in divers. *Undersea Biomed Res* 1981; 8 (4): 209-217
2 Morrison JB, Florio JT and Butt WS. Observations after loss of consciousness under water. *Undersea Biomed Res* 1978; 5 (2): 179-187
3 Juhn MS and Tarnopolsky M. Oral creatine supplementation and athletic performance: a critical review. *Clin J Sport Med* 1998; 8 (4): 286-297
4 Juhn MS and Tarnopolsky M. Potential side effects of oral creatine supplementation: a critical review. *Clin J Sport Med* 1998; 8 (4): 298-304

CMDR Robyn Margaret Walker, MB BS, Dip DHM, RAN, is the Officer in Charge, Submarine and Underwater Medicine Unit, HMAS PENGUIN, Middle Head Road, Mosman, New South Wales 2088, Australia. Phone + 61-02-9960-0333. Fax + 61-02-9960-4435. E-mail <Robyn.Walker@defence.gov.au>.

ADJUNCTIVE THERAPY IN DECOMPRESSION ILLNESS: PRESENT AND FUTURE

Richard E Moon

Key Words
Decompression illness, drugs, treatment.

Historical background

When attempting to evaluate the value of adjunctive treatment, it is instructive to examine case descriptions from an era when none were available. In Edward Ellsberg's book, *Men Under the Sea*, is a dramatic description of air recompression therapy of a diver with a severe case of the bends, experienced during the salvage of the submarine *S-51* in 1925.[1]

> [After a 60 minute dive to 132 feet, and two hours of in-water decompression]…the tenders finished undressing the divers, leaving the *Falcon's* fantail a mess of wet lead shoes, lead belts, helmets, hoses, and sodden diving rigs, and the three, still in their underwear, hurried below for supper, already somewhat late.
>
> Five minutes later, seated on a bench before the heavily laden mess table, L'Heureux, still as merry as ever, suddenly collapsed, pitched forward on the table, unconscious!

No need to ask questions in that company. "The bends" and a bad case of it! No one wasted time in futile first aid measures. Hastily his shipmates seized the silent figure of L'Heureux, unceremoniously rushed him up the steep ladder to the deck above…

In through the round steel door of the recompression tank went L'Heureux's inert form, one diver dragging his head, another pushing on his legs. Running from the wardroom came Surgeon Flotte, to dive through the opening almost on L'Heureux's heels. The door clanged shut behind him. On went the compressed air, hissing gently into the chamber as was customary. Hastily Surgeon Flotte felt L'Heureux. No sign of heartbeat. The man was completely out, might die at any moment, might perhaps already be dead from bubbles of air clogging his heart. It was no time for routine measures. At any cost those bubbles must be reduced to a size small enough to pass through the heart valves, to allow circulation to continue. And only high air pressure could compress them enough for that.

Dr. Flotte sprang for the air valve and twisted it wide open (apparently, in those days the insider tender operated the chamber). Immediately the low hiss of the incoming air changed to a loud roar and, under the terrific pressure of the high pressure air banks, air started to pour into that recompression chamber. The needle on the caisson gauge jumped like a race horse getting away from the barrier, continued rapidly round the dial. Twenty pounds, 40, 50. Dr. Flotte's ears began to ring. That was as high in pressure as we had ever gone before on anybody. But no stop now. Sixty pounds. Blood oozed in Flotte's nose and mouth, but still he kept the roaring in full blast. He must get the pressure up on L'Heureux, never mind himself. Seventy pounds, with the valve wide open, the needle still racing up the dial. Eighty pounds, a higher pressure by far than anybody on that diving job had ever before been subjected to, either on the bottom or in the tank, and, worst of all for Flotte, taken in one swift rush!

Eighty pounds (55 m equivalent depth) was enough. Flotte shut off the air. Dizzy from the sudden impact of high pressure, ears ringing excruciatingly, he bent over L'Heureux, tore off his shirt. The diver's chest was covered with purple splotches, the result of the bursting of a myriad small blood vessels from expanding air. But that was a minor result of "the bends." The major question was circulation. Had he got those heart bubbles down before L'Heureux's heart had stopped forever?

Flotte bent over his chest, listened, then smiled wanly. His heroic treatment had succeeded. A faint heartbeat became perceptible, L'Heureux began to breathe again. The bubbles, compressed to one-sixth their previous size by the sudden application of

pressure, were passing out of the heart; blood was beginning to pump through it once more.

Gradually then Flotte began to release the air from the chamber, decompressing L'Heureux by regular stages. But in spite of working over him all night through, in spite of everything that his medical skill could suggest, Flotte was never able to bring L'Heureux back to consciousness. Through the long hours he lay there as the air pressure went down, limp, unconscious, apparently paralyzed in some degree, simply breathing feebly.

At 3 A.M., Dr. Flotte emerged from the recompression chamber, weak and dazed from his own exertions and the shock of high pressure. He sought out Lieutenant Hartley, skipper of the *Falcon*.

"Everything that pressure can do for L'Heureux's been done. Everything that I can do for him here has been done. He's paralyzed and he's nearly gone. If we're going to save L'Heureux's life, we've got to get him to a hospital right away!"…At 7 A.M. in the early dawn, we transferred the still unconscious L'Heureux to the ambulance and sadly headed back to sea...

That was mid-November. When we landed him, L'Heureux had been a man of something over 160 pounds weight. Within a few weeks, partial paralysis, including his kidneys, resulting from "the bends," had wasted him away to a skeleton of 70 pounds, and there for months he hovered precariously between life and death. Not until late the following July, after an eight-month struggle in the hospital, did he finally recover sufficiently to be discharged.

As an example of a severe case of decompression illness, probably with severe hypotension, one can only speculate as to the outcome that might have been achieved if the doctor had the tools available to measure blood pressure and administer intravenous fluids.

