

ORIGINAL ARTICLE

Sudden unexplained death in adults caused by intracranial pathology

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Sudden unexplained deaths as a result of intracranial lesions in adults are an important component of medicolegal practice and are best examined as a combined effort by a forensic pathologist, or a histopathologist experienced in coroner's necropsies, and a neuropathologist. Analysis of case material on file in the University of Glasgow's departments of forensic medicine and science, and neuropathology showed that the principal causes were sudden unexplained death in epilepsy (SUDEP), intracranial haemorrhage, either natural or after trauma, purulent meningitis or an abscess, and tumours. The mechanisms of death are considered to be the rapid increase of intracranial pressure caused by bleeding into the various compartments of the brain, or an acute obstructive hydrocephalus, and in cases where death is very rapid, autonomic and/or neurochemical dysfunction.

The practices of forensic medicine and neuropathology not infrequently come together in the investigation of cases of sudden death, which in a large number of instances is the result of intracranial pathology. This paper is based on the joint experience of the two departments in the west of Scotland.

DEFINITION OF SUDDEN UNEXPLAINED DEATH IN ADULTS

Sudden unexpected or unexplained natural deaths comprise the vast majority of deaths encountered in the practice of forensic pathologists in the UK. In England and Wales, approximately 80% of cases reported to the coroner will be natural deaths. In Scotland, the number of cases reported to the procurator fiscal, which undergo postmortem examination, where death is the result of natural causes, will be slightly less. This disparity reflects the more restrictive coroners' laws in England and Wales, whereby the certifying doctor must have seen the deceased during their last illness, usually within 14 days of death, failing which a coroner's necropsy will be required. This is not the case in Scotland, where any registered medical practitioner can legally issue the death certificate.

The definition of sudden unexpected or unexplained death is not entirely straightforward, and the two are not always interchangeable. Mason defines sudden death as "unexpected death following so rapidly from the onset of symptoms that the cause of death could not be certified with confidence by a medical practitioner familiar with the patient".¹ Although the World Health Organisation accepts a limit of 24 hours between the onset of symptoms and death (cited by Knight²), this is considered too long an interval by many practitioners and pathologists, and a much shorter time interval of within a few hours of apparently good health³ or of one hour is preferred.² This is a separate category of death from those that remain unexplained after full postmortem examination, including further investigations—for example, toxicology and histology. For the purposes of our paper, we interpret unexplained as meaning unexplained at the time of death and sudden as dying within one hour of onset of symptoms, or where the deceased was found dead unexpectedly.

SOURCES OF MATERIAL

The department of forensic medicine and science at the University of Glasgow provides a postmortem examination service for the former region of Strathclyde in Scotland, the population of which is approximately 2.7 million. Almost all cases of suspicious deaths within this region and also a considerable proportion of natural, suicidal, and accidental deaths are examined. Approximately 60% of 1500–2000 necropsies each annum comprise sudden unexpected or unexplained deaths. The records of the department have been reviewed for deaths involving epilepsy, intracranial haemorrhage, meningitis, and tumours (table 1).

The department of neuropathology provides a tertiary reference service for most of the hospitals in the central and the western parts of Scotland, including the city of Glasgow. This forms the basis of about two thirds of the 800–900 specimens referred for examination each year. The remaining one third consists of material referred for medicolegal purposes, which is the major source of the cases falling within the definition of sudden unexplained death in adults, and is the basis of some of the findings described in our paper. The most common causes of death in these circumstances are associated with epilepsy, intracranial haemorrhage, either natural or after trauma, and acute bacterial meningitis.

SUDDEN DEATH FROM NATURAL CAUSES

Sudden unexplained death in epilepsy

Epilepsy has long been associated with an increased risk of death other than from trauma or drowning.^{4–5} It is now recognised that individuals with epilepsy are at an increased risk of sudden unexplained death (SUDEP), which is not attributable to either of these causes.^{6–8} The incidence of these unexpected deaths is different in various population groups—for example, in specific hospitals,^{9–12} or in the general population with epilepsy^{6–15}—and this is reflected in rates, which can vary from 0.4–1.35/1000 person years,¹⁵ to 4.9/1000 person years.⁹ Ficker and colleagues⁶ gave a risk approximately 24 fold greater than that of the general population, and Leestma and

Abbreviations: DAI, diffuse axonal injury; DVI, diffuse vascular injury; SUDEP, sudden unexplained death in epilepsy

Table 1 Principal intracranial causes of sudden death in adults (from the department of forensic medicine archives)

Cause of death	Total no. of cases	Years reviewed	Cases/year (approx.)
Epilepsy (SUDEP)	131	1991–6	22
Intracerebral haemorrhage	15	1995–8	4
Spontaneous subarachnoid haemorrhage	41	1995–8	10
Subdural haematoma	24	1995–8	6
Extradural haematoma	2	1995–8	<1
Bacterial meningitis	4	1995–8	1
Brain tumours	1	1995–8	<1

colleagues¹³ reported a prevalence of SUDEP of 1/370 to 1/1110 patients with epilepsy/year, with a risk of 1/200 for people with severe epilepsy.

More recently, attempts have been made to standardise terminology, and in 1996 a workshop agreed the definition of SUDEP as “that of a sudden unexpected witnessed or unwitnessed non-traumatic and non-drowning death in patients with epilepsy with or without evidence of a seizure and excluding documented status epilepticus where necropsy does not reveal a toxicological or anatomical cause for death”.¹⁶

Several risk factors for such deaths have been identified and include young adults, male sex, early onset of epilepsy, poor seizure control, multiple drug treatment, history of generalised tonic/clonic seizures, treatment non-compliance/low levels of anticonvulsant drugs on postmortem testing, alcohol abuse, unwitnessed seizures, and body position.^{10 13 15 17–19} Information about the circumstances of death is often difficult to obtain. However, death is often preceded by witnessed fits, with these comprising 67% of cases in the series of Kloster and Engelskjøn¹⁷ and 50% in the study by Leestma and colleagues¹³; in addition, SUDEP often occurs while the person is asleep, comprising between 40–60%^{17–18} and 79% of cases.²⁰

The investigation of these deaths is variable; in some series only a minority of patients had a postmortem examination.⁹ In some studies, postmortem values of anticonvulsants were subtherapeutic or negative.^{8 13 17 18} In addition, despite a proportion showing abnormalities,^{13 18 21 22} the brain is often not formally examined by a neuropathologist.

A retrospective review of cases from the department of forensic medicine and science during the years 1991–6 showed that a relatively constant proportion of deaths was attributed to epilepsy (0.7–1.8%). During this period there were 131 such cases, of which 119 had a history of epilepsy; 84 were male (2 : 1; male : female ratio), with an age between 3 and 74 years, but with the majority occurring in the 30–40 age range, and 43% had a history of alcohol abuse. In approximately a third of the cases a history of the circumstances of the death was not available, in another third the deceased had a witnessed seizure before death, and in almost 50% of cases the circumstances suggested that the patient had died during their sleep.

At necropsy, abnormalities that might have been associated with a seizure were bruising of the tongue in 17%, and in 7.6% petechial haemorrhages in the mucous membranes were described. The brain was submitted for formal neuropathology in 41 of the 131 cases (31.3%). In keeping with previous findings,²² there were abnormalities in about 66% of the cases, most often evidence of recent or old contusional damage, alcohol abuse, and hypoxic damage. In three cases, mesial temporal sclerosis was seen. Where the brain was cut unfixed at the time of postmortem examination, abnormalities were noted in only eight of 90 cases. Postmortem toxicology was performed in 101 of the cases and of the 81 cases in which the results were available, only 65 were tested for anticonvulsants. In these cases, analysis was negative in just over a third and subtherapeutic values were identified in most of the others.

