidence of venous obstruction. Yoo and colleagues (80) measured the epidural pressure with an air pouch system in one of their patients, and found no abnormality either. In the treatment of 3 patients with medically uncontrollable ICP secondary to subarachnoid haemorrhage, Jaeger et al (81) noted that DC not only controlled the ICP but improved tissue oxygenation in the underlying brain. Stiefel et al (89) performed DC in 7 patients (5 with severe TBI and 2 with poor grade subarachnoid haemorrhage) for intracranial hypertension refractory to a stepwise approach to medical management. They found a significant improvement in ICP as well as brain tissue oxygenation after DC. It seems logical that the larger the craniectomy,

the less likely the cortical surface will be compromised by the craniectomy margins as the pressure is dissipated over a large surface area.

Chapter 6: Clinical and Experimental Reports of DC and Outcome

As discussed previously, DC is a procedure that has been employed for raised ICP in various circumstances for more than a century. It has been used for TBI, cerebral infarction, inoperable brain tumours, intracerebral haemorrhage and subarachnoid haemorrhage. Most of the clinical and experimental reports focus on its role in the management of secondary raised ICP after hemispheric infarction and posttraumatic diffuse brain swelling. The centrality of raised ICP as a secondary factor in the posttraumatic course and the high incidence of poor outcome of head injuries has already been emphasised. So why is there not greater clarity regarding the role of DC in the management of head injuries? The answer to this question is complex – in part it relates to the nature of head injuries, in part to the manner in which the procedure has been used and reported in the literature.

Why has DC not been shown to be of Benefit to Outcome?

The nature of head injury is such that numerous variables influence the presentation and outcome of patients who sustain severe TBI. Included amongst these are the age of the patient, the type of injury (focal versus diffuse, open versus closed), the severity of the insult, the presence of surgical mass lesions, the effectiveness of pre-hospital management, the initial clinical condition, hypotension, hypoxia, the degree of brain swelling, the contribution of raised ICP, sepsis, hyperglycemia, and the promptness of medical or surgical treatment. As discussed in the Chapter 3, institutional and reporting bias produces significant

variation of results in various head injury studies, influenced by the study design, the clinical condition of patients operated on, the timing of the procedure, and the methods of evaluating clinical outcome. Furthermore, computed tomography and ICP monitoring were not available in the era when some of the more negative reports on DC were published, making these very difficult to compare with more recent studies. And probably most importantly, DC is often performed in desperate and emergent situations to control life-threatening raised ICP, usually when other methods have failed. Because failure to control ICP acutely in this setting will usually lead to death or severe disability, this is not a context which lends itself to a double-blind, controlled, randomised trial.

The type of surgical procedure employed varies between different centres. Bifrontal (4, 79, 80, 91), unilateral or bilateral hemispheric (70, 74, 89, 92, 93) subtemporal, posterior fossa, circumferential (94), small and large craniectomy – all have been described. Some centres remove bone only and leave the dura intact (68), while others open the dura widely and place a pericranial graft for maximal dural expansion. Even temporal lobectomy has been described as part of the operation to maximally decompress the space around the tentorial incisura (95). Furthermore, many reports have a broader definition of decompresssive craniectomy, also including in their data operations for the removal of significant mass lesions, such as acute subdural haematomas and intracerebral haematomas (3, 79, 89, 93, 95, 96). These are considered as DC when the bone is not replaced. Combining patients who have had operations for pure cerebral oedema with those in whom a mass lesion was removed does not provide useful

comparative data, as the benefit (or risk) of the bone removal alone cannot be evaluated.

Although the inclusion or exclusion of mass lesion removal is a significant factor, even more important has been the variable timing of the procedure. DC is conventionally regarded as an option in the treatment for raised ICP when medical therapy has failed. The medical therapies employed, and the criteria for abandoning medical therapy in favour of surgery show wide variation. Because raised ICP is associated with poor outcome and uncontrolled ICP is a significant factor causing secondary injury due to brain shifts and cerebral ischemia, it is reasonable to assume that the longer that patients are exposed to raised ICP the more likely the patient will have a poor neurological outcome. Therefore, when DC is performed late in the posttraumatic course of patients who have had prolonged exposure to raised ICP, the lack of benefit shown is hardly surprising.

Unfortunately, many of the earlier reports are hampered by the late timing of the procedure, or its application for patients with little hope of a functional outcome (vide infra). The benefit (or lack thereof) of DC in a setting in which irreversible injury has likely occurred is not comparable to its use in a more aggressive attempt to control DC early in the course of raised ICP. Taking into account all these factors, it is not surprising that there is huge variability in the reports of outcome after head injury and the impact that DC has made.

Experimental Reports of DC

There have been numerous experimental reports investigating DC in various animal models of TBI and focal cerebral ischemia. The impact of the operation on ICP, perfusion and brain oedema was discussed in the previous chapter. With regard to the clinical outcome in these animal studies, the following reports are worth noting.