In fact, information about adjunctive treatment was recorded many years earlier, both by Alphonse Jaminet, physician responsible for the men constructing the bridge across the Mississippi River at St. Louis, beginning in 1868, and Andrew Smith, Surgeon to the New York Bridge Company during construction of the Brooklyn Bridge, in 1872. For the treatment of bends Jaminet recommended whiskey or beef broth.[2] Smith's recommendations included ergot by mouth or hypodermically, morphine or atropine for pain, friction with or without stimulating linaments, local hot water baths, an alcoholic stimulant, with ginger, for epigastric pain. For paralysis, he recommended cold douches and frictions to the spine, cups or leeches. Venesection was a possible recommendation for coma.[3-5] The efficacy of these treatments remains unreported.

Current treatment

Although it is commonly assumed that decompression illness (DCI) is a disease that is easily treatable, at least in recreational divers, treatment is considerably less than uniformly successful. Statistics from the Divers Alert Network indicate that after completion of a course of hyperbaric oxygen therapy one third of divers have residual symptoms.[6] The challenge is to find ways to improve the prognosis for those divers, especially ones with neurological symptoms who cannot receive immediate recompression with oxygen, who in general respond less well to recompression treatment.

Accepted modern day adjunctive therapy may consist of surface oxygen, fluid resuscitation, management of plasma glucose, corticosteroids, anticoagulants and management of core temperature.

SURFACE OXYGEN

Oxygen delivery kits for divers are widely available. The Divers Alert Network (DAN) sells a number of models of a demand flow apparatus and a rebreather kit. Other rebreathing systems are available in Australia and Switzerland.[7,8] The rationale for administration of oxygen on the surface is that by excluding nitrogen from the inspired gas the tissue blood PN_2, and then tissue PN_2 are reduced and the gradient for diffusion of gas out of the bubble into the blood increased. For patients who are hypoxaemic, due to aspiration or pulmonary barotrauma, correction of the low PO_2 is another benefit.

Evidence that surface oxygen works was provided by Dr Annane and colleagues,[9] who injected air into the carotid arteries of dogs until bubbles could be seen on a CT scan of the brain. They then compared the rate of resolution of cerebral air under two conditions: spontaneous breathing with room air and mechanical ventilation with 100% oxygen. CT scans of the brain were obtained every minute and revealed that bubbles resolved more quickly under the latter condition.

Data from the Divers Alert Network (DAN) also supports the benefit of surface oxygen (see Figures 1 and 2). While present evidence suggests a beneficial effect before recompression, it is not yet confirmed that ultimate outcome is improved.

FLUID RESUSCITATION

Dr Jaminet measured the specific gravity of urine in St Louis Bridge caisson workers. From his observations it can be discerned that workers who had symptoms of DCI had higher urine specific gravity than those who had no symptoms,[2] from which it reasonable to hypothesize that

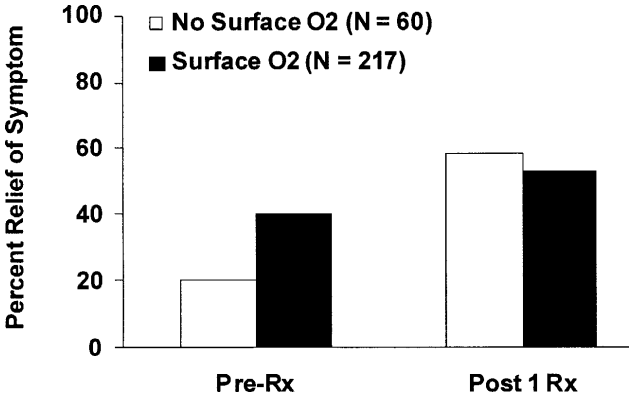

Figure 1. Percentage of divers with difficulty walking reporting complete relief before and after a single recompression treatment (from Divers Alert Network). Surface O_2 administration is associated with relief of symptoms prior to recompression (P = 0.003).

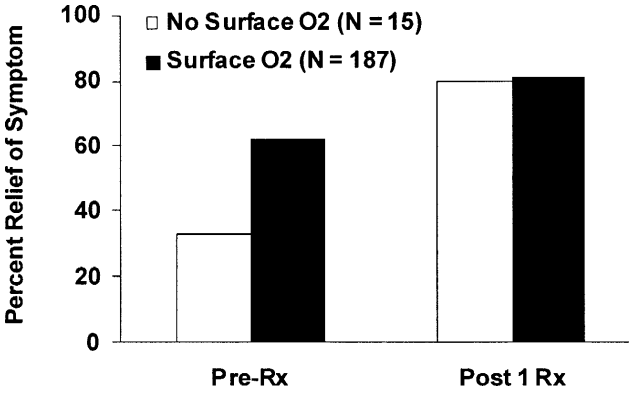

Figure 2. Percentage of divers with altered consciousness reporting complete relief before and after a single recompression treatment (from Divers Alert Network). Surface O_2 administration is associated with relief of symptoms prior to recompression (P = 0.029).

dehydration was either a result of bends or a predisposition to it.

Since then investigators in Zurich published a report describing two experimental divers with severe bends, in whom plasma volume was formally measured using a radioactive tracer. In these cases the venous haematocrit was close to 70% and the measured plasma volume significantly below normal, implicating plasma can leak into the interstitial space.[10] A study by Dr Boussuges and colleagues in France examined outcome after treatment of DCI as a function of initial haematocrit.[11] The investigators observed that those who had neurological sequelae, had a significantly higher haematocrit at presentation compared with those who recovered. These clinical data provide strong circumstantial evidence that fluid resuscitation is beneficial for severe bends.

There is indirect evidence that aggressive hydration can result in more rapid elimination of anesthetic gases,[12] suggesting that a similar approach in divers with decompression illness may accelerate the washout of excess inert gas. Indeed, interventions which increase central blood volume and cardiac preload, and hence raise cardiac output, such as supine position and head down tilt significantly increase the rate of inert gas washout.[13,14] Fluid administration may therefore be advantageous even in divers who are not dehydrated.

