

metabolism of chloramphenicol is impaired in neonates and therefore significantly lower doses are required to prevent toxicity.¹⁴ Drug toxicity is not restricted to the fetus and the newborn infant; sodium valproate hepatotoxicity is thought to be related to enhanced omega oxidation.¹⁵ This pathway is enhanced by polypharmacy and certain metabolic diseases, it also appears to be enhanced in children younger than 3 years. These examples illustrate the importance of increasing our knowledge of drug metabolism in children to minimise toxicity while ensuring efficacy.

Initiatives

Medicines for adults are evaluated to ensure that they meet acceptable standards of safety, quality, and efficacy, whereas in children they are often not evaluated. This unsatisfactory situation resulted in the setting up of a joint working party between the (then) British Paediatric Association and the Association of the British Pharmaceutical Industry, and the publication of a joint report on the licensing of medicines for children in May 1996.¹⁶ At the same time there was discussion in the Europe Community regarding the guidance on clinical investigation of medicinal products in children. After consultation involving health professionals throughout the European Community a new guidance has been issued (March 1997), which came into force in September 1997.¹⁷ The new guidance is a major step forward because of its emphasis on the need for product testing in children. It divides medicinal products into four categories with the following recommendations:

- (1) Diseases affecting children exclusively—trials of medicinal products in children may start before any adult human exposure
- (2) Diseases that mainly affect children, are of particular gravity in children, or have a different natural history in children—clinical trials in children are needed at an early stage in clinical development following demonstration of safety and reasonable (phase I and II) evidence of efficacy in adults
- (3) Diseases occurring in adults and children for which there is currently no treatment—as point 2
- (4) Diseases occurring in adults and children for which treatment exists—clinical trials in children should usually follow completion of adult phase III trials.

This is a sensible approach that should encourage the pharmaceutical industry to concentrate on clinical trials for conditions in children where there is either no or inadequate treatment at present.

Response

The new guidance also encourages pharmaceutical companies to carry out trials in children where the product is likely to be used in children. In the past there was no pres-

sure on the pharmaceutical company to carry out trials in children. The recent report by the House of Commons health committee on the specific health needs of children and young people confirmed that the present system was unacceptable.⁶ The Royal College of Paediatrics and Child Health through its medicines committee has shown that it is keen to cooperate with both the pharmaceutical industry and the regulatory authorities. The Medicines Control Agency in the UK has played a leading role in the development of the new guidance for Europe. We hope that pharmaceutical companies respond to the challenge of ensuring that medicines used in children are evaluated scientifically.

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Epidemiology of head injury

Head injury is recognised as a major public health problem that is a frequent cause of death and disability in young people and makes considerable demands on health services. Epidemiological data are required to initiate appropriate preventive measures and to plan necessary services. However, reliable statistics are difficult to extract from routinely collected data.

International statistics for accidental deaths and road accident deaths do not identify head injuries, but they do

indicate differences in accident rates between countries and over time. For example, road traffic accident (RTA) deaths are more than twice as frequent in France, Australia, and the USA as in the UK or the Netherlands, but in developed countries they are steadily decreasing each year.¹ In developing countries accident rates are increasing as traffic increases, and they greatly exceed those of developed countries. Asked about the main health hazard of the next decade a Chinese professor of public health

replied “the motorcycle”. Head injuries account for one quarter to one third of all accidental deaths, and for two thirds of trauma deaths in hospital. They are also the main cause of lifelong disability after trauma.

While the codes of the International Classification of Diseases do allow some estimates of the frequency of head injuries from routine statistics on deaths and hospital discharges, the 10 codes that cover head injury are variably applied; moreover, multiple injuries and transfers after first admission make estimates inaccurate. Injury severity scores used for trauma in general have been shown to be very inaccurate when applied to head injuries. Although people who present to hospital but are not admitted are a major part of the head injury problem for hospitals, no routine statistics are published for accident and emergency departments. Data published from clinical series are mostly from neurosurgeons whose selection criteria for transfer vary widely and whose population base can seldom be defined, making these data of limited use for epidemiology.

The best sources are therefore research surveys, of which there have been several from different countries in the past 10–20 years.¹ The problem with these surveys is the variation in the definition of head injury and its severity. Most definitions of head injury depend on evidence of a blow to the head, and exclude facial injuries and foreign bodies in the nose and ears. Scalp, skull, and brain can be injured independently of each other, so that only a proportion of patients with head injuries have initial brain injury. About half of all attenders at accident and emergency departments have a scalp laceration and 15% have some evidence of brain damage, but only 2% a skull fracture.² One prominent US epidemiologist suggested that only patients with brain damage should be counted as head injuries—that is, those with some impairment of consciousness either before reaching hospital or on arrival.³ But that overlooks the fact that patients with mild injuries without obvious brain damage make a considerable impact on the health care system, both as attenders at accident and emergency departments who are sent home and as admissions. The concern is that a small minority of patients with these mild injuries have serious complications: intracranial haematoma, brain swelling, intracranial infection or epilepsy. They are also important in exploring patterns of causation as the basis for prevention strategies, because most mild injuries might have been more severe with only slightly different circumstances. As for defining severity, most countries use the Glasgow coma scale⁴: the score can range from 3 to 15 and a convention has emerged that patients with a coma score of 8 or less are classed as severe and those with a score of 13 or more as mild, the others being classed as moderate. Paediatric coma scales have been developed for assessing younger children.⁵

The only systematic data on attenders to accident and emergency departments are from surveys carried out across Scotland in 1974 and 1985, and in one district general hospital in Glasgow in 1984.² These provide a dataset of 12 000 attenders, which indicates that about 10% of all new attenders at accident and emergency departments present with head injuries. Studies have also been done of all admissions and of neurosurgical unit transfers throughout Scotland.⁶ Head injury deaths can be difficult to ascertain from hospital surveys because about half of them occur at the scene and because many fatalities have multiple injuries.⁷

Another source of confusion is the definition of a child. In all our studies we have used under 15 years, but others use under 16 years and some children's hospitals accept only patients of 12 or under. Some studies in other countries classify by decades and record all those under 20 as children. In regard to cause and injury type, complications,

Table 1 Percentage of patients younger than 15 years in different head injury series in Scotland

Accident and emergency department attenders	40–50%
Admissions	31%
Neurosurgical unit transfers	25%
Deaths in neurosurgical unit	20%
Operated intracranial haematoma	11%

Based on data from Brookes *et al.*²

Table 2 Percentage of people with head injuries presenting to accident and emergency departments with brain damage (Scotland 1985)

	Children (n = 2118)	Adults (n = 3124)
All	7%	23%
Falls	6%	26%
Road traffic accidents	27%	32%

Based on data from Brookes *et al.*²

and mortality, 15–20 year olds are much more like young adults than children.

The proportion of children in each of the different categories of head injuries varies greatly,² from nearly half of attenders to 20% of deaths (table 1). About half of accident and emergency child attenders are younger than 10 years, but only a fifth of the severely injured and a third of fatalities are patients younger than 5. Male patients make up more than 70% of attenders over the age of 5 but only 60% of the younger children are male.

There are 4011 attenders, 400 admissions, and 5.3 deaths per 100 000 children per year.¹ Age specific rates for deaths and admissions from head injury in the UK across all ages show the peak incidence in the 15–30 age range, but for attenders at accident and emergency departments, this peak is younger than 10 years.¹ Although the case fatality rate for admitted children is only 0.7%, a fifth of the rate for all ages, the large number of admissions together with the number of deaths before admission means that head injury is an important cause of death in childhood. According to Sharples *et al.*,⁵ head injury is the most common cause of death between 1 and 15 years, accounting for 15% of all deaths, and for 25% of deaths in the 5–15 years age group.

Neuropathologists in Glasgow have compared detailed necropsy findings in 87 children aged 2–15 years with those for 360 adults.⁸ The frequency of contusions, diffuse axonal injury, ischaemic brain damage, and intracranial haematoma was similar in adults and children. However, bilateral cerebral swelling was three to four times more common in children. In 40% of those the swelling was not accompanied by contusions, ischaemic brain damage or intracranial haematoma—one or more of which are usual in adults with brain swelling.

The vast majority of patients with head injuries coming to accident and emergency departments, and of those admitted, have mild injuries. In the Scottish studies, 80% of admissions of all ages were for mild injuries, two thirds having neither a skull fracture nor evidence of brain damage, nor an extracranial injury requiring admission in its own right, and two thirds were discharged in less than 48 hours. These admissions reflect extreme caution before guidelines based on statistically calculated risk factors were published (see later).

Of accident and emergency attenders in Scotland, only 1% of children had impaired consciousness on arrival at hospital, while 6% had recovered from brief impairment of consciousness. The incidence of brain damage in adults was more than three times that for children, with 5% impaired on arrival and 18% recovered from impaired consciousness. In children brain damage was much more common after an RTA than a fall, but no such difference was found in adults (table 2).

Table 3 Causes of head injury in children in Scotland

	RTA	Fall	Assault
A & E attenders	9%	57%	6%
A & E attenders with brain damage	34%	45%	2%
Admissions	23%	55%	5%
Neurosurgical unit transfer	43%	28%	4%
Severe injuries	75%	12%	3%
Deaths in neurosurgical unit	71%	22%	2%

Data from Brookes *et al*³ and Jennett *et al*.⁹

A & E, accident and emergency department; RTA, road traffic accidents.

Table 4 Causes for accident and emergency department attenders in Scotland

	Children	Adults
Falls	57%	33%
RTA	9%	16%
Assaults	6%	29%
Type of RTA		
Pedestrian	42%	23%
Bicycle	32%	9%
Passenger	20%	58%

Based on data from Brookes *et al*.²

RTA, road traffic accidents.

The distribution of causes of head injury in children varies greatly according to severity, with falls predominant for accident and emergency attenders and admissions, and RTA the major cause only for neurosurgical unit transfers, severe injuries, and deaths (table 3).³⁻⁹ For those attending accident and emergency departments, assaults and RTA are more common in adults than in children (table 4). Moreover the distribution of victims of RTA with head injuries are different for children, with fewer car occupants and more pedestrians and cyclists. Among fatal RTAs concerning children, pedestrians are even more common, 69% in the Newcastle series.¹⁰ Most bicycle injuries in children are sustained during play off the road and do not involve collision with another vehicle. In some reports these are classified as recreational rather than road accidents. However, most serious injuries are from the minority of bicycle accidents that do involve collisions with other vehicles.

The high incidence of unsafe behaviour by children as a cause of both pedestrian injuries and those caused by bicycle collisions was noted by the Newcastle team.¹⁰ In that study most child occupants in cars who were fatally injured were not wearing seat belts, and few bicycle fatalities had been wearing helmets. The value of bicycle helmets for children has been studied in Australia¹¹ where use is now mandatory in several states. It has been suggested that built-in safety features for restraints in cars should become the rule.¹² However, most of the recent reduction in child death rates from road accidents in England and Wales appears to be because there are fewer child pedestrians and cyclists as more children travel by car.¹³

Assaults form a small minority of childhood injuries in the UK and are often sustained in play. In the United States, firearms are a frequent cause of injury, mostly the result of children playing with their parents' guns. Even the Newcastle series had four fatal shotgun injuries, all from accidents while playing with parents' guns.¹⁰ In that study fewer than 5% of fatal injuries were non-accidental.

A matter of some concern and controversy is the need to admit children with mild injuries to hospital for observation. If unnecessary, this adds unjustifiable stress to the injured child. The main reason for keeping patients under observation is the fear of complications, particularly acute intracranial haematoma. The Newcastle study found one third of avoidable deaths after head injury were because of missed or late diagnosis of this complication.⁵ In 1984 guidelines for the admission of adults with head injuries emphasised the importance of skull fracture and impaired

consciousness as risk factors for intracranial haematoma,¹⁴ and suggested that these criteria should reduce the number of mildly injured patients unnecessarily admitted. More recently, additional data have been published, including those for children, based on the epidemiological studies in Scotland.¹⁵ These showed that the risk of intracranial haematoma in children is about one sixth of that in adults. However, the risk factors are exactly the same in children, skull fracture being a more potent factor than impaired consciousness. These data indicate the low risk of haematoma in children without skull fracture, only 1 in 500 develop a haematoma even if there is impaired consciousness. Yet in a series of 900 patients in Glasgow operated because of intracranial haematomas there were more children than adults who had been fully conscious, some of them without a skull fracture. Others have questioned the value of skull x ray in assessing head injuries in children.¹⁶

In Scotland between 1974 and 1985 the admission rate for patients with head injuries for all ages fell from 23% to 15%, mostly because fewer children were admitted—10% compared with 20% of adults in 1985.² Of those with impaired consciousness on arrival at the accident and emergency department, 25% of children and 16% of adults were sent home—most often because no skull fracture was found. A skull x ray was done in 58% of all children, but in 88% of those with brain damage. Reduction in unnecessary admissions, particularly of children for whom this can add psychological trauma, is to be welcomed. The decision to send a child home will depend on full consciousness having been regained and there being no reason to suspect a skull fracture, but may also be influenced by home circumstances. Moreover, it needs to be associated with adequate counselling of parents about the need for rapid return to hospital in the event of new symptoms, supported by a card listing warning symptoms and giving the telephone numbers for contacting the hospital.

Conclusions

Head injuries are less common in the UK than in many other countries, but they are still a major problem for health services. Children account for half of attenders at accident and emergency departments after head injury, a third of admissions, a quarter of severe injuries, and a fifth of deaths. Head injuries account for 15% of deaths of children aged 1–15 years, but the rate is falling because of fewer road accident deaths. Fewer than 10% of attenders have any evidence of brain damage, and most admissions are patients with mild injuries. Causes vary according to severity, road accidents accounting for fewer than 10% of attenders but for more than 70% of severe and fatal injuries. Many injuries on the road are to pedestrians. Fewer children need to be admitted if risk factors for complications in mild injuries are carefully assessed.

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Evidence-based dilemmas in pre-school vision screening

What should policy makers do with systematic reviews that fail to find evidence of effectiveness for interventions currently provided in the NHS? Is no evidence of effectiveness sufficient evidence of no effectiveness? The systematic review process has made great progress in minimising the influence of personal bias in the selection and critical appraisal of evidence. By bringing together in one place and critically appraising all the relevant studies, these reviews can show the fragility of the evidence on which some current practice is based.

Policy makers in the NHS take the results of these reviews seriously and expect to be able to act on their findings. But clinicians argue that it is wrong to close down a service, which might be doing good, just because the research evidence of effectiveness is poor. The review of pre-school vision screening commissioned by the NHS Health Technology Assessment Programme¹ raises this dilemma and presents policy makers with a difficult decision. This report's most startling finding was that the reviewers could not identify any robust studies showing that amblyopia (the main target condition of pre-school vision screening programmes²) causes any problems to children or adults. One researcher who tried to find performance differences between amblyopic students (as opposed to people blinded in one eye in adulthood or blindfolded in one eye for the purpose of an experiment) and students with monocular refractive errors was not able to document disabilities that he considered likely to affect everyday life.³ Health professionals have always assumed that reduced vision in one eye must cause problems, and in occupational health services health professionals have been responsible for the development of policies that exclude people with amblyopia from certain occupations on these grounds. The best documented consequence of amblyopia, however, appears to be that blindness may ensue if the good eye becomes damaged or diseased in later life. The incidence of this problem has been reported in a single study from Finland,⁴ which was not methodologically robust. The problem is certainly rare compared with childhood amblyopia, which has a prevalence of 1–2% and is unlikely to be sufficiently common to justify treating all childhood amblyopes. Surprised by these findings, the authors of the review went on to undertake a qualitative study that suggested that people who have suffered from amblyopia since childhood have difficulty in specifying any way this has affected them. It may, however, be difficult for people to perceive that they cannot perceive something of which they have no experience.

The second finding of the review was that it was not possible to identify trials of treatment for amblyopia that included a “no treatment” control group. The natural history of amblyopia has only been studied in an indirect way and for short periods, and the studies that have been done suggest that amblyopia may sometimes regress spontaneously. Given the lack of studies on the natural history of the

condition, the results of observational studies of treatment impact (which show an average improvement of around two lines on a Snellen chart) and studies comparing one treatment regimen with another, cannot be interpreted with any confidence. The evidence for clinicians' belief in the efficacy of amblyopia treatment therefore comes largely from animal studies in which amblyopia has been artificially created in kittens and monkeys. The pharmaceutical industry would never be allowed to market a drug that had not been thoroughly tested in humans. It seems unlikely that the public would, if they knew, approve of other types of interventions being done on their children on the basis of animal studies alone.

An incidental finding of the qualitative study was that many adults and children were clear that the treatment (wearing glasses and intermittent patching of the good eye) had had an important and negative impact on their quality of life as children and on the lives of their families.⁵ The children did not like wearing glasses or patches, and some parents had felt distressed at enforcing these on their children. They persisted for two reasons, however. Firstly, because they were concerned that if they did not their children's sight might cause problems in later life and secondly, because they felt that good parents should do for their children what was prescribed by health professionals.

The review found one prospective controlled study and a small number of retrospective observational studies that confirmed beliefs that primary orthoptic screening is an efficient way of identifying children with this condition. In the face of the evidence that the condition may not be disabling, that there are no robust studies of treatment impact, and that the psychological and practical consequences of treatment could be a problem for families, this evidence may be redundant. This review set out to investigate the efficacy of screening and therefore concluded that screening is not effective, not because the screening programme cannot identify children efficiently, but because there is no evidence that treatment is either effective or necessary. It has therefore called into question the provision of orthoptic services as well as screening services and has presented policy makers with an added dilemma.

Although amblyopia is regarded as the main target condition for this programme, pre-school vision screening also identifies other conditions that are sufficiently common to warrant screening, for example, non-cosmetically obvious squints (phorias and microsquints) and refractive errors. Cosmetically disturbing squints are by definition obvious to the casual observer and therefore do not need to be screened for. Spectacle correction is effective in correcting refractive errors. There is, however, no clear evidence that pre-school children benefit from correction of the minor refractive errors that are common in childhood, and there is good evidence that children with these defects, who are old enough to make choices for themselves, often choose not to wear glasses.⁶ Glasses are sometimes prescribed to