A 1968 study by Moody et al (97) raised the concern that, while DC may preserve life, the poor quality of survival may offset that benefit. The authors reported an experiment with 20 dogs which they subjected to brain injury involving inflation of an epidural balloon. Ten dogs acted as controls and 10 others were treated with bilateral DC. Both groups were subjected to hyperventilation therapy. The brains were examined at death or at day 10 after injury in the survivors. All 10 controls died within 12 hours of inducing the lesion. Increased survival was found in the treated group, with some of the animals surviving the full 10 days, but the quality of survival was exceptionally poor. No evidence of tonsillar herniation was seen at post-mortem in the treatment group but haemorrhagic necrosis was noted at the craniectomy site. The criticism of this study centres on the severity of the 100% mortality model chosen by the authors - all controls died within *12 hours* of inducing the lesion, which may not be the ideal model for *salvageable* head injury. The same findings may not have occurred in a less severe model in which some salvage of useful brain function could be reasonably achieved.

Doerfler and colleagues (98) studied 68 rats after inducing focal ischaemic injury with an endovascular method of middle cerebral artery (MCA) occlusion. Twenty

animals were in the control group, while the rest were treated with DC in 4 groups of 12 each, respectively 4, 12, 24, and 36 hours after lesioning. Mortality in the control group was 35%, while none of the craniectomised animals died. Additional benefit was demonstrated by decreased infarct size and improved neurological outcome in the treatment group. The best results were seen in the animals that were treated with decompression early (at 4 hours). Doerfler and co-workers (99) again studied ischaemia in rats in a more recent experiment to investigate the impact that DC had on cerebral perfusion. Thirty-six rats were subjected to endovascular MCA occlusion and had perfusion- and diffusion-weighted magnetic resonance scans performed at intervals of 4, 24, 48, 72, and 168 hours thereafter. There were 12 controls, 12 animals that had DC performed at 4 hours post-occlusion, and 12 that underwent DC after 24 hours. There was no change in perfusion in the group treated at 24 hours, but the early group (DC performed at 4 hours) demonstrated increased cortical perfusion through collateral vessels. Again, there was decreased infarct size and improved neurological performance in the treated animals.

Forsting et al (100) also demonstrated benefit with DC after MCA occlusion in 30 rats (control group 20 animals). Mortality in the control group was 35%, and 0% in the treated group. The treated group also showed a diminished infarct size and better neurological performance.

Gaab and co-workers (101) recommended not only craniectomy but aggressive resection of any oedematous or contused brain at the same time, suggesting that this approach produces the best experimental results based on the data from their

study of ICP, EEG and cerebral metabolism in cats subjected to cold-lesioning. The assumption was made that the oedematous and contused area would become necrotic anyway. However, clinical outcome was not evaluated and the approach can be criticised because it cannot be ascertained with certainty that viable tissue is not present within the oedematous region.

Clinical Reports of DC for Severe TBI

Commonly cited early clinical studies that reported little, if any, benefit from DC include those by Clark et al (94), Kerr et al (102), Cooper et al (103), Venes and Collins (104), and Kjellberg and Prieto (91). In 1968 Clark and co-workers (94) described the use of circumferential craniotomy in 2 patients with head injuries, one of whom had decerebrate posturing, and the other who had no response to painful stimulus; both had bilaterally fixed pupils. In the same year Kerr and colleagues (102) reported 2 patients, both of whom were decerebrate, one with a unilaterally fixed pupil and the other with bilaterally fixed pupils. In 1971 Kjellberg and Prieto (91) reported 73 patients, 89% of whom had decerebrate posturing, with unilateral or bilaterally fixed pupils. Of the 13 patients in the 1975 series by Venes and Collins (104), 11 had evidence of brainstem dysfunction at the time of surgery. And finally, 50 head-injured patients were treated with hemicraniectomies in the 1976 series by Cooper et al (103). All of the patients had acute subdural haematomas, and all but 2 were in a premorbid state, demonstrating decerebrate posturing and/or pupillary abnormalities. In fact, 23 had bilaterally fixed pupils and 27 had absent corneal reflexes. Given the preoperative condition of the patients in

these reports it is unsurprising that surgery failed to demonstrate more significant clinical benefit.

From the evidence in more recent reports where ICP was monitored, there appears to be a general consensus that DC results in significant ICP reduction (4, 68, 70, 71, 73, 75, 77, 78, 79, 80, 84, 89, 95, 105, 106, 107). There has been only one attempt at a randomised trial. Taylor and colleagues (68) reported a series of 27 paediatric patients with severe TBI, accumulated over a 7-year period. Thirteen patients underwent bitemporal craniectomy, compared with 14 patients treated with conventional medical management. The operative technique involved the removal of a relatively small disc of temporal bone bilaterally (only 3-4cm diameter) without opening the dura. This procedure was relatively conservative compared with that employed in other series, which incorporated not only larger craniectomy defects but also wide opening and grafting the dura. The other limitation of the study was the long time period over which the patients were accumulated, during which changes to the target cerebral perfusion pressure were made. The ICP reduction achieved was understandably modest (9.8mmHg in the operative group compared with 7.0 mm Hg in the conventionally treated group). However, they also demonstrated a lower frequency of later spikes of ICP and there was a trend towards better outcome in the group treated with DC.