The most appropriate intravenous fluids for resuscitation of patients with DCI are either isotonic crystalloids (e.g. Ringer's solution, normal saline) or colloids. Rapid administration of hypotonic fluids to patients with injured brains can contribute to cerebral edema;[15] glucose-containing IV fluids could worsen neural injury (see below). Hypertonic saline (7.2%; 8 x normal) has been used in head injured patients with some success in reducing cerebral edema,[16] but has not been tested in patients with DCI.

For mild bends oral fluids may suffice. Rehydration after oral fluid administration is related to the rate of transport of water and electrolytes across the intestinal mucosa and the rate at which ingested fluid is delivered to the intestine. The gastric distention that occurs after oral fluid intake stimulates gastric emptying. However, the gastric emptying rate may be reduced by protein, or glucose concentrations greater than 5% (252 mOsm/kg). Maximum water absorption occurs at a sodium concentration of 60 mM and glucose concentration in the range of 80-120 mM. While most commercially available soft drinks and juices have an osmolality higher than plasma, water absorption is greater when osmolality is low.[17] An ideal solution for rehydration in diarrhea (possibly approximating the requirement in DCI) has been suggested as containing approximately 30-60 mM sodium, 70-150 mM glucose and osmolality of around 240 mOsm/kg.[18,19]

Plain water is almost always available, though its ingestion stimulates a urine output that is disproportionate to the degree of rehydration. Ingestion of electrolyte-free water causes a decrease in plasma osmolality and inhibition of ADH secretion. Urine output is then increased in response to the hypo-osmolality, and thus does not necessarily indicate adequate rehydration.[20,21] Studies of rehydration in normal volunteers in whom dehydration of 4% of body weight (12% reduction in plasma volume) was induced by exposure to a hot, dry environment indicate that administration over four hours of fluid equal to the volume lost, using water, failed to normalize plasma volume, although urine output had increased to 180-380 ml/hour.[20] Even after an additional 24 hours of ad lib fluid intake plasma volumes were 2.4-5.5% below pre-test values.

Although almost all commercially available beverages are low in sodium and high in carbohydrate, some

drinks marketed as "sports drinks" contain glucose and electrolytes that are close to ideal. If this is not available, a reasonable palatable oral rehydration fluid with appropriate electrolyte and carbohydrate concentration can be improvised by mixing one part orange or apple juice with two parts water and adding half a teaspoonful of salt to one liter of the mixture. Alternatively, in lieu of adding salt, one part sea water diluted with 9 parts fresh water can be used to dilute the juice. Provided the patient is not vomiting, an intake of 1,000-2,000 ml per hour for 1-2 hours is safe and usually well tolerated.

End points for fluid therapy should at least include normal hemodynamics and hematocrit. Urine output should exceed 1 ml/kg per hour, keeping in mind that if large volumes of hypotonic oral fluids are used, the urine output may falsely reflect the degree to which plasma volume repletion has occurred. Fluid should not be withheld just because an ideal liquid is not available.

HYPERGLYCAEMIA

There is evidence that hyperglycaemia can worsen central nervous system injury in both brain[22] and spinal cord,[23,24] probably due to accelerated production of lactate, and the ensuing intracellular acidosis. The effect probably becomes significant above a threshold plasma glucose of around 200 mg/dl (11 mM).[25,26] Administration of even small amounts of glucose, for example one litre of intravenous 5% dextrose solution, may worsen neurological outcome, even without significant hyperglycemia.[27,28]

Further evidence is available from a recent study of middle cerebral artery occlusion, in which both PO_2 and glucose were manipulated after inducing focal cerebral ischaemia of the parietal cortex of rabbits by cauterization of the right middle cerebral artery.[29] Serum glucose was varied between 2.8 mM and >28 mM; arterial PO_2 was either 50 mmHg or 150 mmHg. During hyperglycaemia, intracellular pH was reduced, mitochondrial function assessed by NADH redox state was impaired and infarct volume was greater than during hypoglycaemia.

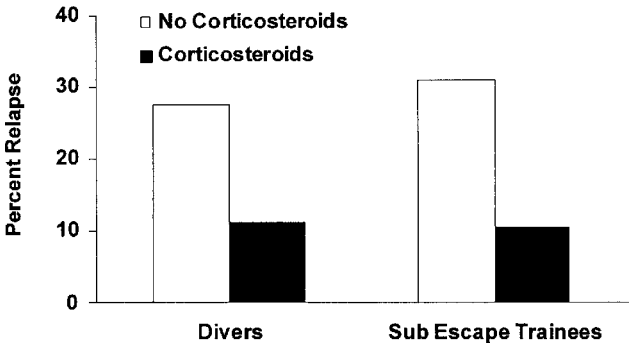

Figure 3. Relapse after arterial gas embolism as a function of whether corticosteroids were administered (from a retrospective study by Pearson and Goad).[36] Corticosteroid administration was associated with a significantly lower probability of relapse (P = 0.02).

Unless it is necessary to treat hypoglycemia, it is best to avoid the administration of glucose-containing intravenous solutions, and to measure plasma glucose if there is reason to suspect hyperglycaemia (e.g. if high dose corticosteroids are administered). Although there are relatively few diabetic divers, in glucose intolerant individuals stress and administration of corticosteroids can cause significant elevation of plasma glucose, which may require treatment.

MANAGEMENT OF CORE TEMPERATURE

Studies in which body temperature has been manipulated shortly after brain injury have shown that hypothermia can be beneficial, while hyperthermia is detrimental.[30-32] In a recent study patients with severe head injury (Glasgow coma scale 3-7) were randomly assigned to receive standard therapy or to be cooled to 33°C, kept at 32-33°C for 24 hours and then rewarmed. At 3 and 6 months after injury, for the patients with scores of 5 to 7, hypothermia was associated with significantly improved outcomes. The facility to induce and manage hypothermia is not widely available, and the observations need to be repeated before introducing the technique into routine practice. Thus, while diving doctors should not yet feel compelled to make divers with neurological injuries cold, it is worth a vigorous effort to be sure they do not become febrile.

CORTICOSTEROIDS

Steroids have been tried in most neural injuries, including DCI, and there have been several studies in animals. In a canine preparation, dexamethasone 1 mg/kg given before embolisation appeared to have a therapeutic effect upon the somatosensory evoked response amplitude, but when given afterwards there was no significant effect. Dr James Francis and colleagues, using methylprednisolone 20 mg/kg and recompression in spinal cord decompression sickness in dogs, observed no beneficial effect on somatosensory evoked responses within 250 minutes after treatment.[33]

Since then a study in patients with spinal cord trauma showed that methylprednisolone 30 mg/kg as a bolus, followed by 5.4 mg/kg/hour for 23 hours, was associated with greater recovery of motor function after 6 months.[34] In another study all patients received a bolus of methylprednisolone 30 mg/kg.[35] They were then randomized to receive methylprednisolone 5.4 mg/kg per

hour for either 24 or 48 hours. A third group received tirilazad mesylate 2.5 mg/kg every 6 hours for 48 hours. Patients treated within 3 hours of injury had equivalent outcomes at 6 weeks and 6 months. For those in whom therapy was initiated between 3 and 8 hours the patients treated with methylprednisolone for 48 hours did best, and those treated for 24 hours did least well.

Drs Pearson and Goad, in 1982, performed a retrospective study of relapse after arterial gas embolism, and reported a significantly lower incidence of relapse in patients who received one dose or more of corticosteroids (Figure 3).[36]

Whether corticosteroids should be administered routinely to divers with neurological DCI therefore remains undecided. On the basis of the information from studies in spinal cord trauma, if corticosteroids are administered they should probably be given early, preferably within the first 8 hours after symptom onset.

ANTICOAGULANTS

Evidence exists that bubbles in blood can initiate platelet adhesion and activation.[37-41] Conditions that could promote platelet aggregation might include large volumes of intravascular bubbles and sluggish blood flow, such as in the epidural venous plexus in severe decompression sickness.[42,43] Vascular obstruction due to bubbles could then be compounded by formation of fibrin clot. Anticoagulation of patients with neurological decompression illness might therefore seem reasonable.

However, in a study of arterial gas embolism in dogs,[44] in which somatosensory amplitude was the end-point, prostaglandin I_2 (PGI_2), indomethacin and heparin, and all possible combinations, were tested. None of the drugs singly or in double combinations were effective in returning somatosensory evoked potential amplitude toward normal. Only the combination of all three had any significant effect.

Anticoagulation may carry with it some risk. Tissue haemorrhage has been observed in animal and human decompression sickness of both the spinal cord and inner ear.[45-48] There has therefore been some reluctance to induce full heparinization in DCI. However, immobility due to spinal cord decompression illness is associated with deep vein thrombosis (DVT), and sometimes fatal pulmonary embolism.[49] Therefore, at least DVT prophylaxis is recommended for such patients.

The future

The initial event in decompression illness (DCI) is the formation of bubbles within tissue, which can cause immediate effects such as mechanical distortion and vascular occlusion leading to ischaemia. If reduction of oxygen delivery is extreme, rapid cellular death may occur due to depletion of ATP and loss of ionic membrane gradients. If, because the mechanical effects or ischaemia are less severe, immediate cell death does not ensue, then secondary injury mechanisms may ensue. Fibrin clot formation may occur, initiated by platelet activation. Ischaemia can initiate a cascade of events that includes excitatory neurotransmitter release, increase in intracellular calcium, sodium and zinc, increase in extracellular potassium, activation of proteases, adherence of leukocytes to endothelium in the ischaemic area, generation of reactive oxygen species such as superoxide and lipid peroxidation.[50] One of the effects of intracellular calcium influx is activation of the enzyme nitric oxide synthase, which catalyzes the formation of nitric oxide from arginine and oxygen. The resulting excess of nitric oxide (NO) can combine with superoxide anion (O_2^-), producing peroxynitrite ($ONOO^-$), a substance that can initiate DNA damage. This leads to activation of the nuclear repair enzyme poly(ADP-ribose) polymerase (PARP), which catalyzes attachment of ADP ribose units from NAD to nuclear proteins following DNA damage. This process consumes energy, and there is strong evidence that excessive activation of PARP after ischaemic cell injury can lead to cell death by energy depletion.[51] Compared with wild-type mice, animals with disruption of the gene that encodes PARP have 80% reduction in infarct volume after two hours of middle cerebral artery occlusion.[51] Evidence of PARP activation in the brain has been observed in humans after cardiac arrest,[52] and it has been suggested that PARP inhibitors could provide a potential therapy in acute stroke.[53] Indeed, treatment of rats with a PARP inhibitor significantly reduced the lesion volume that resulted from a 90 minute period of cerebral ischaemia.[54,55]

Clinical observation indicates that patients usually respond to treatment with hyperbaric oxygen hours, or even days after the insult, supporting the notion that immediate cellular death cannot be the only mechanism for DCI, and that there may be a “window of opportunity” in which adjunctive agents could limit secondary effects of bubbles pending definitive treatment with hyperbaric oxygen. Development of such agents should be a high priority for diving medicine. However, while in the USA per year there are approximately 1,000 cases of decompression illness, 1.5 million new cases of cerebrovascular disease occur. The vast weight of research effort is therefore directed toward the latter, and to the extent that DCI is due to ischaemia, solutions are likely to come from studies primarily directed toward treatment of stroke. Several potentially useful compounds may soon be available, as shown in Table 1.

LIGNOCAINE

Lignocaine is a promising agent of particular

TABLE 1

PARTIAL LIST OF ADJUNCTIVE AGENTS THAT HAVE BEEN INVESTIGATED IN CENTRAL NERVOUS SYSTEM ISCHAEMIA, TRAUMA OR DECOMPRESSION ILLNESS

(† indicates an absence of data in DCI.)

Compound	Mechanism	Animal Studies	Human Studies
Ancrod (viprinex)	Reduced fibrinogen	Neuroprotective in focal ischaemia[83]	Initial data favourable;[84,85] study ongoing †
Aspirin	Cyclooxygenase inhibition, anti-platelet effects		Anecdotal efficacy in DCI[86]
Clomethiazole	$GABA_A$ agonist	Neuroprotective in focal ischaemia and spinal cord injury[87,88]	Under investigation in stroke: initial report showed no effectiveness, although possibly effective in subgroups[89] †
Diaspirin cross-linked hemoglobin	Increased O_2 delivery	Neuroprotective in spinal cord ischaemia, cerebral ischaemia[90,91]	†
Doxycycline	Neutrophil inhibition	Improved outcome after AGE[92]	†
DPQ (3,4-dihydro-5-[4-(1-piperidinyl)butoxy] -1(2H)-isoquinolinone)	PARP inhibition	Neuroprotective in focal ischaemia[55]	†
Heparin and low MW heparin	Anticoagulation	Ineffective alone in AGE[44] but demonstrated to inhibit leukocyte rolling and sticking[93]	Possibly useful in preventing DVT in paraplegia due to DCI
Indomethacin	Cyclooxygenase inhibition, anti-platelet effects	Ineffective alone in AGE[44,] reduced pulmonary oedema due to venous gas embolism[94]	†
Isoproterenol	Increased intracellular cAMP	Reduced pulmonary oedema due to venous gas embolism[94]	†
Lignocaine	? inhibition of leukocyte activation	Improved outcome after AGE[56-58,94]	Reduced neurological deficit after CP bypass,[96] anecdotal improvement in DCI[61,62] and AGE[63]
Lubeluzole	Sodium channel blocker, inhibition of glutamate release	Neuroprotection after 9 minutes of bilateral and carotid artery occlusion hypotension in rats.[97] Lubeluzole and diaspirin cross-linked hemoglobin combination reduced infarct volume after focal cerebral ischaemia in rats[98]	Preliminary evidence supports effectiveness in human stroke[99] †

TABLE 1 (Continued)

PARTIAL LIST OF ADJUNCTIVE AGENTS THAT HAVE BEEN INVESTIGATED IN CENTRAL NERVOUS SYSTEM ISCHAEMIA, TRAUMA OR DECOMPRESSION ILLNESS

(† indicates an absence of data in DCI.)

Compound	Mechanism	Animal Studies	Human Studies
Methylprednisolone	? free radical scavenger	Effective in preventing paraplegia after aortic cross clamping (30 mg/kg before and after).[100] Acute study: 20 mg/kg ineffective in spinal cord DCS[33]	154 mg/kg over 23 h reduced 6 month morbidity in traumatic spinal cord injury[34] †
Mg^{2+}	NMDA, Ca^{2+} antagonist	Neuroprotection in spinal cord ischaemia[101,102]	†
Nicardipine	Inhibition of intracellular calcium influx, vasodilatation	Accelerated neurological recovery in dogs with hyperbaric oxygen after 5 min. global cerebral ischaemia[103]	†
Nifedipine	Inhibition of intracellular calcium influx, vasodilatation	Reduced pulmonary edema due to venous gas embolism[94]	†
Nimodipine	Inhibition of intracellular calcium influx, vasodilatation	Inconsistent effects after spinal cord injury[104-106]	Not useful in stroke[107] †
NMDA blockers	Prevention of Ca^{2+} entry	Neuroprotective in focal ischaemia[108,109]	Under investigation in stroke[110] †
Perfluorocarbons (e.g. Oxygent™)	Inert gas scavenger, improved O_2 delivery	Improved outcome after AGE, DCS[73,74,76,78,80,82,111]	†
Tirilazad	Free radical scavenger	Neuroprotective in spinal cord injury[112-114]	Evidence of efficacy in traumatic spinal cord injury[35] †
Tissue plasminogen activator	Clot lysis		Effective in human stroke[115] †

interest because it is already on the market, and with both animal and human data suggesting a benefit. Dr Evans showed that anesthetized cats pretreated with lignocaine experienced less decrement in somatosensory evoked potential amplitude compared to control animals after vertebral artery embolization with air.[56] A beneficial effect was also observed when lignocaine was administered after embolization.[57] Dr Dutka and colleagues have also demonstrated that lignocaine-treated embolized dogs recover with significantly more SEP amplitude after recompression than dogs treated with recompression alone.[58] Lignocaine treatment attenuated the neurological injury produced by retrograde cerebral perfusion in dogs.[59] A randomized trial in humans by Dr Mitchell and colleagues demonstrating that lignocaine infusion improves outcome after cardiopulmonary bypass[60] and four cases of apparent benefit of lignocaine administration in decompression illness[61,62] and arterial gas embolism[63] support the animal data and provide a strong rationale for a study of lignocaine treatment in acute decompression illness in humans.

The mechanism of the apparent beneficial effect of lignocaine in this context is unknown, but may only be related to bubbles indirectly. Anecdotal evidence supports its use in ischaemic myelopathy due to scoliosis surgery.[64] High doses (160 mg/kg) may reduce the oxygen requirement of CNS tissue not only by inhibiting electrical activity, but also by blocking sodium and potassium ion leak fluxes.[65] Lignocaine (total 6 mg/kg) has been reported to reduce neurological damage in dogs after hypothermic circulatory arrest.[66] Lignocaine also inhibits the release of calcium from mitochondria into the cytosol during ischaemia,[67] and to attenuate extracellular glutamate accumulation.[68] Lignocaine has been observed to attenuate the acute lung injury produced by pancreatic enzymes.[69] A study demonstrating that intravenous lignocaine attenuates the pulmonary damage induced by aspiration of hydrochloric acid, mediated at least in part by inhibition, sequestration and activation of neutrophils, suggests that lignocaine may inhibit the elaboration of oxygen free radicals induced by gas embolism.[70]

Intravenous administration of lignocaine requires an infusion pump and the capability of dealing with untoward effects such as seizures. "Field" use of lignocaine, using injection of 200-400 mg into the deltoid muscle, produces plasma concentrations in the therapeutic range for arrhythmia prophylaxis for up to two hours.[71]

PERFLUOROCARBONS

Perfluorocarbons have an extremely high solubility for a variety of gases, including N_2 and O_2, providing a rationale for their use in DCI. Intravenous administration of perfluorocarbons could provide a gas trap to accelerate diffusion of nitrogen from bubbles into the blood, while simultaneously enhancing O_2 delivery. Intravenous pretreatment of animals with perfluorocarbons prior to intracarotid air injection is protective against neural injury and retinal injury.[72-76] Similar protection has been observed for cardiac damage after coronary air embolism and cardiorespiratory effects after venous gas embolism.[77,78] Inert gas elimination from muscle is enhanced by perfluorocarbons.[79] Rats with decompression illness treated with intravenous FC-43 and 100% O_2 survived significantly longer than controls receiving 6% hetastarch or saline.[80-82] A new perfluorocarbon (Oxygent™, Alliance Pharmaceutical Corp., San Diego, California, USA) is expected to be approved shortly by the American Food and Drug Administration. Testing in DCI will be needed to show efficacy in humans. It will also be important to demonstrate that it does not promote O_2 toxicity.

Summary

Surface oxygen appears to be efficacious, at least whenever there is some delay to recompression treatment. First aid measures should ideally include airway management and assuring adequacy of ventilation, fluid resuscitation and maintenance of blood pressure. Other principles include avoidance and treatment of hyperglycaemia and hyperthermia. Deep vein thrombosis prophylaxis is recommended for divers with severe leg weakness.

In the near future several pharmacological agents may become available to protect against neurological damage during the pre-recompression interval.

References

1 Ellsberg E. *Men Under the Sea*. New York: Dodd, Mead & Co., 1939; 115-119

2 Jaminet A. *Physical Effects of Compressed Air and of the Causes of Pathological Symptoms Produced on Man by Increased Atmospheric Pressure Employed for the Sinking of Piers in the Construction of the Illinois and St. Louis Bridge*. St. Louis, Missouri: Ennis, 1871

3 Smith AH. *Effects of High Atmospheric Pressure Including the Caisson Disease*. Brooklyn, New York: Eagle Print, 1873

4 McCullough D. *The Great Bridge*. New York: Avon Books, 1972

5 Phillips JL. *The Bends*. New Haven, Connecticut: Yale University, 1998

6 Divers Alert Network. *Report on Decompression Illness and Diving Fatalities*. Durham, NC: Divers Alert Network, 2000

7 Komesaroff D. Oxygen administration in diving accidents. *SPUMS J* 1998; 28: 20-25

8 Wendling J. Normobaric oxygenation in dive accidents: a challenge for the developers of oxygen delivery systems. *SPUMS J* 1997; 27: 101-104

9 Annane D, Troche G, Delisle F et al. Effects of mechanical ventilation with normobaric oxygen therapy on the rate of air removal from cerebral arteries. *Crit Care Med* 1994; 22: 851-857

10 Brunner F, Frick P and Bühlmann A. Post-decompression shock due to extravasation of plasma. *Lancet* 1964; 1: 1071-1073

11 Boussuges A, Blanc P, Molenat F, Bergmann E and Sainty JM. Haemoconcentration in neurological decompression illness. *Int J Sports Med* 1996; 17: 351-355

12 Yogendran S, Asokumar B, Cheng DC and Chung F. A prospective randomized double-blinded study of the effect of intravenous fluid therapy on adverse outcomes in outpatient surgery. *Anesth Analg* 1995; 80: 682-686

13 Balldin UI, Lundgren CEG, Lundvall J and Mellander S. Changes in the elimination of ^{133}Xe from the anterior tibial muscle in man induced by immersion in water and by shifts in body position. *Aerosp Med*

1971; 42: 489-493

14 Vann RD and Gerth WA. Physiology of decompression sickness. In *Proceedings of the 1990 Hypobaric Decompression Sickness Workshop*. Pilmanis AA. Ed. Brooks Air Force Base: Armstrong Laboratory, 1990: 35-51

15 Drummond JC, Patel PM, Cole DJ and Kelly PJ. The effect of the reduction of colloid oncotic pressure, with and without reduction of osmolality, on post-traumatic cerebral edema. *Anesthesiology* 1998; 88: 993-1002

16 Munar F, Ferrer AM, de Nadal M et al. Cerebral hemodynamic effects of 72% hypertonic saline in patients with head injury and raised intracranial pressure. *J Neurotrauma* 2000; 17: 41-51

17 Cunha-Ferreira RMC, Elliott EJ, Brennan EA, Walker-Smith JA and Farthing MJG. Oral rehydration therapy: a solution to the problem. *Ped Res* 1987; 22: 108-?

18 Elliott EJ. The role of human perfusion techniques in the assessment of oral rehydration solutions. *Acta Paediatr Scand* 1989; 364 (Suppl): 31-39

19 Cunha-Ferreira RMC. Optimising oral rehydration solution composition for the children of Europe. *Acta Paediatr Scand* 1989; 364 (Suppl): 40-50

20 Costill DL and Sparks KE. Rapid fluid replacement following thermal dehydration. *J Appl Physio*l 1973; 34: 299-303

21 Nose H, Mack GW, Shi XR and Nadel ER. Role of osmolality and plasma volume during rehydration in humans. *J Appl Physiol* 1988; 65: 325-331

22 Pulsinelli WA, Levy DE, Sigsbee B, Scherer P and Plum F. Increased damage after ischemic stroke in patients with hyperglycemia with or without established diabetes mellitus. *Am J Med* 1983; 74: 540-544

23 Drummond JC and Moore SS. The influence of dextrose administration on neurologic outcome after temporary spinal cord ischemia in the rabbit. *Anesthesiology* 1989; 70: 64-70

24 Hemmila MR, Zelenock GB and D'Alecy LG. Postischemic hyperglycemia worsens neurologic outcome after spinal cord ischemia. *J Vasc Surg* 1993; 17: 661-668

25 Lam AM, Winn HR, Cullen BF and Sundling N. Hyperglycemia and neurological outcome in patients with head injury. *J Neurosurg* 1991; 75: 545-551

26 Li PA, Shamloo M, Smith ML, Katsura K and Siesjo BK. The influence of plasma glucose concentrations on ischemic brain damage is a threshold function. *Neurosci Lett* 1994; 177: 63-65

27 Lanier WL, Stangland KJ, Scheithauer BW, Milde JH and Michenfelder JD. The effects of dextrose infusion and head position on neurologic outcome after complete cerebral ischemia in primates: examination of a model. *Anesthesiology* 1987; 66: 39-48

28 Wass CT and Lanier WL. Glucose modulation of ischemic brain injury: review and clinical recommendations. *Mayo Clin Proc* 1996; 71: 801-12

29 Anderson RE, Tan WK, Martin HS and Meyer FB. Effects of glucose and PaO_2 modulation on cortical intracellular acidosis, NADH redox state, and infarction in the ischemic penumbra. *Stroke* 1999; 30: 160-170

30 Pomeranz S, Safar P, Radovsky A, Tisherman SA, Alexander H and Stezoski W. The effect of resuscitative moderate hypothermia following epidural brain compression on cerebral damage in a canine outcome model. *J Neurosurg* 1993; 79: 241-51

31 Wass CT, Lanier WL, Hofer RE, Scheithauer BW and Andrews AG. Temperature changes of ≥ 1°C alter functional neurological outcome and histopathology in a canine model of complete cerebral ischemia. *Anesthesiology* 1995; 83: 325-335

32 Ginsberg MD and Busto R. Combating hyperthermia in acute stroke: a significant clinical concern. *Stroke* 1998; 29: 529-534

33 Francis TJR and Dutka AJ. Methylprednisolone in the treatment of acute spinal cord decompression sickness. *Undersea Biomed Res* 1989; 16: 165-174

34 Bracken MB, Shepard MJ, Collins WF et al. A randomized, controlled trial of methylprednisolone or naloxone in the treatment of acute spinal-cord injury. Results of the Second National Acute Spinal Cord Injury Study. *New Engl J Med* 1990; 322: 1405-1411

35 Bracken MB, Shepard MJ, Holford TR et al. Administration of methylprednisolone for 24 or 48 hours or tirilazad mesylate for 48 hours in the treatment of acute spinal cord injury. Results of the Third National Acute Spinal Cord Injury Randomized Controlled Trial. National Acute Spinal Cord Injury Study. *JAMA* 1997; 277: 1597-1604

36 Pearson RR and Goad RF. Delayed cerebral edema complicating cerebral arterial gas embolism: Case histories. *Undersea Biomed Res* 1982; 9: 283-296

37 Philp RB and Gowdey CW. Platelets as an etiological factor in experimental decompression sickness. *J Occup Med* 1969; 11: 257-8

38 Philp RB, Schacham P and Gowdey CW. Involvement of platelets and microthrombi in experimental decompression sickness: similarities with disseminated intravascular coagulation. *Aerosp Med* 1971; 42: 494-502

39 Warren BA, Philp RB and Inwood MJ. The ultrastructural morphology of air embolism: platelet adhesion to the interface and endothelial damage. *Br J Exp Pathol* 1973; 54: 163-72

40 Thorsen T, Dalen H, Bjerkvig R and Holmsen H. Transmission and scanning electron microscopy of N_2 microbubble-activated human platelets in vitro. *Undersea Biomed Res* 1987; 14: 45-58

41 Thorsen T, Klausen H, Lie RT and Holmsen H.

Bubble-induced aggregation of platelets: effects of gas species, proteins, and decompression. *Undersea Hyperbaric Med* 1993; 20: 101-19

42 Hallenbeck JM, Bove AA and Elliott DH. Mechanisms underlying spinal cord damage in decompression sickness. *Neurology* 1975; 25: 308-316

43 Hallenbeck JM. Cinephotomicrography of dog spinal vessels during cord-damaging decompression sickness. *Neurology* 1976; 26: 190-199

44 Hallenbeck JM, Leitch DR, Dutka AJ, Greenbaum LJ Jr and McKee AE. Prostaglandin I_2, indomethacin and heparin promote postischemic neuronal recovery in dogs. *Ann Neurol* 1982; 12: 145-156

45 Elliott DH and Moon RE. Manifestations of the decompression disorders. In *The Physiology and Medicine of Diving. 4th Edition*. Bennett PB and Elliott DH. Eds. Philadelphia, Pennsylvania: WB Saunders, 1993: 481-505

46 Broome JR and Dick EJ Jr. Neurological decompression illness in swine. *Aviat Space Environ Med* 1996; 67: 207-213

47 Landolt JP, Money KE, Topliff ED, Nicholas AD, Laufer J and Johnson WH. Pathophysiology of inner ear dysfunction in the squirrel monkey in rapid decompression. *J Appl Physiol* 1980; 49: 1070-82

48 Antonelli PJ, Parell GJ, Becker GD and Paparella MM. Temporal bone pathology in scuba diving deaths. *Otolaryngol Head Neck Surg* 1993; 109: 514-21

49 Spadaro MV, Moon RE, Fracica PJ et al. Life threatening pulmonary thromboembolism in neurological decompression illness. *Undersea Biomed Res* 1992; 19 (Suppl): 41-42

50 Lipton P. Ischemic cell death in brain neurons. *Physiol Rev* 1999; 79: 1431-1568

51 Eliasson MJL, Sampei K, Mandir AS et al. Poly(ADP-ribose) polymerase gene disruption renders mice resistant to cerebral ischemia. *Nature Med* 1997; 3: 1089-1095

52 Love S, Barber R and Wilcock GK. Apoptosis and expression of DNA repair proteins in ischaemic brain injury in man. *Neuroreport* 1998; 9: 955-959

53 Pieper AA, Verma A, Zhang J and Snyder SH. Poly (ADP-ribose) polymerase, nitric oxide and cell death. *Trends Pharmacol Sci* 1999; 20: 171-181

54 Lo EH, Bosquehamilton P and Meng W. Inhibition of poly(ADP-ribose) polymerase - reduction of ischemic injury and attenuation of N-methyl-D-aspartate-induced neurotransmitter dysregulation. *Stroke* 1998; 29: 830-836

55 Takahashi K, Pieper AA, Croul SE, Zhang J, Snyder SH and Greenberg JH. Post-treatment with an inhibitor of poly(ADP-ribose) polymerase attenuates cerebral damage in focal ischemia. *Brain Res* 1999; 829: 46-54

56 Evans DE, Kobrine AI, LeGrys DC and Bradley ME. Protective effect of lidocaine in acute cerebral ischemia induced by air embolism. *J Neurosurg* 1984; 60: 257-263

57 Evans DE, Catron PW, McDermott JJ, Thomas LB, Kobrine AI and Flynn ET. Therapeutic effect of lidocaine in experimental cerebral ischemia induced by air embolism. *J Neurosurg* 1989; 70: 97-102

58 Dutka AJ, Mink R, McDermott J, Clark JB and Hallenbeck JM. Effect of lidocaine on somatosensory evoked response and cerebral blood flow after canine cerebral air embolism. S*troke* 1992; 23: 1515-1520

59 Wang DX, Wu XM, Zhong YF et al. Effect of lidocaine on improving cerebral protection provided by retrograde cerebral perfusion: A neuropathologic study. *J Cardiothorac Vasc Anesth* 1999; 13: 176-180

60 Mitchell SJ, Pellett O and Gorman DF. Cerebral protection by lidocaine during cardiac operations. *Ann Thorac Surg* 1999; 67: 1117-1124

61 Drewry A and Gorman DF. Lignocaine as an adjunct to hyperbaric therapy in decompression illness: a case report. *Undersea Biomed Res* 1992; 19: 187-190

62 Cogar WB. Intravenous lidocaine as adjunctive therapy in the treatment of decompression illness. *Ann Emerg Med* 1997; 29: 284-286

63 Mitchell SJ, Benson M, Vadlamudi L and Miller P. Cerebral arterial gas embolism by helium: An unusual case successfully treated with hyperbaric oxygen and lidocaine. *Ann Emerg Med* 2000; 35: 300-303

64 Klemme WR, Burkhalter W, Polly DW, Dahl LF and Davis DA. Reversible ischemic myelopathy during scoliosis surgery. A possible role for intravenous lidocaine. *J Pediatr Orthop* 1999; 19: 763-765

65 Astrup J, Sorensen PM and Sorensen HR. Inhibition of cerebral oxygen and glucose consumption in the dog by hypothermia, pentobarbital, and lidocaine. *Anesthesiology* 1981; 55: 263-8

66 Zhou Y, Wang DX, Du MY et al. Lignocaine prolongs the safe duration of circulatory arrest during deep hypothermia in dogs. *Can J Anaesth* 1998; 45: 692-698

67 Zhang YL and Lipton P. Cytosolic Ca^{2+} changes during in vitro ischemia in rat hippocampal slices: Major roles for glutamate and Na+-dependent Ca^{2+} release from mitochondria. *J Neurosci* 1999; 19: 3307-3315

68 Terada H, Ohta S, Nishikawa T, Mizunuma T, Iwasaki Y and Masaki Y. The effect of intravenous or subarachnoid lidocaine on glutamate accumulation during transient forebrain ischemia in rats. *Anesth Analg* 1999; 89: 957-961

69 Kiyonari Y, Nishina K, Mikawa K, Maekawa N and Obara H. Lignocaine attenuates acute lung injury induced by a combination of phospholipase A(2) and trypsin. *Crit Care Med* 2000; 28: 484-489

70 Nishina K, Mikawa K, Takao Y, Shiga M, Maekawa N and Obara H. Intravenous lidocaine attenuates acute lung injury induced by hydrochloric acid aspiration in rabbits. *Anesthesiology* 1998; 88: 1300-1309

71 Koster RW and Dunning AJ. Intramuscular lidocaine for prevention of lethal arrhythmias in the prehospitalization phase of acute myocardial infarction. *New Engl J Med* 1985; 313: 1105-1110

72 Menasché P, Pinard E, Desroches AM et al. Fluorocarbons: a potential treatment of cerebral air embolism in open heart surgery. *Ann Thorac Surg* 1985; 40: 494-497

73 Spiess BD, Braverman B, Woronowicz AW and Ivankovich AD. Protection from cerebral air emboli with perfluorocarbons in rabbits. *Stroke* 1986; 17: 1146-9

74 Cochran RP, Kunzelman KS, Vocelka CR et al. Perfluorocarbon emulsion in the cardiopulmonary bypass prime reduces neurologic injury. *Ann Thorac Surg* 1997; 63: 1326-32

75 Herren JI, Kunzelman KS, Vocelka C, Cochran RP and Spiess BD. Horseradish peroxidase as a histological indicator of mechanisms of porcine retinal vascular damage and protection with perfluorocarbons after massive air embolism. *Stroke* 1997; 28: 2025-30

76 Herren JI, Kunzelman KS, Vocelka C, Cochran RP and Spiess BD. Angiographic and histological evaluation of porcine retinal vascular damage and protection with perfluorocarbons after massive air embolism. *Stroke* 1998; 29: 2396-403

77 Spiess BD, McCarthy RJ, