HEAD INJURY FOR NEUROLOGISTS

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Trauma is the leading cause of death and long term disablement in young persons. Head injury accounts for about 30% of traumatic deaths and a higher proportion of long term disablement. Historically the emphasis of reviews on head injury has concentrated on the acute phase of treatment and has thus adopted a neurosurgical perspective. As a result, much of the content is peripheral to neurological practice, and the consequences of traumatic brain injury (TBI) remain the business of somebody, and as a result nobody, else. An underlying assumption is presumably that anyone can diagnose injury to the head, which is usually true, but determining whether, and to what extent, coexisting injury to the brain contributes to a clinical problem may not be so simple. A night in an accident and emergency department, neurological consultations on the intensive therapy unit or general or psychiatric wards, or involvement in a personal injury case will soon make this evident.

Neurological contact with patients with TBI is likely to increase with developing interest in neuroprotection and restorative neurology, drug treatments of specific impairments, increasing evidence of effectiveness of rehabilitation programmes after TBI,[1] and improved methods of imaging demonstrating evolving and residual brain damage. This paper aims to describe the sequelae of TBI that impact on current and future neurological practice. A detailed discussion of its rehabilitation is omitted.

CAUSES AND CONSEQUENCES: EPIDEMIOLOGY

In the UK, about 2% of the population attend casualty each year after a head injury. Of these 80–90% are not admitted. Of those 200–300 per 100 000 admitted, 20–40% stay for more than 48 hours and only 5–10% have injuries sufficient to warrant neurosurgical transfer.[2] About 20% of neurosurgical patients achieve a good outcome. Previously the prevalence of long term disablement has been estimated at between 100–439 per 100 000. However a recent one year follow up of patients with all severities of injury in a population of nearly 3000 admitted over one year by five Glasgow hospitals[3] estimated a prevalence of 3000–4500 per 100 000. Perhaps, as the study suggests, previous estimates have failed to account for a less than good outcome in the large numbers of patients admitted after "mild" TBI. This estimate is indirectly corroborated by the incidental finding of healed contusions in 2.5% of 2000 consecutive necropsies in a general hospital. Further studies are needed.

In the UK urban population, only 20% of patients admitted after TBI have been involved in a road traffic accident, which more frequently results in death and more serious injury. The majority of the remainder result from falls and assaults that are often, especially in younger persons, alcohol related, and alcohol may be detectable in up to 60% of patients hospitalised after TBI. Poor judgement, imbalance, and blackouts, whether the result of alcohol, epilepsy, recreational drug use, psychosis or previous brain damage of any cause including trauma, predispose to head injury. Recreational and organised sport accounts for only a small percentage of admitted injuries.

PATHOLOGY

The description some 40 years ago of diffuse axonal injury (DAI) provided an organic basis for post-concussional symptoms. This was contrary to the previous view that concussion was a reversible physiological phenomenon, without detectable pathology: understandably post-concussional symptoms were regarded by many as having a non-organic basis. An eloquent neuropathological description[4] of a pattern of primary and secondary focal and diffuse damage after all severities of injury has emerged, relevant to the understanding of residual impairments and the exploration of neuroprotective strategies, even after minor injury. This is now supplemented by the understanding that damage at the moment of impact is followed by a cascade of potentially modifiable events over hours, days, and possibly weeks, in parallel with the synthesis and release of factors promoting neural recovery.

Primary mechanical injury to axons and blood vessels results from rotational and translational accelerations. Rotational acceleration causes diffuse shearing/stretch of axonal and vascular cell

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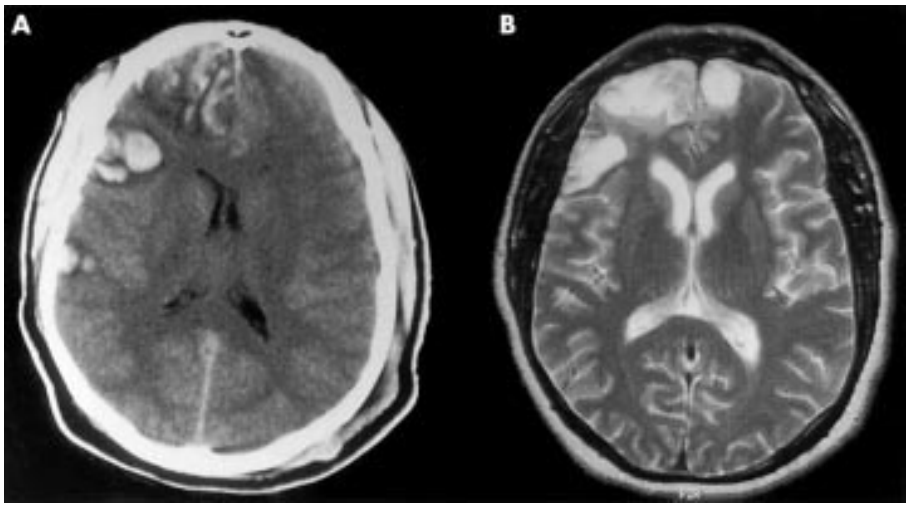

Figure 1 Thirty six year old man: assault. (A) Computed tomography (CT) acutely shows superficial haemorrhagic frontotemporal contusion, mainly on the right with some involvement of the medial aspect of the left frontal lobe, and mass effect with distortion of the anterior horn of the right lateral ventricle. (B) Subsequent T2 weighted magnetic resonance imaging (MRI) shows cystic encephalomalacia and gliosis at the sites of the previous contusions.

membranes, increasing their permeability ("mechanoporation"). Irreversible changes result when intracellular calcium influx triggers proteolysis, breakdown of the cytoskeleton, and interruption of axonal transport—marked, within 2–3 hours, by the accumulation of β amyloid precursor protein, the formation of axonal bulbs (retraction balls), secondary axotomy, and an inflammatory response. DAI typically occurs in deep parasagittal white matter, and extends centripetally with increasing injury severity: in the white matter of the parasagittal cortex "glide contusions" result from vascular shear injury; in the internal capsule, associated with shearing injury to branches of the lenticulostriate arteries and deep haematomas in the region of the basal ganglia; in the corpus callosum and fornix; and in the dorsolateral quadrant of the upper brain stem. Translational acceleration causes focal haemorrhagic contusions which largely involve the frontal and temporal lobes (fig 1), and extradural (arterial) and subdural (venous) haematomas—primary events which, with delayed contusional haematomas and swelling, secondarily result in mass effects and ischaemia (fig 2), and the biochemical cascade of injury.

IMAGING

New structural and functional imaging techniques contribute usefully to one's understanding of a patient's clinical problems. Magnetic resonance imaging (MRI) reveals more abnormalities than *x* ray computed tomography (CT), both early and late after TBI. New MRI techniques are increasingly able to inform the process of injury. However, MRI is difficult to perform acutely in a ventilated, unstable patient, and it will require much effort to establish whether advanced CT and MRI can significantly contribute to questions about pathogenesis, neuroprotective and restorative strategies, and prognosis.

Studies of T1/T2 weighted, T2 weighted fluid attenuated inversion recovery (FLAIR), and T2* gradient echo MRI sequences early and late post-injury confirm that those with a worse outcome have more damage. This is measured by number and volume of lesions resulting from contusions and large deep haemorrhages (T1, T2, FLAIR, and T2*), and the residual haemosiderin of microvascular shearing injuries (T2*) and degree of atrophy, both helpful markers of DAI. Direct imaging of hemisphere DAI (grade I DAI), rather than additional posterior callosal (grade II DAI) or dorsolateral midbrain (grade III DAI) lesions, both of which predict a worse outcome if haemorrhagic (fig 3), is less easily available. In white matter that appears normal on conventional MRI, diffusion tensor imaging (DTI) may reveal evidence of loss of neuronal and glial cells (increased diffusivity) and parallel fibre tracts (reduced anisotropy) (fig 4), while magnetic resonance spectroscopy may show a reduction in N-acetyl aspartate, consistent with neuronal loss. Acute studies of perfusion/diffusion mismatch on MRI could inform use of acute treatments, though this needs further study. Single photon emission computed tomography with technetium-99m hexamethylpropylene amine oxime may show areas of hypoperfusion that may or may not correlate with changes on structural MRI. The functional correlates of such perfusion defects are currently unclear.[5]

No imaging technique at present predicts outcome in group studies more reliably than simple clinical observation using admission Glasgow coma score (GCS) or duration of post-traumatic amnesia (PTA). At an individual level, however, the presence and characteristics of abnormalities early or late after injury may assist in the interpretation of neuropsychological or other clinical findings. For example, in a comatose patient with a spastic quadriparesis, imaging may differentiate a central midbrain haemorrhagic coning injury with relative preservation of the cerebral hemispheres and a reasonable outcome, from the haemorrhagic dorsolateral midbrain lesions associated with grade III DAI and a poorer outcome. After minor injury, changes on FLAIR and/or T2* may indicate that at least some of the patient's complaints are organic. As always, imaging changes should be interpreted in the context of other findings and never in isolation.

CLINICAL CONSEQUENCES OF TBI

The early physical, cognitive, affective, and behavioural consequences of TBI are initially associated with disordered arousal and awareness. Later there are attentional, executive, and memory problems. A few simple measures can be used to record injury severity and outcome (table 1). Even after severe injury under 10% of patients fail to mobilise long term, but almost all have some degree of neuropsychological deficit. Occasionally after coning from an extradural, in the absence of DAI cognition may be relatively preserved while independence is limited by severe neurophysical impairment, as a spastic–ataxic quadriparesis from midbrain damage (fig 2), so the patient is effectively "locked-in".

Glasgow coma score

The GCS introduced by Teasdale and Jennett in 1974[6] provides the best initial measure of severity of head injury. The score is

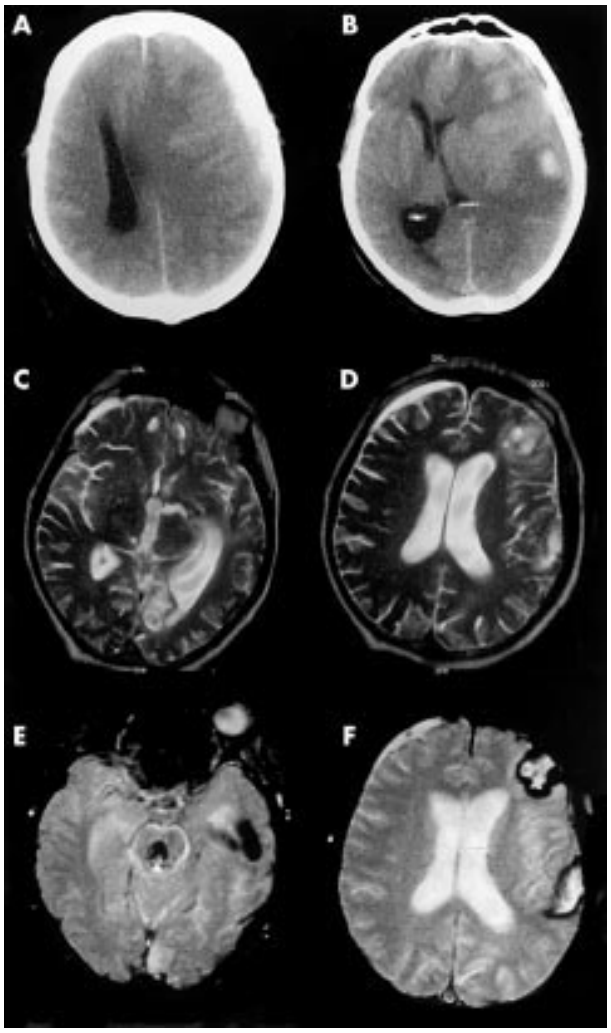

Figure 2 Thirty four year old man: deteriorated over seven days after a fall before presenting unconscious. Initial CT head scan shows mixed density subdural containing isodense and hyperdense components (A), and (B) cerebral contusions in the left frontal and temporal lobes, left hemisphere swelling, pronounced midline shift, and left uncal herniation; there is also evidence of left posterior cerebral artery (PCA) territory ischaemia and contralateral hydrocephalus. MRI six weeks later shows a shallow right frontal subdural collection, the left hemisphere swelling has resolved, the left PCA infarct has matured, and there are additional signs of residual damage in the frontal lobes, right thalamus, and left inferior anterior capsule (C, D). A T2 gradient echo sequence demonstrates the previous contusions (F) and the presence of blood breakdown products in the midbrain following haemorrhagic midbrain (E) infarction caused by transtentorial herniation. The low signal intensity in the left mid-temporal region is caused by partial volume of the petrous bone.