Polin et al (4) used a novel approach to achieve a relatively comparative control group from patient data accrued in the Traumatic Coma Databank (TCDB). Each of their 35 patients who underwent DC for cerebral swelling due to TBI were matched with one to four controls from the TCDB based on age, gender,

preoperative GCS and maximum preoperative ICP. Although there are limitations to the validity of this method of comparing outcomes, the data obtained is nevertheless useful for comparison. In the treated group ICP was significantly lower compared with the controls at day 3 post-injury. Overall mortality appeared improved but the difference was not statistically significant. However, subgroup analysis was more revealing. Improved favourable outcome was seen in the paediatric subset. Mortality was also significantly reduced for patients who were operated within 48 hours of injury and in whom the maximum ICP was less than 40 mmHg, with favourable outcome reported in 60%, compared with the matched controls. Other reports also suggest improved outcome with earlier application of DC for selected patients, based on the rationale of intervening before irreversible secondary injury is established (3, 68, 70, 77, 78).

The timing of DC in most of the reports shows wide variation, with many including in their data procedures performed very late after the injury. Gaab et al (74) reported 37 patients, 18 of whom had unilateral craniectomies and 19 who had bilateral craniectomies performed. The interval to surgery ranged widely, from 5 hours to 10 days. Mortality was 14% and all the deaths directly related to brain injury occurred in patients who had an initial GCS of less than 4, who also had unilateral or bilateral pupillary abnormalities. In the study by Guerra and colleagues (3), the range of interval to surgery was 12 hours to 18 days in a series of 57 patients over 20 years. Other reports also included patients operated on between 6-11 days after injury (75, 78, 79, 95).

In addition to the study of Polin et al cited above, other reports also suggest that DC may be of particular benefit in paediatric TBI. Favourable outcome in children was reported by Taylor et al (68), Ruf et al (77), and Simma et al (78), Berger et al (105), and Josan and Sgouros (106). The pressure-volume index (PVI) as a measure of intracranial compliance was explored in Chapter 5. In children the PVI is lower (15); therefore the apparent benefit of DC in these studies may relate to the fact that ICP in children is more sensitive to changes in volume. Also, in children, delayed deterioration is more likely to be due to diffuse brain swelling and raised ICP than is the case with adults, in whom haematoma is more common (23, 24, 28, 29).

Clinical Reports of DC for Hemispheric Infarction

Although patients with ischaemic strokes are not directly comparable to patients with severe TBI, there are certain principles relevant to the management of raised pressure and the risk/ benefit ratio of DC that are helpful in determining the potential role for the procedure in TBI.

Mortality in patients with large hemispheric infarctions may be as high as 70-80% (72, 108). It would appear that early, aggressive management of raised ICP with early DC does confer benefit in selected patients. Cho et al (72) recently reported a series 52 patients with malignant MCA infarction. Diagnosis was based on diffusion-weighted magnetic resonance imaging because of its increased diagnostic sensitivity in the early period compared with CT scanning. From the 52 patients, the authors identified 3 groups: one group had DC performed within 6

hours (early DC), one group had DC performed between 8-216 hours (late DC) because of later arrival, and one group was treated without surgery because consent was refused. These groups were similar with regard to age and preoperative GCS. Mortality in the early DC group was 9%, in the late DC group 37%, and in the non-operated group 80%.

Robertson et al (109) raised the concern that an aggressive approach may result in more disabled survivors. In their group of 12 patients who underwent DC, the proportion of disabled survivors was higher. However, their approach was significantly different in that DC was done only once the patients demonstrated signs of herniation despite maximal medical therapy. Rengarachy et al (110) and Carter et al (92) also performed DC for patients who were unresponsive to conventional medical therapy and who demonstrated 'uncal herniation and impending death'. However, Woertgen and colleagues (111) reported on the course of 48 patients with ischaemic strokes. Mortality was 26%, and the patients who underwent early DC fared best. Contrary to expectation, they found no patients in the vegetative group. In the series of 32 patients by Rieke et al (108) there was a mortality of 76% in the conservatively treated group compared with 34% in the operated group. Schwab and co-workers (112) found that mortality could be reduced to 16% if surgery was performed *before* signs of herniation developed.

Chapter 7: Early Decompressive Craniectomy in Children with Raised Intracranial Pressure due to Severe Traumatic Brain Swelling: A Case Series

Objective

The description of the experience at Red Cross Childrens Hospital with decompressive craniectomy (DC) for children with raised ICP secondary to brain swelling associated with severe TBI.

Background

Although DC has been used for various conditions causing raised ICP for more than a century, it has remained a controversial procedure, particularly for severe TBI. The lack of a definitive answer to the question of the role of DC in trauma is a result of the difficulty in designing and completing randomised trials in severe head injury. This difficulty is compounded by the lack of conformity in the world literature: various surgical techniques, differences in indications for the procedure, and the wide range in the interval prior to intervention. With particular reference to the latter, there is now a growing enthusiasm for the earlier use of DC, before irreversible injury secondary to prolonged raised ICP has occurred, recognising that a significant limitation in earlier reports is the practice of performing the operation late in the course of refractory ICP elevation as a salvage procedure for patients unlikely to benefit from any heroic intervention by that stage.