The cause of death was certified by the pathologist in most cases as either epileptic seizure or epilepsy. In a small number of cases, death was ascribed to status epilepticus or asphyxia. This variety of terminology can be confusing, particularly when in some instances the basis for implicating a seizure or asphyxia is not clearly apparent from the information available.^{9 23} It is also misleading and potentially distressing to the relatives of the deceased.²⁴ Annegers *et al* reported that the incidence of ischaemic heart disease is increased in patients with epilepsy.²⁵ It is possible, given that deaths from epilepsy essentially result in a negative postmortem examination, that SUDEP deaths may be underestimated, especially if an additional pathology is found, such as coronary artery atheroma. In the absence of any clear circumstantial evidence, such as a witnessed seizure, the cause of death may well be ascribed to the pathology rather than the epilepsy. The 1996 workshop recommended that if a death remains unexplained after a full necropsy, including toxicology and examination of the heart, it should be certified as witnessed or unwitnessed sudden unexpected death/known epilepsy.

“SUDEP deaths may be underestimated, especially if an additional pathology is found”

Sudden death owing to non-traumatic intracranial haemorrhage

Sudden death may occur as a result of rapid bleeding into any one or more of the intracranial compartments—extradural, subdural, subarachnoid, or intraventricular spaces—or into brain substance. The causes vary depending upon age and anatomical location of the haemorrhage. In most instances there is bleeding into more than one intracranial compartment. For example, rupture of a saccular aneurysm may be associated with a subdural haematoma, bleeding into the subarachnoid space, and an intracerebral haematoma, which in the course of expanding may in turn rupture into the ventricular system. In contrast, a primary intracerebral haematoma is rarely associated with a subdural haematoma, although it may present at the surface and be associated with subarachnoid bleeding; more commonly it extends medially into the ventricles.

Sudden death from ruptured saccular aneurysm

There has been some uncertainty about the frequency with which ruptured intracranial saccular aneurysms are associated with either instantaneous or very rapid death. Early medicolegal literature,^{26 27} based on surveys of large numbers of patients who died before or on arriving at a hospital, found that 60% of the patients died immediately after rupture of the aneurysm. The mean age was 46 years and at necropsy there was massive subarachnoid haemorrhage in 96% of the cases, subdural haemorrhage in 22%, and intracerebral haemorrhage in 43%; in addition, patients with saccular aneurysms of the posterior part of the circle of Willis or arising from the internal carotid artery showed a greater tendency to die at the time of rupture than those with aneurysms arising from other arteries.²⁷

Studies have shown that 8–10% of deaths from a ruptured intracranial saccular aneurysm occur suddenly, before reaching hospital.^{28–30} In discussion, particular emphasis was placed on the exceptionally high fatality rate in patients with ruptured saccular aneurysms arising from the posterior circulation of the circle of Willis. A few hospital based studies have also suggested a somewhat higher mortality after rupture of posterior circulation saccular aneurysms,^{31 32} whereas others have failed to detect any differences in outcome.^{33–36}

The frequency of posterior circulation saccular aneurysms has been variably reported as between 5% and 10% of all intracranial aneurysms,^{32 33 37} whereas in some referral based medical centres the frequency of posterior circulation aneurysms may approach 20%.^{35 38} The under representation of posterior circulation aneurysms in most other series of patients with subarachnoid haemorrhage is explained, in part, by the high early mortality associated with a rupture before the patient receives medical attention. For example, sudden death has been recorded in 10% of all aneurysmal subarachnoid haemorrhages.³⁰ However, of the cases caused by rupture of a posterior circulation aneurysm in other epidemiological studies, the proportion of patients succumbing to subarachnoid haemorrhage before reaching medical attention ranged from 3% to 17%.^{28 39 40}

The case files of the department of forensic medicine and science were reviewed for deaths caused by a non-traumatic subarachnoid haemorrhage in the years 1995–8. There were 41 cases of sudden or unexpected death. In most of these cases, the distribution of the subarachnoid haemorrhage was described as mainly basal or diffuse. In seven of the 41 cases, the source of the bleeding was not identified, and in one case the haemorrhage was the result of a vascular malformation. In 27 of the remaining 33 cases, the ruptured aneurysms arose in the anterior circulation of the circle of Willis, and in only six was a ruptured posterior circulation aneurysm responsible for death. Therefore, it seems that the frequency with which massive subarachnoid haemorrhage has been attributed to saccular aneurysms arising from either the anterior or posterior part of the circle of Willis can be explained by case selection and referral patterns.

At necropsy, the diagnosis of massive subarachnoid haemorrhage is self evident. However, because of the large amounts of freshly formed blood clot it is often difficult to locate the saccular aneurysm unless the brain is examined when fresh. The subarachnoid membrane should be removed with forceps and the ventral surface of the brain washed with isotonic saline. Even with the use of a dissecting microscope it may not be possible to identify the source of the subarachnoid haemorrhage in at least 5–10% of cases, raising the possibility that the cause is rupture of a small saccular aneurysm, which had been completely obliterated by the “blow out” of the blood vessel.

The role of physical or emotional stress—for example, minor assault or a verbal argument—when someone dies from a natural disease process shortly after the event is a not uncommon medicolegal problem. Such deaths most frequently result from subarachnoid or intracerebral haemorrhage or cardiac disease, with death possibly occurring as a consequence of a rise in blood pressure as a result of the stress. To establish a causal link there must be at least a clear temporal association between the stressful event and death.

Intracerebral haematoma

Massive haemorrhage into brain substance is characterised clinically by an abrupt onset and rapid evolution. In one study in a medicolegal practice, 393 cases of intracerebral haematoma were identified, of which 40% originated within the basal ganglia, 16% in the pons, 15% in the thalamus, 12% in the cerebellum, and 10% in the cerebral white matter.⁴¹ In 75% of the cases, the intracerebral haematoma had ruptured into

the ventricular system, 15% had presented at the surface within the subarachnoid space, and in 6% there was an associated subdural haematoma. In 35% of the cases, individuals were found dead or were dead on arrival at a hospital. The files of the department of forensic medicine revealed a total of 15 sudden deaths from an intracerebral haemorrhage in the four years 1995–8, 11 of which occurred in 1998.

“Massive haemorrhage into brain substance is characterised clinically by an abrupt onset and rapid evolution”

Most large intracerebral haematomas occur in middle aged men with hypertension, or in the elderly. There are occasional examples caused by rupture of a vascular malformation or in association with a blood dyscrasia, sickle cell disease, or anti-thrombolytic treatment. There are also a small number of cases on record where there has been massive haemorrhage into a pre-existing tumour. These days, intracerebral and subarachnoid haemorrhage are seen increasingly in association with drug abuse and possibly binge alcohol drinking. The drugs most commonly associated with this are ecstasy (MDMA; 3,4-methylenedioxymethamphetamine), other amphetamines, and cocaine. The rupture of the aneurysm is thought to be a consequence of a rise in blood pressure that occurs in these situations, or possibly a vasculitis.^{42 43}

Sudden death caused by intracranial infection

Although intracranial infection occurs most frequently in children, there are examples in adults, principal among which are sudden unexplained deaths caused by either acute bacterial meningitis or in association with a large cerebral abscess. Invariably, acute bacterial meningitis is secondary to a bacteraemia in adulthood, and is most commonly caused by pneumococci and meningococci. Review of the department of forensic medicine archives for 1995–8 revealed only two cases in each of 1995 and 1997. At necropsy, the brain may be greatly swollen and the sulci filled by a cloudy, pale yellow/green exudate, which, in meningococcal meningitis, may be so slight as to be difficult to identify. Acute bacterial meningitis is frequently associated with social and economic deprivation, and alcohol abuse, and is classically associated with pneumonia, a compromised immune system, and an absence of the spleen. It is usually possible to culture pneumococcus from samples taken after death, but this is uncommon in the case of meningococcal meningitis, although the diagnosis may be suspected if there is other evidence of meningococcal disease, such as petechial haemorrhages and purpura of the mucous membranes and skin, and haemorrhagic necrosis of the adrenal glands. This diagnosis can be confirmed by the detection of specific meningococcal capsular polysaccharides in the blood.⁴⁴

Chronic suppurative otitis media or occasionally long standing infection of other sinuses may be forerunners of a brain abscess. Usually chronic, the abscess has a grey and rather translucent capsule, with its effective size often increased by brain swelling. Therefore, an abscess acts as an intracranial expanding lesion. Additional complications are rupture of the abscess into the ventricular system to produce an acute purulent ventriculitis, or rupture into the subarachnoid space to produce an acute purulent meningitis. Review of the department's archive identified two cases of sudden unexplained death caused by brain abscesses, both in heroin addicts. Apparently, symptoms had been masked by the drug habit and failure of the health care services to recognise the potential importance of a discharging ear.

Sudden death caused by brain tumours

Intracranial tumours are said to account for 8% of non-traumatic intracerebral haemorrhage, in about half of which it may be the first manifestation,^{45 46} and in a small proportion of

these cases the patients die very rapidly. In our experience, it is a rare cause of sudden death, only one case being identified in the files of the department of forensic medicine from 1995 to 1998. In the literature, of the primary brain tumours glioblastoma multiforme predominates⁴⁷; other tumours that have been reported to present in this way include oligodendroglioma, medulloblastoma, lymphoma, teratoma, and pituitary adenoma (as a result of apoplexy). Of the metastatic intracranial tumours bronchial carcinoma, choriocarcinoma, and melanoma are the most common.

Colloid cysts of the third ventricle are also associated with acute neurological deterioration and can be a cause of sudden death in adults.⁴⁸ Small lesions may remain silent to be found only at necropsy. Larger cysts may occlude the foramina of Munro and in some instances they are not anchored to adjacent structures but have sufficient movement to act as a ball valve. The wall is usually a thin membrane enclosing a homogenous soft opaque hyaline-like material.

SUDDEN DEATH ASSOCIATED WITH TRAUMA

The principal neuropathological findings may be diverse and range from a brain that may appear to be relatively normal, to one in which there are multiple petechial haemorrhages, or one that shows massive subarachnoid or subdural haemorrhage. Whereas there is an observable abnormality in the last three situations, which at least provides a structural basis for sudden death, the first situation makes it difficult to achieve a satisfactory clinicopathological correlation.

Death with minimal evidence of traumatic brain injury

In our experience, there are several cases each year in which the circumstances associated with death strongly suggest that trauma is the most important contributing factor. Thus, there may be both external and internal evidence of trauma, with some injuries to the thoracic and abdominal cavities, but insufficient in amount and severity to provide a satisfactory explanation for death, or indeed evidence of trauma may be confined to the head. Under these circumstances there is a reasonable expectation that the cause of death may lie within the skull and that examination of a fixed brain might provide the answer. All too often this is not the case—although there may be some evidence of trauma, with a thin film of subdural haemorrhage and minimal surface contusions, slicing of the brain often fails to reveal any evidence of internal damage, including either parenchymatous or intraventricular haemorrhage. Therefore, uncertainties remain about the exact mechanism of death and may remain even after extensive histological studies.

Traumatic intraventricular haemorrhage

Variable amounts of recent haemorrhage within the ventricular system are often found, either as an isolated finding or in association with multiple haemorrhages, principally within midline structures (see below). The source of the haemorrhage may be difficult to determine, but has been attributed to tearing of small blood vessels in the walls of the ventricular system, including the interventricular septum and in the choroid plexus,⁴⁹ therefore reflecting a degree of injury consistent with “inner cerebral trauma”.⁵⁰ In addition, the deformation of central portions of the brain may cause sufficient dilation of the ventricular system to result in the rupture of small blood vessels beneath the ependyma.⁵¹ Sometimes, it is caused by extension of midline haemorrhages into the ventricular system, or there is evidence of diffuse brain damage.⁵²⁻⁵⁴

Diffuse vascular injury

The forensic pathologist not infrequently undertakes a necropsy on a patient who has died rapidly, usually with features of external trauma to the head, but without obvious

external abnormality of the brain. Under these circumstances, neuropathological examination after a period of fixation is likely to show multiple petechial haemorrhages throughout the brain, especially in the brain stem and in the white matter of the anterior portions of the frontal and temporal lobes adjacent to the thalamus. The hind brain haemorrhages have been referred to in the past as primary brain stem haemorrhages,⁵⁵ but in our experience they are more appropriately considered as a primary type of diffuse brain damage, in view of their wide distribution throughout the cerebral hemispheres and the brain stem.⁵⁶

Although it is undoubtedly true that patients with this pattern of multiple petechial haemorrhages in the brain die either instantaneously or within a few minutes, increasing experience has shown that there are some patients with this type of acute vascular pathology who survive the initial injury only to die some hours later. This suggests that there is likely to be a spectrum of traumatic damage characterised by multiple small haemorrhages in the brain (diffuse vascular injury; DVI) that may be remarkably similar to that seen in diffuse axonal injury (DAI).

Both DVI and severe DAI,⁵⁷⁻⁵⁸ previously called shearing injury,⁵⁴⁻⁵⁹⁻⁶⁰ are the most severe forms of diffuse traumatic brain injury occurring predominantly after road traffic accidents,⁶¹ but not exclusively so.⁶²⁻⁶³ It has been suggested that such petechial haemorrhages are indicative of damage of a type and distribution that is incompatible with life.⁵⁵⁻⁶⁴

Isolated traumatic subarachnoid haemorrhage

Some bleeding into the subarachnoid space is probably the most common finding after head injury. Larger amounts may occur, usually in association with cortical contusions and/or skull fractures, in road traffic accidents or falls from a height, but occasionally this bleeding is massive and is the principal finding in cases of sudden unexplained death.⁶⁵⁻⁶⁶

This entity is said to occur typically in a “young, healthy, but intoxicated male who receives a minor blow, immediately collapses, and dies within minutes”.⁶⁷⁻⁶⁸ Certainly, most subjects are men and have been involved in moderate degrees of violence, with blunt impact injury to the lateral or posterolateral neck, demonstrable at necropsy after appropriate dissection.⁶⁹ In one case,⁷⁰ however, traumatic subarachnoid haemorrhage resulted from violent jerking of the head to avoid a blow. Although immediate collapse is the norm, there have been documented instances in which death has been delayed by up to 60 minutes after injury.⁷¹ In cases where death has occurred rapidly, there are usually considerable amounts of subarachnoid haemorrhage in the posterior fossa: rarely is this associated with real damage to the brain stem.⁷²⁻⁷⁴ The site of damage to the vasculature remains uncertain, but it is generally accepted that in over 66% of the cases a tear occurs in the vertebral artery, either in its intracranial or extracranial course.⁷¹⁻⁷⁵⁻⁷⁶ Some studies have demonstrated fractures of the transverse process of the upper cervical spine at the same level as the arterial injury in a large number of cases.⁶⁸⁻⁷⁰⁻⁷²

Difficulty remains in identifying the source of haemorrhage at necropsy, further compounded by the possible occurrence of artefactual tears during the course of examination. Several techniques have been described to identify the site of vascular rupture⁷⁷: these include en bloc removal of the hind brain and upper cervical spinal cord, and block dissection or suboccipital exposure of the neck, combined with defleshing or postmortem angiography.⁶⁸ Another technique that reportedly yields good results involves the cannulation of the proximal vertebral arteries in the neck and flushing with isotonic saline while inspecting the ventral surface of the brain stem for escaping fluid, the calvaria having been removed previously.

The role of alcohol and its contribution to the head injury remains controversial. Between 40% and 100% of subjects are

said to be intoxicated with alcohol,⁷⁸ and it is suggested that this may be associated with violent jerking of the head and neck owing to slow protective responses.² The vasodilatory role of alcohol is also unclear. However, alcohol intoxication is a common finding in any violent death. Other theories include the effects of direct trauma,⁶⁹ characterised by the triad of massive basal subarachnoid haemorrhage, the absence of a ruptured saccular aneurysm or vascular malformation, and the demonstration of blunt force injury to the lateral or ipsilateral portion of the neck. Other authors have invoked hyperextension with some rotation and/or flexion of the neck.

Extradural haematoma

Although the classic history of an extradural haematoma is of a "lucid" or "latent" interval after the injury before lapsing into unconsciousness, allowing most patients to reach hospital and surgical intervention, Knight² states that this is so often not the case that no diagnostic reliance can be placed upon it. Very occasionally, they present as a sudden death, an extradural haematoma being the cause of death in only one patient in the department of forensic medicine files from 1995 to 1998. The typical postmortem finding is of a skull fracture at the point of impact, usually the parietotemporal area, overlying the localised dark red blood clot arising from a tear in the middle meningeal artery, or one of its branches. The pathologist must distinguish an acute extradural haematoma from the brown, friable artefactual "heat haematoma" found in some fire deaths.

The minimum volume required to form a significant space occupying lesion and thus potentially produce a fatal outcome is variably reported between 35 and 100 ml. The site and presence of a fracture can vary, with an intact skull being reported in about 15% of cases.⁷⁹

Subdural haematoma

As with an extradural haematoma, a patient with a pure subdural haematoma may experience a lucid interval before unconsciousness, and thus may reach hospital before death. Therefore, such cases do not fall within the boundaries of our paper. Despite this, in our experience, an acute subdural haematoma is seen more frequently as a cause of sudden, unexpected death than an extradural haematoma, possibly reflecting a high incidence of alcohol abuse and resultant failure to seek medical attention. In the four years of records reviewed from the department of forensic medicine it accounted for 24 sudden deaths, the annual numbers varying from two to 12.

Subdural haematomas most frequently result from falls and are thus commonly associated with skull fractures. Whereas in extradural haematoma, the fracture and the blood clot invariably underlie the point of impact, the blood clot in subdural haematomas is often diffuse and may be unilateral or bilateral, and may not correspond with the fracture line. This reflects the different mechanism of injury, a subdural haematoma resulting from tearing of bridging veins in the subdural space as a result of a rotational movement. The site of bleeding cannot always be identified at necropsy. The development of an acute subdural haematoma, comprising dark red fluid and/or clotted blood, can be very rapid. A sufficient volume to cause death can accumulate in as little as 30 minutes.⁸⁰

MECHANISMS OF DEATH

Sudden death in epilepsy

The circumstantial evidence is consistent with the current view that death associated with epilepsy is seizure related. Central apnoea is known to occur in epileptic seizures,^{81 82} and the common occurrence of pulmonary oedema at autopsy would be in keeping with this. Other theories include seizure associated cardiac arrhythmia⁸¹ or arrhythmia associated with antiepileptic drug withdrawal.⁵

When death is very rapid

In deaths from trauma where there is minimal evidence of brain injury on examination, the failure to identify specific structural changes, no doubt, reflects the speed with which death has occurred, and sudden death after trauma may be a consequence of massive neurochemical or autonomic dysfunction in the absence of identifiable structural change. When death is virtually instantaneous the mechanism remains uncertain. In cases of subarachnoid haemorrhage, it is likely that the sudden enveloping of the brain stem by blood from a ruptured saccular aneurysm induces an autonomic discharge, causing dysrhythmia or cardiac arrest, severe ischaemia of the brain stem by the induction of intense vasospasm, or a rapid rise in intracranial pressure and a pronounced reduction in the cerebral perfusion pressure. In those patients who have large bleeds in the immediate vicinity of the ventricular system, particularly within the posterior fossa, there may also be an element of acute obstructive hydrocephalus.

In a high proportion of the cases there are flame shaped subendocardial haemorrhages along the outflow tract of the left ventricle. Such lesions may occur in association with cardiac dysrhythmias and may be the proximate cause of death. These various abnormalities have been ascribed to autonomic discharge via the lower cranial nerves or to high concentrations of systemic adrenaline/noradrenaline as part of the "stress response".⁸³⁻⁸⁵

Raised intracranial pressure

The most common mechanism of death is raised intracranial pressure as a result of an intracranial expanding (space occupying) lesion, as in intracerebral, extradural, and subdural haematoma, tumour, or abscess. If the haemorrhage is massive, there is a rapid rise in intracranial pressure, the cerebral circulation ceases, and death may ensue. Under these circumstances, the conventional features of shift, distortion, internal herniation, and secondary haemorrhage in the brain stem may either be incompletely formed or absent.

When the rise in intracranial pressure is less rapid, then there is a lateral shift of the midline structures and the appearance of internal herniae. A supracallosal hernia occurs when the ipsilateral cingulate gyrus herniates under the free edge of the falx. The pericallosal arteries may be selectively compromised; however, patients dying within one hour rarely show infarction in the territories of the pericallosal arteries. A small wedge of pressure necrosis may occur in the cortex of the cingulate gyrus where it is in contact with the falx.

A tentorial hernia occurs when there is displacement of the uncus and the medial part of the ipsilateral parahippocampal gyrus through the tentorial opening. The medial part of the temporal lobe pushes towards the midline and over the free edge of the tentorium. The midbrain is narrowed in its transverse axis. The aqueduct is compressed and the contralateral cerebral peduncle is pushed against the opposite free edge of the tentorium (Kernohan notch). The third cranial nerve becomes angled over the artery and there may be haemorrhage into it. As the hernia enlarges it produces a groove on the upper surface of the adjacent cerebellar hemisphere. As with the supracallosal hernia, a wedge of pressure necrosis often accompanied by haemorrhage may occur along the line of the groove in the parahippocampal gyrus. If it is not haemorrhagic the wedge of pressure necrosis may only be identifiable microscopically.⁸⁶ Haemorrhage and infarction occur mainly adjacent to the midline in the tegmentum of the midbrain and in the tegmental and basal parts of the rostral pons.⁸⁷ However, such secondary damage may be absent in cases of sudden death. A tonsillar hernia—downward displacement of the cerebellum through the foramen magnum—is more severe when it is the result of an infratentorial lesion rather than a supratentorial expanding lesion.

When there is a severe tonsillar hernia, the posterior inferior cerebellar arteries may be so compressed that infarction occurs in the inferior part of one or both cerebellar hemispheres. Herniation can only be said to be present if there is impaction of the tonsils in the foramen magnum producing a depression on the ventral surface of the medulla, where it has been compressed against the foramen magnum, or if there is necrosis of the tips of the tonsils.

A common association with an infratentorial expanding lesion is the increase in the size of the third and lateral ventricles—hydrocephalus (see below).

Acute obstructive hydrocephalus

In obstructive hydrocephalus it is the site of the lesion, rather than its nature, that is of importance. If there is a small lesion in a crucial site adjacent to a ventricular foramen—for example, the aqueduct in the midbrain—then it is of much greater importance than a large expanding lesion in a frontal or occipital lobe. However, the abnormality need not be adjacent to the ventricular system because any process, such as meningitis or subarachnoid haemorrhage, which results in obliteration of the subarachnoid space (particularly at the level of the tentorial opening) will obstruct the free flow of cerebrospinal fluid. It follows that hydrocephalus will develop rapidly from any lesion in the posterior fossa.

In essence, the ventricular system proximal to the obstruction enlarges. If there is obstruction of an interventricular foramen one lateral ventricle enlarges; if it is in the third ventricle or the aqueduct both lateral ventricles enlarge; if it is at the exit foramina of the fourth ventricle the entire ventricular system enlarges; if the obstruction is in the subarachnoid space at the level of the tentorium again the entire ventricular system enlarges, on this occasion the hydrocephalus is communicating in type.

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