the sum of the scale's three measures of eye opening, and best motor and verbal responses. This ranges from a score of 3 for a patient with no motor or verbal response or eye opening to painful stimuli, to 15 for a patient who is orientated, follows commands, and has spontaneous eye opening. Patients who do not follow commands, speak or open their eyes, with a score of 8 or less, are by definition in coma. TBI is defined as *mild* by an admission GCS score of either 13 or 14–15, *moderate* by a score of 9–12 or 13, and *severe* by a score of 3–8. The score on admission, and its prognostic usefulness, are obviously easily confounded by factors other than TBI, particularly sub-

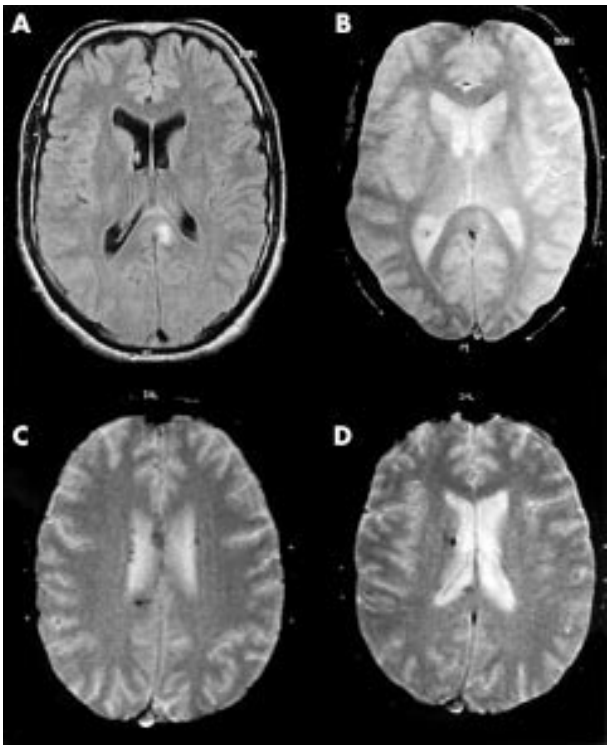

Figure 3 Grade II diffuse axonal injury (DAI). Patient 1: 26 year old man, one week post-traumatic amnesia (PTA) after a fall skiing. Fast fluid attenuated inversion recovery (FLAIR) image (A) showing signal abnormality in splenium of corpus callosum to left of midline; corresponding T2* gradient echo sequence (B) shows no evidence of susceptibility at this site, in keeping with a non-haemorrhagic lesion. Patient returned to work with minor constraints. Patient 2: 32 year old male, three months PTA, community independent, not working. T2* susceptibility effect representing blood products in the subependyma, mid and right posterior body of the corpus callosum, and subjacent to the superior frontal gyri (C, D). Normal T1/T2 weighted sequences.

stance misuse, but its sequential recording after admission plays a crucial role in recording early progress and in management.

Post-traumatic amnesia

PTA is the period following TBI when continuous memory fails. Patients are confused and disorientated, and lack the capacity to store and retrieve new information. They have a wide range of cognitive problems compared with patients with chronic isolated memory difficulties, consistent with a confusional state,[7] and are often agitated. Islands of memory or recollection of events may surface before the end of PTA. Inability to remember events before injury—retrograde amnesia—may last seconds, days, months, or even years, and can shorten during recovery. The duration of PTA, but not of retrograde amnesia, is a useful predictor of outcome. PTA can be estimated either prospectively using validated clinical rating scales combining tests of orientation, as a surrogate for confusion, and various aspects of memory (for example, the Galveston orientation and amnesia test), or retrospectively using datable landmarks in the clinical history. Prospective measurement of PTA is seldom routinely performed but can be done at the bedside by using simple tests of orientation (in person, place, and time) or attention (for example, reciting months forward) to mark the resolution of confusion.

Agitated behaviour is frequent during PTA, and should not be confused with maladaptive aggressive behaviours, or

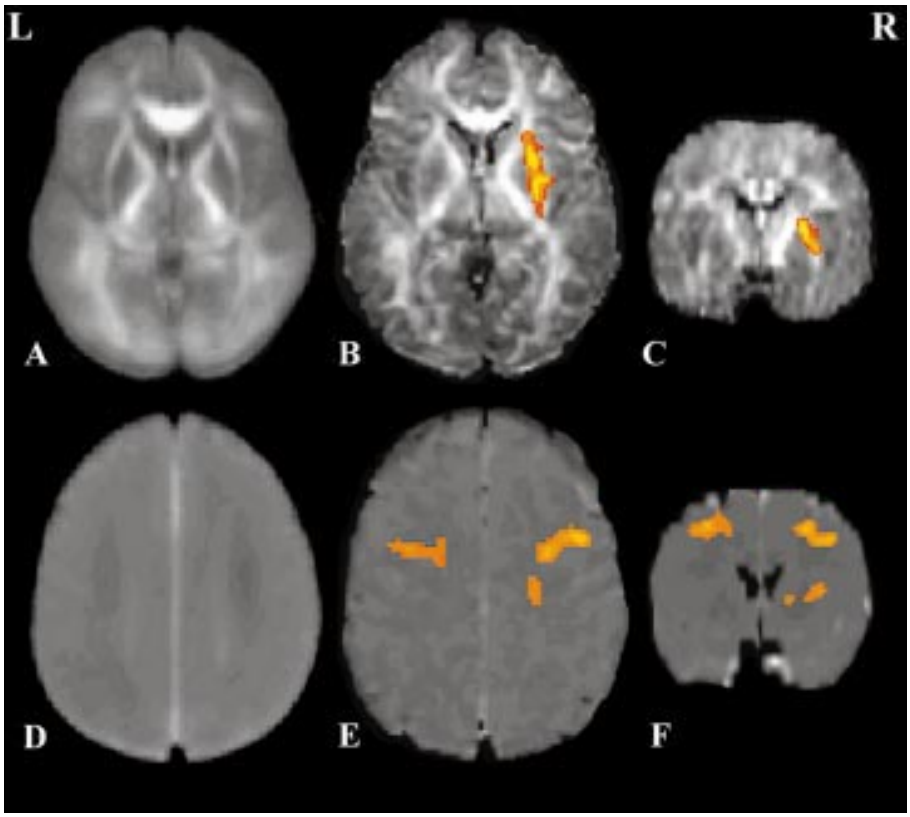

Figure 4 Thirty year old man, dysexecutive and resolved left hemiparesis nine months after road traffic accident; CT and conventional MRI normal. Diffusion tensor imaging (DTI) compared on a voxel-by-voxel basis with 30 healthy controls (A and D). Regions of reduced fractional anisotropy (B and C) and increased mean diffusivity (E and F) identified, suggesting a loss of structural organisation and expansion of the extracellular space caused by DAI. Note that right on the image is the patient's right. Courtesy Dr F Rugg-Gunn.

Abbreviations

AED: antiepileptic drug
DAI: diffuse axonal injury
DTI: diffusion tensor imaging
FLAIR: fluid attenuate inversion recovery
GCS: Glasgow coma score
GOS(E): Glasgow outcome scale (extended version)
MRI: magentic resonance imaging
PTA: post-traumatic amnesia
TBI: traumatic brain injury

psychoses, occurring late post-injury, long after the cessation of PTA. Treatment, for which there is almost no evidence base, comprises the introduction of a structured environment with reduction of distraction and stimulation, sometimes with drug treatments. Reasonable prescriptions are, initially, haloperidol 5–10 mg and diazepam 10 mg intravenously, or droperidol 5–10 mg and lorazepam 2 mg intramuscularly, and/or, as maintenance, oral risperidone 0.5–4 mg per day, carbamazepine 400–800 mg per day, or buspirone 15–90 mg per day.

Neurophysical problems

Almost any focal neurological deficit can result from TBI and will reflect the site(s) of damage. Approximately 25% of severely injured patients escape obvious focal neurological deficit, more after mild and moderate injury.

Unlike stroke, significant long term trunk and limb weakness is uncommon and problems result largely from spastic hypertonus, sometimes leading to contractures, clumsiness, and uncoordinated muscle contraction, ataxia, and imbalance. Hemiparesis when present may be contralateral to contusions or the deep large haematomas associated with DAI, or ipsilateral to mass lesions that have caused compression of the contralateral cerebral peduncle against the tentorial edge from herniation. Alternatively, brain stem injury associated with DAI or coning results in a variable asymmetrical spastic–ataxic quadriparesis, sometimes with titubation and/or a disabling ataxic tremor in the "good" arm. Dystonic limb movements may be delayed in onset and appear as strength improves, occasionally accompanied by central neurogenic ("thalamic") pain that confusingly may seem localised to joints. Compression mononeuropathies can complicate the picture, as may coexisting spinal injury or, in older people, a cervical spondylotic myelopathy worsened by hyperextension at the time of the head injury.

After severe injury, subacute deterioration not from systemic complications may be the result of hydrocephalus caused by organisation of ventricular or subarachnoid bleeding, and often usefully responsive to shunting. Early after injury hydrocephalus is not easily confused radiologically with atrophy, but the two may be difficult to distinguish if late ventricular dilatation develops. In the elderly, chronic subdural haematomas may become large without becoming symptomatic, often after mild or forgotten head injury, and subsequently spontaneously resorb (fig 5); in younger patients these present as drowsiness, papilloedema, new headache, or hemiparesis and require evacuation.

Cranial neuropathies occur in about 10% of admitted and 30% of severe injuries. Frontal injury, basal skull fracture, and pressure effects account for most.

Complete or incomplete absence or distortion of smell and taste are well recognised, particularly after frontal or occipital injuries, and seldom improve after more than six months following injury. Anosmia can cause occupational difficulties and is occasionally associated with cerebrospinal fluid rhinorrhoea.

Table 1 Consequences of traumatic brain injury: basic measures of injury severity and outcome

Glasgow coma scale (GCS)	**Post-traumatic amnesia (PTA)**
Eye opening (E)	<5 mins: minimal
4 spontaneous	5–60 mins: mild
3 to speech	1–24 hours: moderate
2 to pain	1–7 days: severe
1 nil	1–4 weeks: very severe
Motor response (M)	4–12 weeks: extremely severe
6 obeys	12–24 weeks: exceptionally severe
5 localises	>24 weeks: devastating
4 withdraws	**Glasgow outcome scale (GOS)**
3 abnormal flexion	1 Dead
2 extends	2 Vegetative
1 nil	3 Severely disabled (requires assistance or supervision for some activities during every 24 hours)
Verbal response (V)	4 Moderately disabled (independent indoors and outdoors but disabled)
5 orientated	5 Good recovery (resumes normal life; may have minor impairments)
4 confused conversation	
3 inappropriate words	
2 incomprehensible sounds	
1 nil	
Score (E+M+V) = 3–15	

GCS and GOS from Jennett and Teasdale[6]; PTA categories unvalidated, adapted from Jennett and Teasdale[6] and other sources,

Visual symptoms are common after TBI and mainly result from oculomotor dysfunction, refractive error shifts, damage to the cornea and intraocular structures, visual field loss caused by anterior and posterior visual pathway damage, and visual perceptual deficits.

Visual blurring and monocular diplopia may be caused by corneal trauma, injury to the contents of the anterior chamber including the lens, vitreous tears, and subhyaloid haemorrhages. Blot and flame shaped retinal haemorrhages, and papilloedema, are not uncommon after severe TBI. Traumatic optic neuropathies usually affect the tethered portions of the nerve at the entry and exit of the optic canal; they may be partial and sometimes accompany relatively minor ipsilateral frontal injury. Severe injury may result in damage to the intracranial optic pathways. It may cause bilateral visual field defects from chiasmal injury, usually due to direct mechanical damage and sometimes accompanied by pituitary dysfunction. DAI involving the optic tract(s) or radiation(s), or direct trauma, coning with compression of a posterior cerebral artery, or global ischaemia may all involve the primary visual or association cortices and cause visual field and/or visual perceptual deficits.

Double vision may result from the breakdown of a previously compensated squint, or orbital injuries and fractures. Isolated third, fourth or sixth nerve palsies, occasionally bilateral or combined, are well recognised and usually resolve over time. Central disorders of eye movement, sometimes accompanied by moderately dilated, light-near dissociated pupils or accommodation spasm, are usually the result of severe injury, and may represent the midbrain injury of grade III DAI. Aspects of Parinaud's syndrome including lid retraction (Collier's sign) are seen occasionally as the result of relatively minor primary brain stem injury, documentable on MRI, presumably caused by direct injury against the tentorial edge. Arteriovenous shunts, classically as carotid cavernous fistulae, can arise after severe injury (fig 6) but occasionally may develop after a relatively minor one. Symptoms and signs comprise chemosis, proptosis, double and blurred vision, and "the hypoxic eyeball syndrome" from increased pressure in veins normally draining the orbit.

Injury to the trigeminal nerve is generally limited to peripheral sensory branches following frontal lacerations or fracture of the upper orbital margin (supraorbital nerve), facial or orbital fractures (infraorbital nerve), or mandibular

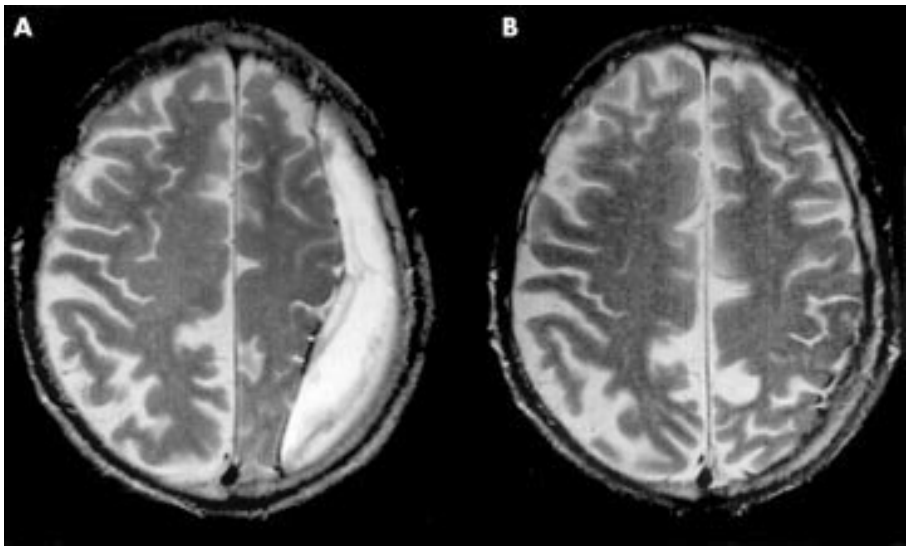

Figure 5 Seventy nine year old man, who experienced a minor blow to head on kitchen cupboard door four weeks before initial scan. Control of Parkinson's disease worse, otherwise well. Axial T2 weighted images six months apart showing complete resolution of left sided subacute mixed signal intensity subdural haematoma.

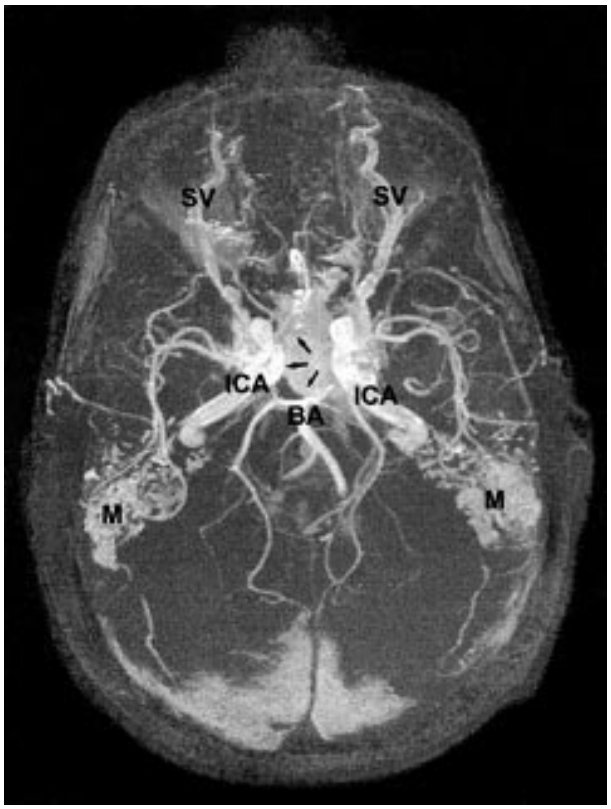

Figure 6 Maximum intensity projection of a three dimensional "time-of-flight" magnetic resonance angiogram demonstrating bilateral carotico-cavernous (CC) fistulae three months after severe TBI in a 17 year old male. There is huge dilatation of the left cavernous sinus into the suprasellar cistern, and abnormal flow in both cavernous sinuses with bilateral retrograde flow into dilated superior ophthalmic veins (SV), resulting in massive bilateral chemosis and proptosis. Balloon occlusion of two fistulae in the cavernous segment of the left internal carotid and coil occlusion of the right CC fistulae resulted in resolution of the proptosis and chemosis, and return of functional vision. ICA, intrapetrous precavernous segments of the internal carotid arteries; BA, basilar artery; M, retained secretions in middle ear and mastoid air spaces. Courtesy of Dr TCS Cox.

fractures (inferior dental nerve). Facial nerve palsies are common, occur with longitudinal or transverse petrous temporal fractures and damage to the middle ear or labyrinth, respectively, are occasionally bilateral, and usually recover fully especially if delayed rather than immediate in onset.

Bloodstained discharge from the ear at the time of injury is usually associated with fracture of the petrous temporal bone, and is followed by a high incidence of audiovestibular problems. Longitudinal fractures usually involve the middle ear, transverse fractures the cochlea and/or eighth nerve, causing complete deafness if bilateral. Profound hearing loss may occasionally persist and cochlea implants prove helpful if the patient is otherwise reasonably able.

Conductive deafness is usually the result of a tympanic membrane perforation or haemotympanum, and resolves over 2–3 months; if not then ossicular discontinuity or fixation may be present and require surgery. Sensory–neural hearing loss is common even after minor head injury, when it often recovers if low tone and persists if high tone. It results from damage to the cochlea or auditory nerve, or to the intracranial auditory pathways, which may also cause tinnitus, abnormal sensitivity to ordinary environmental sounds, and difficulty listening in the presence of background noise.

Benign paroxysmal positional vertigo is the most common vestibular disorder after all severities of head injury.[8] It is often self limiting or treatable by canalith repositioning manoeuvres. Vague symptoms of post-traumatic dizziness may also be attributed, following neuro-otological investigation, to "labyrinthine concussion"—intralabyrinthine haemorrhage—rather than central vestibular pathology. Organic symptoms may develop weeks after injury, but in a significant number of these patients non-organic factors play a part.

The proximal part of the fifth nerve and its ganglion and the lower four cranial nerves (IX, X, XI, XII) are well protected and only damaged by very severe injury and skull base fractures. Dysphagia, dysarthria, and dysphonia are thus usually supranuclear, and pseudobulbar and/or ataxic, in origin.

Cognitive and neuropsychiatric sequelae

After resolution of PTA, overall IQ and posterior cognitive functions of language and visuospatial skills are often relatively intact and the residual neuropsychological deficits may not be easily detected by simple tests of cognitive function. A formal neuropsychological assessment of the patient's memory, attention, and executive skills and their mental speed is thus mandatory, particularly late after severe injury when these problems play a major role in limiting independence.

Organic disorders of behaviour[9] are often seen in tandem with cognitive dysfunction, and are usually described by a carer. Personality changes, of imprecise localising value, include egocentricity, childishness, irritability, aggressiveness, poor judgement, tactlessness, stubbornness, lethargy, disinterest, reduced drive and initiative, and often reduced rather than increased sexual interest. Occasionally more dramatic positive and impulsive, or negative and abulic, behaviours prevail.

Psychiatric sequelae including low mood, depression, and anxiety disorders are common after TBI, and often delayed in onset. Psychiatric illness, fewer years of formal education pre-injury, and a more dependent outcome predispose to the development of these problems.[10] Depression may respond to a selective serotonin reuptake inhibitor or venlafaxine, and psychiatric referral may be necessary. Occasionally obsessive–compulsive disorders and psychoses occur in the absence of obvious premorbid psychiatric history, and the risk of suicide is increased.

EPILEPSY

While post-traumatic epilepsy is yet another psychosocial burden for the severely injured patient, very few have epilepsy sufficiently severe to require complex anticonvulsant regimens or referral for residential investigation and treatment. Nevertheless, its presence precludes driving and may rekindle carer concerns at a time when readjustment to the other consequences of injury is just beginning.

Just as the brain damage resulting from penetrating head injury may increase the risk of epilepsy nearly 600 fold during the first year, so after blunt injury is the risk significantly increased by markers of brain damage; particularly to the cortex, indicated by a (depressed) skull fracture, an intracranial clot requiring surgery, and altered awareness for more than 24 hours associated with radiological evidence of brain contusion.[11 12] As imaging improves it is easy to see how even minor injury followed by only an hour or two of PTA can occasionally be followed by post-traumatic epilepsy from cortical contusion. Following injury, late epilepsy (more than one week post-injury) is predicted by early seizures (12 hours to

one week post-injury), but not by concussive convulsions (occurring seconds after the impact) or immediate epilepsy (occurring up to 12 hours after injury), which are usually regarded as "provoked" seizures and usually do not exempt the patient from driving or require antiepileptic drugs (AEDs). Twenty five per cent of late seizures occur more than two years post-injury, and the risk of seizures even 10 years post-injury in a patient whose risk was 50% initially is still around 3%.

While intravenous phenytoin within 24 hours of high risk injury prevents early seizures, there is no evidence that the early use of either phenytoin or sodium valproate prevents late seizures, even in high risk patients, and the neurobehavioural side effects of phenytoin after TBI have been well documented.[13] As yet[14] there is also no good evidence to support the prophylactic use of AEDs in high risk patients, let alone guidance about how long medication should be taken—a matter often resolved by individual discussion after a fit-free 6–12 months.

The high chance of recurrence after a first late seizure of 65% at one year, even in those without a depressed skull fracture or acute subdural haematoma, make it difficult to avoid prescribing an AED, with its attendant side effects, in such circumstances. The inclination is to focus on seizure control initially either with carbamazepine or lamotrigine, reserving the newer AEDs, such as oxcarbazepine and levitiracetam, for those with troublesome side effects or further seizures. The onset of late seizures is usually not associated with new change on conventional imaging. After a two year remission, discussion about the risks of recurrence after AED withdrawal is appropriate.

Non-epileptiform seizures are rare after severe injury. They may be seen after less severe injuries, sometimes in the context of post-traumatic stress disorder or panic disorder following the index event. Rages and episodic dyscontrol syndromes are (almost) never epileptic.

OTHER PROBLEMS

Other complications (not always neurological) require consideration in the overall assessment of the patient, usually early after severe injury when comorbidities, particularly resulting from extracranial injuries and premorbid illness, may be significant.

Folliculitis involving face and torso is common in younger patients. Pressure sores unfortunately still occur though with reduced frequency as a result of the use of pressure care mattresses. Pronounced weight loss from underfeeding and a post-injury hypercatabolic state may contribute to the development of pressure sores and a poor long term outcome, and should be prevented by early introduction of nutritional support and gastrostomy feeding. Failure of oral feeding may be the result of several factors including an abnormal posture, a tracheostomy, and cognitive and behavioural problems, as well as neurogenic dysphagia.

Later weight gain, which may be considerable, sometimes occurs, and may be associated with identifiable disturbance of pituitary function, most commonly of growth hormone or gonadatrophin secretion. Significant pituitary dysfunction may be accompanied by traumatic chiasmal or optic nerve damage, a pointer to the diagnosis. Deterioration caused by traumatic panhypopituitarism must always be considered in such patients. Hypothalamic damage is well recognised postmortem after head injury and in life is the likely explanation of autonomic overactivity, such as sweating and fever in the absence of identifiable infection. Whether this damage contributes to late behavioural and affective problems is unclear. Incontinence is usually neurogenic and associated with detrusor hyperreflexia. Occasionally, the loss in diurnal variation of vasopressin release after hypothalamic/pituitary damage results in nocturia with nocturnal incontinence. Frequency caused by outflow obstruction and an increased post-micturition residual may be the result of urethral stricture caused by patients pulling on their catheter while confused.

Extraosseous bone formation, heterotopic ossification, is usually para-articular in the region of large joints (hips, shoulders, elbows, knees) and starts several weeks after injury. It may produce local pain; isotope scanning shows early osteoid formation, while later ossification shows on plain *x* rays. It is not known whether the osteogenic transformation of undifferentiated cells is induced by central nervous system injury or factors released by immobilisation osteopenia. Surgical removal of heterotopic ossification is not usually necessary.

MINOR HEAD INJURY AND TBI IN SPORT

Minor head injury[15 16] accounts for 70–80% of admitted head injuries. Disagreement over the extent of resultant morbidity is partly explained by study entry criteria. Patients with a PTA of less than one hour, a minor head injury by Russell and Smith's PTA criteria of 1961, will generally be expected to have a better outcome than those with an admission GCS of 13 or 14. The "post-concussional" symptoms that follow may be somatic (headaches, dizziness, fatigue, sensitivity to light and noise, and sleep disturbance), cognitive (memory, attention, and concentration), or affective (anxiety, depression, and irritability). Most persons report problems and have measurable evidence of difficulties with attention, memory, and efficiency of information processing one week after an admission GCS of 13–15. The majority recover by three months, but about 20% have complaints at one year. This situation is complicated by misattribution to the TBI of symptoms that have a high prevalence in the general population, or can be explained by an earlier head injury, neuro/psychiatric disorder, or alcohol and substance abuse. Early problems, when somatic and cognitive complaints predominate, are largely the result of organic injury including frontotemporal contusions and DAI, often demonstrable on early MRI. Psychological factors including coping style or symptom exaggeration play a significant role in the development of persistent and especially late onset symptoms, which are often affective. Similar symptoms may result from coexisting post-traumatic stress disorder, which at times occurs despite loss of memory of the injury itself. These patients may report intrusions, including nightmares, avoidance behaviours, and hyperarousal, and may respond to cognitive–behavioural exposure techniques. Older age, abnormalities on early imaging, acute elevation of biochemical markers, particularly the serum protein S-100B, an (unlucky) admission GCS of 13, and a PTA of more than one hour, help predict the minority of patients at risk of persistent postconcussional symptoms, who may benefit from formal follow up.

TBI sustained during contact sports[17] is usually minor, often repetitive, but occasionally severe. Severe or mortal injury, such as that sustained while boxing, is usually the result of translational acceleration resulting in an acute subdural haematoma with mass effect and brain swelling. Outcome correlates with time to craniotomy, and thus rapid neurosurgical access is mandatory. Repetitive TBI over a long period results in time in the cognitive, motor, and psychiatric symptoms of

Table 2 Influences on outcome after (traumatic) brain injury

Pre-injury	Injury		Recovery
	Primary*	Secondary	
Genotype	Diffuse	Mass effects	Recovery of neuronal excitability
Age	Axonal	Ischaemia	Network and neuronal reorganisation and regrowth
Sex	Vascular	Seizures	Behavioural adaptations and substitutions
Psychosocial status	Focal	Infection	Systemic and contextual limitations
Comorbidities	Contusions	Systemic factors	
Nutrition	Haematomas (EDH; IDH)	BP, O_2, °C, etc	
Alcohol	↓	↓	
Drugs	Biochemical mediators of necrosis and apoptosis		

*Apart from primary injuries after traumatic brain injury, the table illustrates factors influencing outcome after many sorts of brain injury.
BP, blood pressure; EDH, extradural haematoma; IDH, intradural haematoma (subdural and intracerebral).

dementia pugilistica, reported in boxers, especially those with the APOE-e4 allele genotype, and steeplechase jockeys. Histological changes comprise neocortical neurofibrillary tangles and diffuse amyloid plaques. Exposure to repeated minor head injury in other sports including karate, ice hockey, and American and Association football, is associated with neuropsychological deterioration. Return to play guidelines, currently not universally agreed, are designed to reduce risk of second injury caused by suboptimal competence early post-injury, and also the cumulative effects of repeated concussion.

HEADACHE

Head injury may worsen pre-existing headache or headache may develop de novo. For reasons that are unclear, it is seldom reported after severe head injury. Headache does not appear to be a surrogate for diffuse axonal injury or any other organic brain damage, and is possibly the consequence of injury to the head and meninges, rather than the brain itself. Post-concussional symptoms, caused by neurological damage including vertigo, diplopia, or mild cognitive problems, may contribute to worsening of pre-existing headache, but there is no reason to think that they should cause headaches in patients who "did not know what a headache was" before a minor head injury.

Post-traumatic headache, by definition, starts within 14 days of the injury, or with recovery of awareness, and if it continues for more than eight weeks it is said to have become chronic. Tension-type headache or migraine, with or without aura or a combination of the two, are commonly seen. However, only a minority develop chronic daily headache, often perpetuated by analgesic misuse. Local soft tissue injury, especially to a temporomandibular joint, cervical structures, and rarely the carotid sheath, contribute. Infrequently one may encounter other types of primary headache, such as cluster headache and chronic paroxysmal hemicrania. Occasionally orthostatic headache (low pressure headache from cerebrospinal fluid leak) may occur.

Management depends upon the headache type, combined with a detailed explanation, attention to psychological factors, and physical therapies. In patients with chronic daily post-traumatic headache, withdrawal of misused analgesia and ergotamine, often with prophylactic sodium valproate up to 500 mg three times daily or low dose amitriptyline, have been recommended though not subject to rigorous trial.

THE VEGETATIVE STATE AND LIFE EXPECTANCY

Vegetative patients are wakeful but not aware. Coma for a few weeks after injury, where there is no spontaneous eye opening and vigorous stimulation does not result in awareness, is followed by wakefulness without evidence of self or environmental awareness—the vegetative state. There is preservation of function in the ascending reticular activating system but not in the thalami and cerebral hemispheres.

Following severe TBI, about 10% of patients are vegetative at one month. In 10–15% of these patients, usually over 40 years old, the vegetative state persists until it can be said to be permanent at 12 months, when 30–50% of the original cohort will have died and 40–50% will have regained awareness, mostly within six months. The majority of these remain severely disabled, although a few, usually young, achieve good recovery, rated by the Glasgow outcome scale. About 20% of patients still vegetative at three months will become aware,[18] though none achieve a good outcome. After hypoxic–ischaemic insults prognosis is much worse, only 10% of vegetative patients regaining awareness after one month and hardly any after three months. These data are useful when advising on management of patients on general wards.

In the vegetative state normal sleep/wake cycles occur with other evidence of subcortical reflex activity including orientation towards light, sound or movement, brief tracking of a moving object, withdrawal, grimacing or groaning to pain, tooth grinding and chewing, and grasping reactions, in the absence of evidence of awareness. These often apparently purposeful movements can lead to false hope as well as diagnostic difficulties. Detailed and repeated observations are essential in confirming the presence/absence of reliable awareness and to distinguish the vegetative state from the minimally conscious (aware) state, akinetic mutism, and the locked-in syndrome. Severe thalamic damage, either in association with severe DAI or neocortical hypoxic–ischaemic injury, and occasionally as a result of tentorial coning, is the pathological substrate for the vegetative state.

If individuals survive the first year or two and remain vegetative, life expectancy may be related to a level of care over and above a level adequate to prevent infection, accidents, and pressure sores, and to maintain nutrition. Survival longer than five years is not uncommon, more than 20 years is unusual, and there are reports of the occasional patient surviving for more than 30 years. Life expectancy in aware but profoundly disabled patients is shortened, mainly by immobility and the need for gastrostomy feeding. Strauss and colleagues[19] found that after TBI, in the context of "no" and "poor" mobility, life expectancy was 10–15 years and 18–35 years, respectively, depending on age.

PREDICTION OF OUTCOME

Of all the specific and generic outcome measures available, the five point Glasgow outcome scale (GOS) and its eight point

extended version (GOSE) best capture overall outcome after TBI.[20] Quite apart from their usefulness for group comparisons in clinical trials, they also offer a useful framework for clinical practice. Most models evolved to predict outcome in the longer term seek to differentiate reliably, in the acute neurosurgical setting, those patients with a non-vegetative survival at six or 12 months; these will not be discussed here in detail.

Neurologists are often asked to give some idea of long term outcome in the 10–20% of patients who remain in hospital for more than a few days after TBI. Avoid the temptation of a "target" outcome, and thus an over optimistic or pessimistic prediction, or if possible the "too early to say" statement, which fails to engage the family/carer or colleague. Instead, a best/worst envelope or a functional ceiling, as in "X is likely to walk and may well look after himself but is unlikely to be able to hold down regular paid work", or "Y may regain awareness and the ability to communicate but is unlikely to become independent", suitably expressed, provides a framework for the future and long term planning and is more likely to contribute usefully to expectations and management.

Long term, under 10% of neurosurgical patients fail to walk, at least indoors, but only 20–30% of patients achieve re-employability after severe injury. Acute predictors—admission GCS; present/absent pupillary responses; attendant hypoxic/ischaemic injury; imaging findings, especially depth of lesion; and perhaps biochemical markers—help formulate prognosis when the patient is seen subacutely. Duration of coma and PTA are also useful, providing they are not prolonged by medication or systemic factors. A PTA of two weeks or more predicts inevitable measurable residual cognitive problems, of variable impact; a month of PTA predicts at best a reduced work capacity, at worse some community supervision; and a PTA of three months makes voluntary or subsidised work a likely best outcome while at worst residential placement may be needed.

Eventual outcome is the result (table 2) of interaction between injury severity, restorative processes, and contextual factors. The latter include increasing age over 50 years, social class, personality, family support, premorbid caseness, and genetic make up, particularly the possession of at least one apolipoprotein E e4 allele which is associated with a poorer long term outcome.[21] The complexity of these interactions results in the range that functional predictions must encompass; at first sight this may make the predictions seem of little use but in practice they contribute to a valuable early operational framework.

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