Methods and Materials

Data from the initial part of the series from September 1999-February 2002 was documented retrospectively. From February 2002 to December 2004 cases were recorded prospectively. All cases in which decompressive craniectomy or craniotomy were performed for severe TBI and raised ICP were collected. Decompressive *craniectomy* was defined as an operation for raised ICP due to cerebral swelling in which bone was elevated and not replaced initially, with or without dural augmentation. Decompressive *craniotomy* was defined as an operation for the same condition, in which bone was elevated, dural augmentation was performed, and the bone was replaced loosely at the end of the operation. Exclusion criteria were: age greater than 15, Glasgow Coma Score (GCS) of more than 8 immediately prior to surgery, any concomitant mass lesion evacuated, surgery performed more than 48 hours after the onset of raised ICP or secondary deterioration, and surgery performed for any condition other than that of traumatic brain swelling.

Details of Surgical Technique

In most cases a unilateral craniectomy was performed, incorporating a large frontotempoparietal bone flap. The typical procedure is performed as follows: after the induction of general anaesthesia a large question mark skin incision is made on the side of maximal brain swelling and a large free bone flap is elevated. The dura is opened widely with caution and dural augmentation is accomplished by the interposition of a dural graft harvested from pericranial tissue. Particular attention must be paid to achieving maximal control of brain swelling immediately prior to

dural opening, utilising head elevation, short-term hypocarbia and mannitol. This enables greater control of potential brain herniation when opening the dura. Harvesting the graft prior to dural opening is advised. Durectomy and graft interposition should be accomplished as rapidly as possible. Cottonoid patties are used to protect the cortical surface from the cut edge of the dura and the pericranial graft is interposed medial to the dural edge. If the bone is left out, the musculocutaneous flap is closed over the defect. In selected cases the bone may be replaced after dural augmentation, but only loosely secured so as to allow the bone to be elevated above the brain swelling, with minimal contribution to ICP. An ICP probe is placed in the subdural space at the end of the operation for ICP monitoring in the postoperative period. A single dose of antibiotic is given intraoperatively.

In some patients a bifrontal approach can be used, with or without dural opening. These patients are selected on the basis of bilateral swelling being present, with no midline shift. A large craniectomy is performed, removing the bone in the frontal region on both sides to beyond the coronal suture.

Results

Decompressive operations were performed on 14 patients during this period. Of these, 3 were excluded from analysis. Two patients were excluded because significant mass lesions were removed at the same time, and one patient was excluded because DC was performed for a large middle cerebral artery territory infarct secondary to traumatic vascular injury. In the other 11 patients DC was

performed for traumatic brain swelling causing raised ICP. The details of these patients are shown in Table 1. The median age was 7 years, with a range from 5 to 12. The mechanism of injury was variable. Details of the clinical presentation and deterioration of the patients are shown in Table 2. All patients had a GCS of 8 or less prior to DC being performed. In 10 patients there was a documented clinical deterioration or deterioration in ICP control that occurred after admission. Repeat CT was performed in 6 patients, confirming the progression of swelling. DC was performed in all within 12 hours of this deterioration. In patient number 10 there was no secondary deterioration; DC was performed based on the initial clinical assessment, combined with CT evidence of severe brain swelling and an ICP of 40 mmHg. The majority of patients were operated on less than 48 hours after the injury (9 of 11). In 2 patients surgery was undertaken more than 48 hours after injury due to the onset of delayed brain swelling and raised ICP: in one patient on day 3, and on the other patient on day 5 post-injury. However, in both patients surgery was performed within 12 hours of secondary deterioration. A unilateral approach was chosen in 9 patients and a bifrontal approach in 2. Decompressive *craniectomy* was performed in 7, while *craniotomy* was performed in 4.

Patient number	Age	Mechanism of injury
1	6	fell from a height
2	6	MVA pedestrian
3	11	blunt assault
4	12	fell from a moving vehicle
5	5	crush injury
6	9	MVA pedestrian
7	1	fell from a height
8	7	MVA pedestrian
9	11	GSW left parietal
10	6	MVA pedestrian
11	8	MVA passenger

Table 1: Patient data. MVA, motor vehicle accident; GSW, gunshot wound

No.	Initial presentation	Initial CT	Deterioration
1	GCS 5T, pupils reactive	grade IV swelling	GCS 2T, Hemiparesis, unilateral fixed pupil, HPT, bradycardia
2	GCS 8, pupils reactive	contusions, cisterns open	GCS 4T, unilateral fixed pupil Repeat CT:grade IV swelling
3	GCS 14	contusions, cisterns open	GCS 8 Repeat CT:grade IV swelling
4	GCS 10	contusions, cisterns open	GCS 8, bradycardia Repeat CT:grade III swelling
5	GCS 5T, pupils reactive, hypotensive	contusions, grade IV swelling	GCS 4T, unilateral fixed pupil, bradycardia
6	GCS 5T, polytrauma	grade III swelling	ICP 55 despite medical Rx, sedated, Repeat CT: increased swelling
7	GCS 15, dropped to 8 with temporal EDH, craniotomy for EDH removal	temporal EDH	After EDH removal, GCS dropped again to 5T, unilateral fixed pupil Repeat CT: grade III swelling
8	GCS 6T, polytrauma, hypoxic, hypotensive	contusions, cisterns open, middle cerebral artery branch infarct	GCS 3T, pupils bilaterally fixed, ICP 50 despite medical therapy Repeat CT: grade IV swelling
9	GCS 13, drowsy	parietal contusion, cisterns open	GCS 8, pupils bilaterally fixed, Hemiparesis
10	GCS 3T, pupils fixed, external brain hernia from compound wound, ICP 40	grade III swelling, diffuse axonal injury	Nil
11	GCS 6T, polytrauma, unilateral fixed pupil, brain hernia externally	grade III swelling, bifrontal; contusions, extensive BOS #	GCS 5T, increased ICP despite medical therapy

Table 2: Clinical data. GCS, Glasgow Coma Score; grade III and grade IV swelling, based on criteria from TCDB (36); EDH, extradural haematoma, HPT, hypertension

No.	Outcome
1	GOS 4, aggressive behavioural problems, at special school
2	CSF leak from wound at 2 wks, bone replaced only at 7 months because of an infected granuloma of scalp, bone flap sepsis cognitive deficits, GOS 4
3	no motor deficits, developing well, GOS 5
4	excellent outcome, GOS 5
5	mild hemiparesis, residual oculomotor nerve palsy, GOS 4
6	mild cognitive deficits, no motor deficits, GOS 4
7	excellent outcome, GOS 5
8	R abducens palsy, GOS 5
9	excellent, no deficits, GOS 5
10	died (day 3)
11	GOS 5, bone still to be replaced, mild inco-ordination

Table 3: Outcome

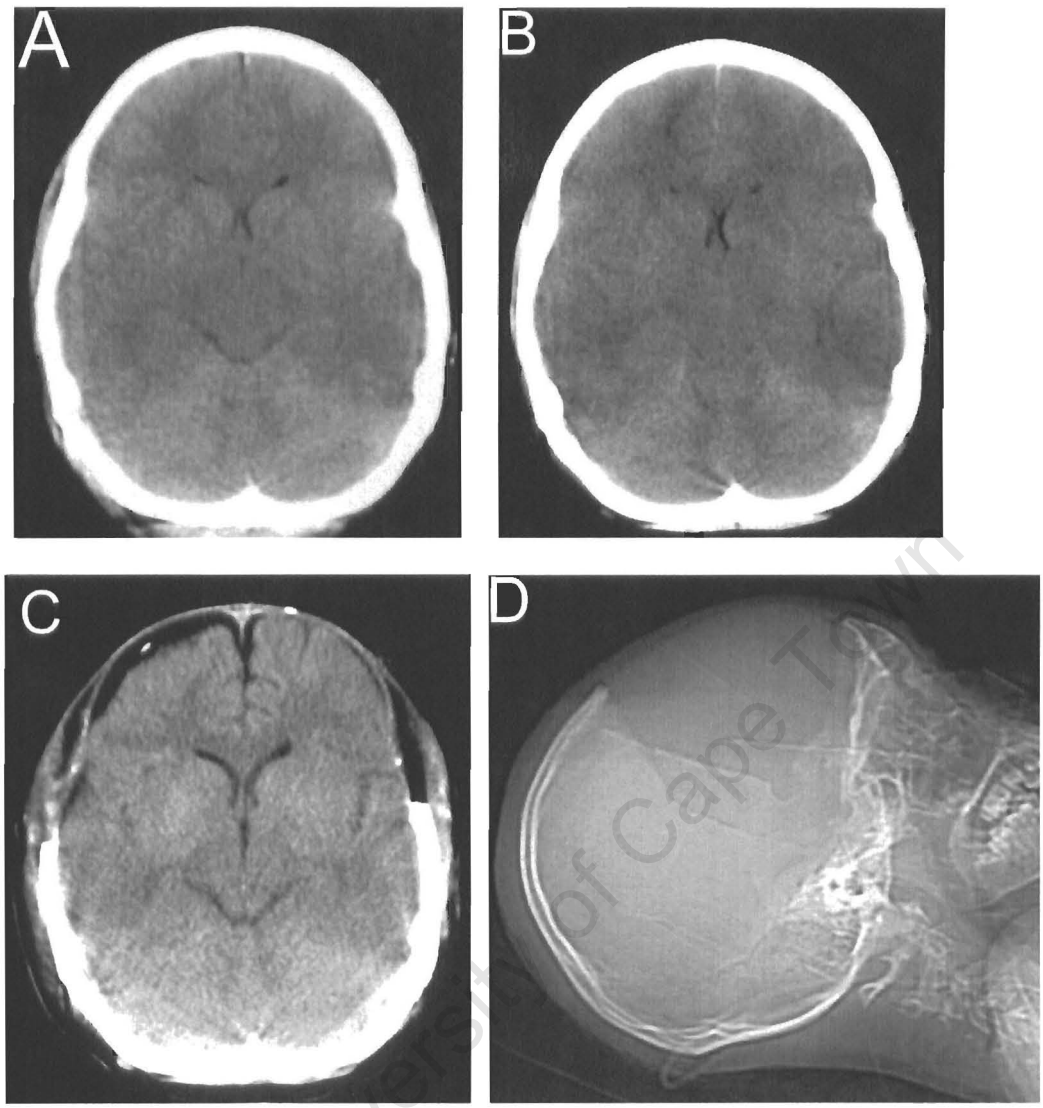

Fig.1 : Patient 6. **A**, Initial CT scan performed after admission, demonstrating open cisterns. **B**, CT scan showing obliteration of the cisterns at neurological deterioration. **C**, CT scan after bifrontal craniectomy, with open cisterns. **D**, CT overview showing the extent of the craniectomy.

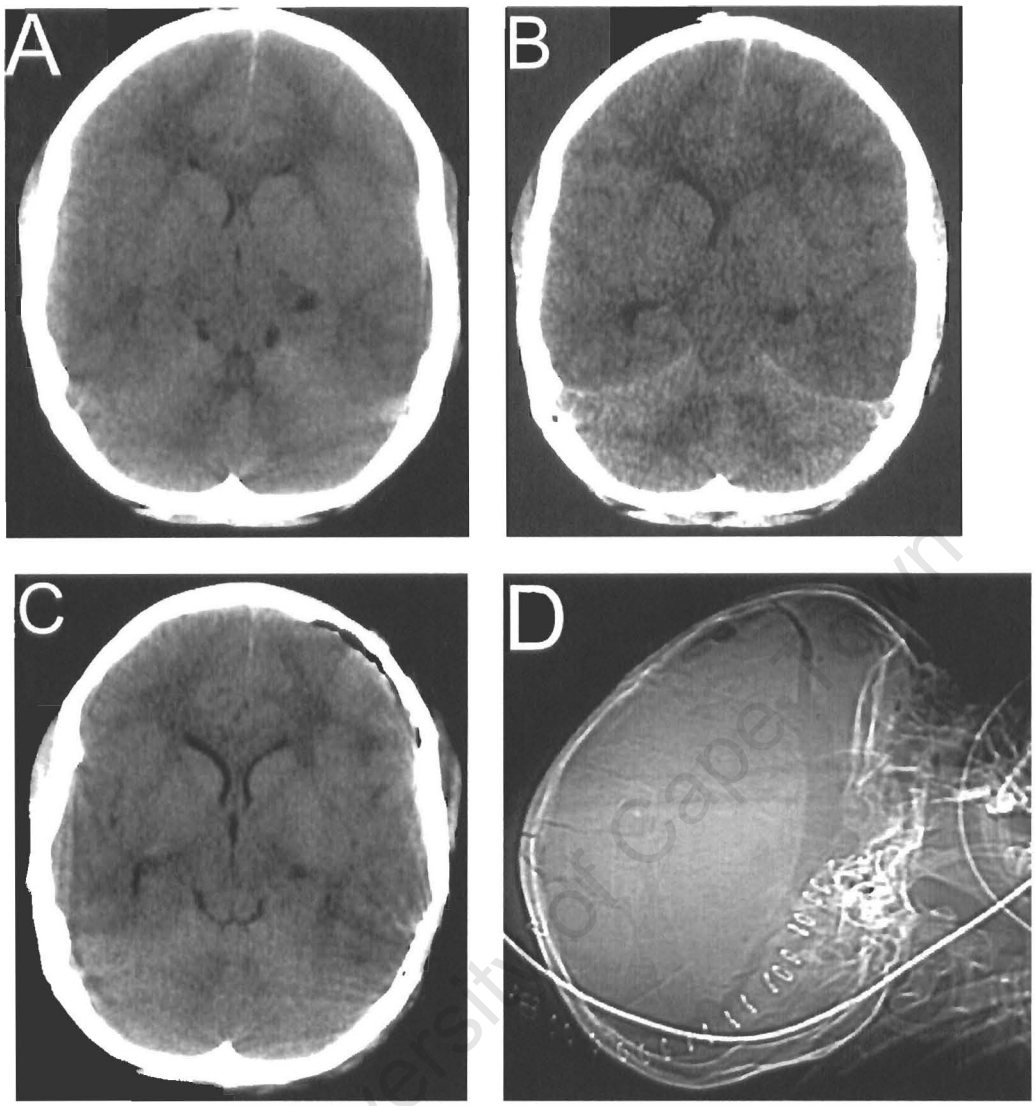

Fig 2: Patient 3. **A**, Initial CT scan demonstrating some cisternal effacement. **B**, CT scan at 24 hours, showing increased swelling with complete obliteration of the cisterns and midline shift. **C**, CT scan 8 hours after unilateral decompressive *craniotomy*. The quadrigeminal cisterns are now patent. **D**, Overview after craniotomy, demonstrating extent of the bone flap.

All patients were managed in a dedicated paediatric intensive care unit (ICU) postoperatively where ICP, CPP, invasive arterial monitoring and ventilatory parameters were recorded.

In all patients ICP was reduced postoperatively: in 5 patients ICP was normalised, and in 5 ICP was significantly lower but medical management was continued for moderate ICP fluctuations, with control of ICP attained in all. In one patient ICP was not monitored in the postoperative period but the clinical improvement was rapid, and associated with re-appearance of the basal cisterns on follow-up CT 24 hours postoperatively. All but one of the patients had a CT scan in the postoperative period. Resolution of shift and re-appearance of the cisterns was seen in all. The pre- and postoperative scans of 2 of the patients are demonstrated in Fig.1 and Fig. 2. Patient 10 (who did not have a postoperative CT) died 3 days after injury. This was the only patient who was admitted with a low GCS from the outset. He had been involved in a motor vehicle accident, demonstrating decorticate posturing with bilaterally unreactive pupils at initial assessment. CT scan obtained within 3 hours of the accident showed severe brain swelling, signs of diffuse axonal injury and loss of grey-white differentiation. Despite the poor prognosis, DC was done after ICP monitor insertion confirmed elevated ICP. Although ICP was normal in the postoperative period, there was no clinical improvement, and the patient subsequently died on day 3.

Median follow-up was 31.5 months for the 10 survivors, with a range of 3 to 66 months. Clinical outcome was measured with the Glasgow Outcome Score (113). A favourable outcome was seen in all of the survivors, with a score of 4 or 5

documented. Details of the clinical outcome are recorded in Table 3. There were few complications related to surgery. One patient developed a temporary CSF leak from the wound in the postoperative period. When the bone flap was replaced electively after 3 months, she developed bone flap sepsis, which required removal of the flap. Another patient developed a CSF hygroma collection beneath the bone flap. This was drained to exclude sepsis but was found to be sterile. In no patient was there any demonstrable increased oedema beneath the bone flap on follow-up CT scan. None of the patients in whom *craniotomy* was done demonstrated subsidence of the flap on follow-up. There was mild resorption of the bone flap in one of the patients from the *craniectomy* group.

Discussion

Despite the passage of more than a century since the procedure was first described, and the publication of numerous experimental and clinical reports on its potential benefits and risks, decompressive craniectomy in trauma has remained a controversial subject. Although the practice of relieving pressure in a confined anatomical space is well established for various compartment syndromes of the limbs or the abdomen the same treatment principle is not easily extrapolated to, or accepted for, raised pressure within the cranial cavity. Compartment syndrome of the limb can be defined as a condition in which 'high pressure within a closed space bounded by fascia and/or bone reduces capillary blood perfusion below a certain level necessary for tissue viability with subsequent neuromuscular dysfunction' (114). Timeous fasciotomy to relieve the pressure urgently and restore adequate blood flow before tissue death occurs is mandatory if the limb is

to be saved. This principle is so well accepted in general surgery that failure to do so when indicated could have medicolegal consequences. However, the same clarity of approach is not evident in treatment for raised ICP. This results from a number of important factors. First, brain tissue is not directly comparable to muscle, and the consequences of 'opening the box' are less predictable. Second, various operative strategies and indications for decompressive craniectomy have been practiced over the years. Third, conducting a randomised trial in this setting is difficult, not only because of the multitude of factors that influence the outcome after severe head injury, but also because this involves a life-threatening condition. And finally, decompressive craniectomy has been used traditionally only as a salvage procedure.

As discussed in previous chapters, numerous experimental and clinical reports have suggested that DC reduces ICP, improves cerebral blood flow and oxygenation, and improves outcome if performed early, before irreversible secondary injury is established. The limitations of earlier studies showing no improvement in outcome have been highlighted in chapter 6. Concerns regarding the possible increase in cerebral oedema beneath the craniectomy were balanced by experimental and clinical reports showing no increase in oedema or brain entrapment, as discussed in chapter 5.

The outcome in this series is noteworthy because of the severity of the brain injury. In chapter 3, the high mortality and poor neurological outcome of survivors after severe TBI are highlighted, along with the various factors associated with poor outcome. From the TCDB data, 47% and 82% of patients with unilateral and

bilateral pupil abnormalities respectively were dead or vegetative at discharge (22), and 84% of patients with grade III diffuse injury (compressed basal cisterns) had a poor neurological outcome. Of the grade IV patients, only 6% had a favourable outcome. The reliability of the state of the cisterns as a predictor of outcome has been confirmed in numerous reports (24, 38, 39). Patients who suffer secondary neurological deterioration due to raised ICP are also known to have a poorer outcome (34).

In this series, all patients had a GCS of 8 or less at the outset or at secondary deterioration, which are the same criteria as used in the analysis of the TCDB data. Five patients had a motor score of 3 or less. All had compressed basal cisterns on CT scan, with grade III or IV swelling by the TCDB criteria. Eight of the 11 patients had pupillary abnormalities prior to surgery; 3 had bilaterally fixed pupils. Ten patients experienced secondary deterioration; the only patient not undergoing secondary deterioration being patient number 10, whose admission GCS was poor. In the only death in this series, the patient probably had a primary brain injury that was incompatible with survival regardless of the intensity of treatment. It could be argued that patients with a prognosis this poor should be treated without treatment strategies as aggressive as DC, but in the acute setting, and particularly with children, it is usually very difficult to withhold any form of treatment even in the most dire circumstances. A favourable outcome (Glasgow Outcome Score of 4 or 5) was seen in all the other patients, despite the severity of the brain injury and the occurrence of secondary deterioration due to brain swelling. Of note, the aggressive approach did not result in any survivors with significant neurological disability.

Craniotomy, as opposed to craniectomy, in which the bone is replaced at the end of the operation, is not commonly practiced. Although this cannot be recommended universally, this may be an option in selected paediatric patients. In children the bone flap is much thinner than in adults; therefore replacement which allows the bone to be elevated above the brain expansion may not compromise the benefit of decompression. This avoids the risks associated with delayed bone flap replacement, which includes that of infection and bone resorption. Subsidence of the bone flap after the cerebral swelling settled was not seen in those patients in whom craniotomy was done. In the craniectomised patients the bone was replaced at an elective date after recovery, there was one case in which infection necessitated removal of the bone flap and was one case of mild resorption of the flap.

There are various opinions on the use of autologous bone flaps. Grant et al (115) reported bone flap resorption in 50% of their childhood and adolescent cases, a surprisingly high figure. However, Iwama et al (116) reported only case of bone flap resorption and one infection in their series of 49 patients. In the latter series the flap was sealed in 3 sterilised vinyl bags and stored at -35 degrees Celsius or -84 degrees Celsius. They suggested that the most important determinant was contiguity between the bone edge and the flap. No recommendation was made for the optimal refrigeration temperature. There is agreement that autoclaving of the flap should not be done as this denatures the bone proteins and limits osteoconduction and osteogenesis (115, 116). Replacement of the bone flap is desirable as soon as recovery has occurred, not only for cosmetic reasons but

also to prevent further injury to the underlying brain. Neurological improvement after cranioplasty has been reported (117), suggesting that it protects the brain from the transmission of atmospheric pressure gradients.

In summary, this is a highly selected series of patients with traumatic brain swelling that underwent DC for raised ICP. It is noteworthy that the outcome was generally favourable despite the severity of the head injury. The one patient who died most likely had a devastating primary injury. The rest all demonstrated secondary deterioration, which may represent the clinical circumstance in which DC is most likely to be beneficial.

Chapter 8: Future Investigation of Decompressive Craniectomy

Obtaining robust evidence from the scientific literature on DC is hampered by the difficulties encountered in head injury trials, as discussed in previous chapters. All available evidence is Class III in quality. Although the randomised trail by Taylor et al (68) is to be commended, the limitations of this trail highlight the challenges that face any institution attempting to produce class I data. Even though the study was prospective and randomised, the evidence obtained was limited to class III with regard to outcome (41) because of concerns about the size and generalizability of the sample. Although the trial was conducted over 7 years, only 13 patients were in the treatment arm. During this time period, a number of changes were made to the targets set for cerebral perfusion pressure. The operative procedure was conservative compared to the practice at most institutions that have published their data, involving the removal of a 3-4cm diameter disc of subtemporal bone bilaterally, without opening and expansion of the dura. The ICP reduction obtained was modest, and there was a trend towards better outcome that was not statistically significant.

Apart from the heterogeneity of TBI patients, one of the biggest challenges in a trial of DC is the slow accumulation of patients and the small sample size that is eventually achieved. This is unavoidable in a single institution, as DC is currently recommended only for a select group of patients. Perhaps the ideal candidate is a TBI patient that demonstrates diffuse brain swelling (without mass lesions) and secondary clinical deterioration, with raised ICP that does not respond to conventional medical management in the acute setting, before permanent

secondary injury is established. This probably represents a small proportion of the head-injured population. During the time period over which an adequate sample size is achieved, it is highly likely that our techniques for brain monitoring will have evolved, improving our understanding of various pathophysiological dynamics, and potentially changing our strategies for treatment. These include tissue oxygen monitoring, microdialysis, PET scanning, transcranial doppler, intracranial compliance evaluation, and assessment of cerebrovascular reactivity.

For a significant prospective, controlled, randomised trial to be achieved, multicentre involvement will be required. Despite the practical difficulties encountered in these trials, and the presence of their own forms of systematic bias, a multicentre trial is probably the only way that the problems encountered in the current single institution studies can be overcome. This would mandate standardisation of the stepwise approach to the management of ICP elevation and agreement on the criteria for abandoning medical therapy. With the current clinical and experimental data available, DC should be evaluated as part of an early and aggressive response to raised ICP in the posttraumatic period, preferably within 48 hours of injury.

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