

brought before parliament in early 1986. The next and obvious stage is to extend the requirement to rear seat occupants. Britain is one of the last of the motorised nations which does not yet require fitting rear seat belts. In depth studies of crashes have shown that one of the limitations to the protection of front seat occupants occurs in frontal collisions when correctly belted front occupants are injured by unrestrained rear seat passengers. If rear seat occupants used seat belts as frequently as front seat occupants do now there would be two benefits: rear seat occupant deaths and injuries would be reduced by some 70%, and there would be a further reduction of some 6% in front seat casualties.<sup>10</sup>

Beyond this obvious measure many technical improvements to restraint systems and car interiors can and should be made. By design, drivers wearing restraints suffer face contacts with the steering wheel in most cars in a crash of more than some 25 mph. The answer lies in better padding or supplementary airbags in the steering wheel together with preloading of seat belts. Anchorage points mounted on the seat improve the lap belt geometry and diminish abdominal injuries due to submarining, which occurs when the pelvis rotates out from under the lap belt section in a frontal collision. But what about the obese, the aged, the pregnant woman, and the child? Have we really provided adequate protection for all those who actually use cars? What about a truly "friendly" interior, in which rational crash protective design has been applied effectively?

In each case the introduction of such protective measures as seat belts, laminated windscreens, head restraints, anti-burst door latches, and airbags represents a potential advance comparable with the introduction of a new drug. In epidemiological terms the benefits and side effects of such measures when used by the population at risk can be profound and often unexpected. And yet these measures do not receive the attention and evaluation from the medical community which they deserve. Perhaps the Rutherford study on the effectiveness of seat belts will generate some new interest in traffic injury research and its prevention. Road accidents cost Britain about £2.5 billion annually. Research into traffic injury reduction has an annual budget of less than one tenth of 1% of that figure. Most other industrialised countries devote far greater resources to the problem. Cannot the success of the seat belt legislation be used as a spur to more effort in tackling the general problems of trauma in our motorised society?

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- 1 Mackay GM. Two years' experience with the seat belt law in Britain. *Proceedings of annual conference of Society of Automotive Engineers Inc.* Warrendale, Pa: Society of Automotive Engineers Inc, 1985. (Paper No 851234.)
- 2 Rumar K, Berggrund U, Jernberg O, Ytterborn U. Driver reaction to a technical safety measure. *Hum Factors* 1978;18:443-54.
- 3 Peltzman S. Effects of automobile regulation. *Journal of Political Economy* 1979;83:677-723.
- 4 Wilde GJS. The theory of risk homeostasis, implications for safety and health. *Risk Analysis* 1982;2:209-55.
- 5 Adams J. The efficiency of seat belt legislation. London: University College, 1981. (*Occasional Paper*.)
- 6 Evans L, Wasielewski P, vonBuseck CR. Compulsory seat belt use and driver risk-taking behavior. *Hum Factors* 1982;24:41-8.
- 7 Ashton SJ, Mackay GM, Camm S. Seat belt use under voluntary and mandatory conditions. *Proceedings of the American Association for Automotive Medicine.* Arlington Heights, Ill: American Association for Automotive Medicine, 1983:65-77.
- 8 Ashton SJ, Thomas PD, Harms P, Mackay GM, Galer MD. Effects of mandatory seat belt use in Great Britain. *Proceedings of Conference on Experimental Safety Vehicles, July, 1985.* Washington, DC: National Highway and Traffic Safety Administration (in press).
- 9 Rutherford WH, Greenfield AA, Hayes HRM, Nelson JK. *The medical effects of seat belt legislation.* London: HMSO, 1985.
- 10 House of Commons Transport Committee. *First report on road safety.* London: HMSO, 1985: 103-1-51.

## Prevention and treatment of brain ischaemia

Cerebral ischaemia is a common and frustrating clinical problem, and a recent symposium issue of the *British Journal of Anaesthesia* on the topic should interest clinicians from many disciplines.<sup>1</sup> Despite a wealth of experimental data, only limited, often anecdotal information seems to be available on the efficacy of alternative treatments for patients with brain ischaemia. Consequently clinicians still feel relatively powerless to influence the outcome after ischaemic insults and emphasise the importance of preventive measures; yet episodes of cerebral ischaemia may often neither be predicted nor be prevented. What interventions, then, might ameliorate ischaemic brain damage by modifying events after the insult?

The pathological events which may culminate in ischaemic brain damage include cardiorespiratory arrest, stroke, and severe head injury as well as some operative procedures such as carotid endarterectomy, cardiopulmonary bypass, and induced hypotension. The ensuing lesion may be focal or global and may be exacerbated by complicating factors such as pre-existing cerebrovascular disease or hypertension, impaired autoregulation, hypoxaemia, or seizures. Thus, in contrast with many of the techniques used in studies on animals, accidental ischaemic insults are often complex. Moreover, the results of animal studies are influenced by both the nature of the ischaemia (global or focal, complete or incomplete, permanent or transient) and the timing of treatment in relation to the insult (before, immediately after, or delayed). Hence we need to be careful in extrapolating the results of laboratory investigations to clinical practice.

The rapid depletion of cellular energy stores after sudden, complete ischaemia<sup>2</sup> leads to failure of the ionic pump, membrane depolarisation,<sup>3</sup> and cellular swelling.<sup>4</sup> There is also a dramatic increase in calcium ions in the cytosol,<sup>3,5</sup> which may be associated with "burst firing" in selectively vulnerable neurones induced by excitatory amino acid neurotransmitters.<sup>6</sup> This intracellular accumulation of calcium may initiate several harmful reactions (including the release of free fatty acids, particularly arachidonic acid, and the production of free radicals of oxygen<sup>5</sup>) and may be the "final common pathway" leading to cell death.

When ischaemia is incomplete these events are modified by the residual flow, which increases the formation of oedema and also provides glucose for anaerobic glycolysis, thereby enhancing lactic acidosis and exacerbating neuronal damage. Similarly, hyperglycaemia, either preceding complete ischaemia or during an episode of incomplete ischaemia, increases the severity of the acidosis and further augments brain damage.<sup>7</sup>

If the decrease in cerebral blood flow is progressive threshold values can be defined for alterations in cerebral electrical activity, electrical silence,<sup>8,9</sup> and membrane failure.<sup>8</sup> Possibly alterations in calcium ion homeostasis may have the lowest threshold of all.<sup>10</sup> Furthermore, in experimental focal ischaemia infarction is ultimately confined to those areas in which flow is reduced below the threshold for membrane failure, even though in the acute stage neuronal function may be disturbed over a larger region—the "ischaemic penumbra."<sup>11</sup>

It is the identification of these thresholds—together with the observation that events occurring during recirculation may initiate or exacerbate cell damage<sup>2</sup>—that suggests that

non-functioning but viable neurones may possibly be "rescued" by prompt intervention. In clinical settings where the risks are known to be high electrophysiological monitoring may be used to detect abnormalities of cerebral electrical activity indicative of ischaemia before neuronal loss is irreversible. The rapid restoration and maintenance of cerebral perfusion and arterial oxygenation, possibly combined with the drug treatment described below, may then prevent or ameliorate brain damage.<sup>12</sup> In clinical practice simple electroencephalographic monitoring—for example, with the cerebral function monitor<sup>13</sup>—is often used to detect ischaemia and may be valuable during induced hypotension,<sup>14</sup> cardiopulmonary bypass, neurosurgery, carotid artery surgery, and in patients with severe head injury.<sup>15,16</sup>

The ultimate outcome after an episode of cerebral ischaemia is undoubtedly influenced by the quality of subsequent supportive care. To restore the cerebral blood flow the systemic blood pressure must be maintained within—or slightly above—the normal range, but extreme hypertension, which might exacerbate the formation of oedema and intracranial hypertension, should probably be avoided. Hypoxaemia and hypercapnia must be prevented at all costs, making artificial ventilation necessary when respiratory function is inadequate; but the place of deliberate hyperventilation (and of prolonged elective ventilation in the absence of respiratory failure) is less clear.<sup>17,18</sup> Seizures increase metabolic demands and may precipitate ischaemic damage in marginally perfused areas of the brain, so anticonvulsants should be given prophylactically and any seizures that do occur treated aggressively. Hyperglycaemia should probably be avoided, both after an ischaemic insult and in high risk settings such as induced hypotension.

The many other therapeutic interventions investigated as adjuncts to supportive care are of uncertain value. These include promotion of reperfusion with heparin, streptokinase, dextran, or oxygen carrying blood substitutes; the administration of prostacyclin; and manipulation of the arachidonic acid cascade. Possibly endogenous opioid peptides may be important in the pathogenesis of ischaemic brain damage since both naloxone<sup>19</sup> and dynorphin<sup>20</sup> may improve the outcome after experimental focal ischaemia, but a recent clinical study of naloxone in acute stroke was not encouraging.<sup>21</sup>

After a focal ischaemic insult oedema is said to cause local rises in tissue pressure, thereby further compromising blood flow,<sup>22</sup> and generalised intracranial hypertension has been described after incomplete global ischaemia.<sup>23</sup> Nevertheless, the value of diuretics and steroids in the management of non-traumatic ischaemic insults is still not clear. In traumatic coma, on the other hand, osmotic diuretics are known to help control intracranial hypertension, but recent evidence has shown that steroids neither reduce intracranial pressure nor improve outcome.<sup>24</sup>

At one time barbiturates were thought to be valuable in brain ischaemia, but a recent study<sup>25</sup> has failed to substantiate earlier claims<sup>26</sup> that thiopentone could ameliorate brain damage when given shortly after experimental global ischaemia. Moreover, a prospective, randomised clinical trial of thiopentone loading after cardiorespiratory arrest found no benefit from such treatment.<sup>27</sup> Furthermore, although it has been repeatedly shown that barbiturates are protective in experimental focal ischaemia (provided reperfusion occurs<sup>28</sup>), clinicians are generally reluctant to expose such patients, who are often conscious, to the hazards of barbiturate coma.<sup>29</sup> In traumatic coma the administration of barbiturates can undoubtedly control intracranial hyper-

tension, and may improve blood flow to ischaemic regions, but such treatment may precipitate hypotension, and the effects on functional outcome are not clear.<sup>29</sup> Etomidate and alphaxalone-alphadolone (Althesin) produce less cardiovascular depression and have been used to control intracranial pressure, but even they may reduce cerebral perfusion pressure,<sup>15,16</sup> and unfortunately neither is now available for clinical use.

Whereas the barbiturates appear to suppress only those aspects of neuronal metabolism related to electrical activity, hypothermia produces generalised cerebral metabolic depression and may, therefore, offer better protection during periods of ischaemia.<sup>30</sup> Practical considerations have inhibited the widespread use of hypothermia, however, although patients with fever are recognised to need active cooling.

The possibility that calcium entry blocking agents might ameliorate ischaemic brain damage is being extensively investigated,<sup>5</sup> and experimental evidence suggests that some,<sup>31</sup> but not all,<sup>32</sup> of these agents may improve neurological outcome after global ischaemia. Calcium blockers may also increase residual flow in focal ischaemia<sup>33</sup> and may be particularly useful for preventing vasospasm—for example, after subarachnoid haemorrhage.<sup>34</sup> They may also impair autoregulation, however, and may increase tissue susceptibility to ischaemic damage.<sup>35</sup> They might act by preventing or reversing the adverse effects of intracellular accumulation of calcium ions as well as by increasing cerebral blood flow.<sup>5</sup>

The efficacy of both cerebral metabolic depressants and calcium entry blockers may be limited by cardiovascular depression. This has encouraged interest in the more specific effects of excitatory amino acid antagonists, which protect against the damage induced by forebrain ischaemia in the rat.<sup>6</sup> Available agents do not cross the blood-brain barrier, however, and focal injection is therefore required.<sup>6</sup>

At present, then, specific treatments for brain ischaemia have proved disappointing, and clinicians are likely to remain sceptical of the relevance of most laboratory studies to clinical practice. It is perhaps unrealistic to expect administration of any single agent significantly to influence outcome after a severe ischaemic insult. Almost certainly multiple therapeutic interventions will be required, including careful supportive care, and these are most likely to be beneficial when started early or when used prophylactically. The only undisputed therapeutic principles in the management of brain ischaemia are to restore systemic blood pressure, ensure adequate oxygenation, avoid hypercapnia, and abolish seizures.

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- Smith G, McDowall DG, eds. A symposium on brain ischaemia. Postgraduate educational issue. *Br J Anaesth* 1985;57:1-130.
- Siesjö BK, Wieloch T. Cerebral metabolism in ischaemia: neurochemical basis for therapy. *Br J Anaesth* 1985;57:47-62.
- Heuser D, Guggenberger H. Ionic changes in brain ischaemia and alterations produced by drugs. *Br J Anaesth* 1985;57:23-33.
- Klatzo I. Brain oedema following brain ischaemia and the influence of therapy. *Br J Anaesth* 1985;57:18-22.
- White BC, Winegar CD, Wilson RF, Hoehner PJ, Trombley JH. Possible role of calcium blockers in cerebral resuscitation: a review of the literature and synthesis for future studies. *Crit Care Med* 1983;11:202-7.
- Meldrum B. Possible therapeutic applications of antagonists of excitatory amino acid neurotransmitters. *Clin Sci* 1985;68:113-22.
- Pulsinelli WA, Waldman S, Rawlinson D, Plum F. Moderate hyperglycemia augments ischemic brain damage: a neuropathologic study in the rat. *Neurology* 1982;32:1239-46.
- Astrup J, Symon L, Branston NM, Lassen NA. Cortical evoked potential and extracellular K<sup>+</sup> and H<sup>+</sup> at critical levels of brain ischemia. *Stroke* 1977;8:51-7.
- Morawetz RB, Crowell RH, deGirolami U, Marcoux FW, Jones TH, Halsey JH. Regional cerebral blood flow thresholds during cerebral ischemia. *Fed Proc* 1979;38:2493-4.

- 10 Harris RJ, Symon L, Branston NM, Bayhan M. Changes in extracellular calcium activity in cerebral ischemia. *J Cereb Blood Flow Metab* 1981;1:203-9.
- 11 Brierley JB, Symon L. The extent of infarcts in baboon brains three years after division of the middle cerebral artery. *Journal of Neuropathology and Applied Neurobiology* 1977;3:217-8.
- 12 Prior PF. EEG monitoring and evoked potentials in brain ischaemia. *Br J Anaesth* 1985;57:63-81.
- 13 Maynard D, Prior PF, Scott DF. Device for continuous monitoring of cerebral activity in resuscitated patients. *Br Med J* 1969;iv:545-6.
- 14 Thomas WF, Cole PV, Etherington NJ, Prior PF, Stefansson SB. Electrical activity of the cerebral cortex during induced hypotension in man: a comparison of sodium nitroprusside and trimetaphan. *Br J Anaesth* 1985;57:134-41.
- 15 Prior JLG, Hinds CJ, Williams J, Prior PF. The use of etomidate in the management of severe head injury. *Intensive Care Med* 1983;9:313-20.
- 16 Bingham RM, Procaccio F, Hinds CJ, Prior PF. Cerebral electrical activity influences the effects of etomidate on cerebral perfusion pressure in traumatic coma. *Br J Anaesth* (in press).
- 17 Gisvold SE, Safar P, Rao G, Moosy J, Bron K, Alexander H. Prolonged immobilization and controlled ventilation do not improve outcome after global brain ischemia in monkeys. *Crit Care Med* 1984;12:171-9.
- 18 McDowall DG. Management of severe head injury. In: Ledingham IMCA, Hanning CD, eds. *Recent advances in critical care medicine*. Edinburgh: Churchill Livingstone, 1983:129-42.
- 19 Zabramski JM, Spetzler RF, Selman WR, et al. Naloxone therapy during focal cerebral ischemia. Evaluation in a primate model. *Stroke* 1984;15:621-6.
- 20 Baskin DS, Hosobuchi Y, Loh HH, Lee NM. Dynorphin (1-13) improves survival in cats with focal cerebral ischaemia. *Nature* 1984;312:551-2.
- 21 Fallis RJ, Fisher M, Lobo RA. A double blind trial of naloxone in the treatment of acute stroke. *Stroke* 1984;15:627-9.
- 22 Iannotti F, Hoff JT, Schielke GP. Brain tissue pressure in focal cerebral ischemia. *J Neurosurg* 1985;62:83-9.
- 23 Senter HJ, Wolf A, Wagner FC. Intracranial pressure in nontraumatic ischemic and hypoxic cerebral insults. *J Neurosurg* 1981;54:489-93.
- 24 Braakman R, Schouten HJA, Dishoek MB-v, Minderhoud JM. Megadose steroids in severe head injury: results of a prospective double-blind clinical trial. *J Neurosurg* 1983;58:326-30.
- 25 Gisvold SE, Safar P, Hendrickx HHL, Rao G, Moosy J, Alexander H. Thiopental treatment after global brain ischemia in pigtailed monkeys. *Anesthesiology* 1984;60:88-96.
- 26 Bleyvaert AL, Nemoto EM, Safar P, et al. Thiopental amelioration of brain damage after global ischemia in monkeys. *Anesthesiology* 1978;49:390-8.
- 27 Abramson NS, Safar P, Detre K, et al. Results of a randomized clinical trial of brain resuscitation with thiopental. *Anesthesiology* 1983;59:A101.
- 28 Selman WR, Spetzler RF, Roessmann UR, Rosenblatt JJ, Crumrine RC. Barbiturate-induced coma therapy for focal cerebral ischemia: effect after temporary and permanent MCA occlusion. *J Neurosurg* 1981;55:220-6.
- 29 Shapiro HM. Barbiturates in brain ischaemia. *Br J Anaesth* 1985;57:82-95.
- 30 Steen PA, Newberg L, Milde JH, Michenfelder JD. Hypothermia and barbiturates: individual and combined effects on canine cerebral oxygen consumption. *Anesthesiology* 1983;58:527-32.
- 31 Vaagenes P, Cantadore R, Safar P, et al. Amelioration of brain damage by lidoflazine after prolonged ventricular fibrillation cardiac arrest in dogs. *Crit Care Med* 1984;12:846-55.
- 32 Newberg LA, Steen PA, Milde JH, Michenfelder JD. Failure of flunarazine to improve cerebral blood flow or neurologic recovery in a canine model of complete cerebral ischemia. *Stroke* 1984;15:666-71.
- 33 Harris RJ, Branston NM, Symon L, Bayhan M, Watson A. The effects of a calcium antagonist, nimodipine, upon physiological responses of the cerebral vasculature and its possible influence upon focal cerebral ischemia. *Stroke* 1982;13:759-66.
- 34 Allen GS, Ahn HS, Preziosi TJ, et al. Cerebral arterial spasm—a controlled trial of nimodipine in patients with subarachnoid hemorrhage. *N Engl J Med* 1983;308:619-24.

## Medical hazards from dogs

Domestic animals are a source of pleasure to many people and may have a beneficial effect on their physical and mental wellbeing.<sup>1</sup> There are, however, public health problems associated with "man's best friend"—the dog—which have recently been extensively reviewed in *Community Medicine*.<sup>2,4</sup>

The size of the British dog population has increased from 3·8 million in 1960 to 6 million in 1979, and this is probably an underestimate. Information on the number of dogbites is also unreliable as many are not recorded. By using data available for England and Wales Baxter estimated that there were 209 000 dogbites a year (4·2/1000 population).<sup>2</sup> Almost twice as many boys and men were bitten as girls and women, with the highest number aged between 5 and 19 years. Others at risk included postmen and delivery men. Not surprisingly, dogbites were most common between April and September, when people move out of doors. Young male dogs were more likely to bite than bitches. The common reasons for biting were self defence, unintentionally during play, and protecting property: only rarely was biting associated with aggression and savagery. The financial cost of bites was estimated as £33·50 a case for hospital treatment (at 1983 prices)—which for England and Wales meant a total cost of £7m a year.

Road traffic accidents where dogs played a direct or indirect part were more difficult to define, quantify, and cost accurately. To extrapolate from police statistics of dog associated road traffic accidents known to Greater Manchester

Police during 1957-77, dogs appeared to have been associated with 0·77% of all accidents. Baxter estimated that for England and Wales the police knew of about 980 000 non-injury accidents, which included 160 000 (16%) associated with dogs.<sup>2</sup> This is probably a gross underestimate, as English law requires a motorist to notify an accident to the police only if another person, vehicle, farm animal, or dog has been injured or damaged and particulars have not been given by anyone else—for example, the owner of the other vehicle or the dog.

Data about accidents on private property, the number of home accident victims, and the percentage who had had dog associated accidents other than dogbites were estimated by using a representative sample from 20 accident and emergency departments in England and Wales during 1976. This suggested that 4360 dog associated home accident victims required hospital treatment.<sup>5</sup>

From the overall figure of roughly 214 000 dog associated injuries in England and Wales each year requiring hospital treatment, 209 000 (98%) would be dogbites, 4000 (1·9%) home accidents other than bites, and 1000 (0·5%) road traffic accidents. Dog associated accidents causing injury were most common in riders of two wheeled vehicles. Baxter estimated the total cost of these (including morbidity, pain, damaged property, loss of earnings, health service costs, as well as police and legal costs) to be £40m annually (1983 prices), with 85% of this due to damaged property.

Other deleterious effects of dogs on human health are difficult to determine as data are limited. Canine faeces and rectal swabs are not collected routinely, and reporting by veterinary practitioners to bacterial laboratories is variable. Many dogs carry human pathogens: at least half *Pasteurella multocida* (estimated to cause 31 000 episodes of wound sepsis in England and Wales); half enteropathogenic bacteria, mostly *Campylobacter* but also *Salmonella* and *Yersinia* (13 000 enteritis episodes); and 10% *Toxocara canis* (16 000 new toxocara infections a year). Around 9000 episodes of human ringworm attributable to dogs occur each year.

Even without any formal statistical information the extent and amount of dog excreta are obvious to most town dwellers. One estimate for an average day deposit of 6 million dogs was 4½ million litres of urine and 1 million kilograms of faeces, equivalent to the urinary output of 3 million humans and the faecal output of 10 million—pollution on a grand scale.<sup>4</sup>

Some of this could be prevented if all dogs had to be both licensed and vaccinated. At present only about half of dogs are licensed, despite the unrealistic dog licence fee of 37½p (since 1878), which has recently gone down (very slightly) to 37p. Indeed, the Department of the Environment loses money on the licences; the Post Office is paid £3·4m for the cost of them, while the annual revenue is only £0·9m. In 1976 a working party on dogs recommended that the annual licence fee should be increased to £5 (which at today's prices might more reasonably be £10), that the control of stray dogs in Great Britain should be transferred from the police to local authorities, and that local authorities should consider setting up discretionary dog warden services.<sup>6</sup> None of these recommendations was implemented, and governments seem loth to take positive action (despite critical comments by the Committee of Public Accounts in 1982).<sup>7</sup> I believe that certification and evidence of vaccination and deworming should be mandatory when initially licensing a dog. The licence fee should be increased to a realistic level and renewed annually with appropriate fines for failure to comply. It might be desirable to have the dog licence number on the dog collar to simplify dealing with stray dogs.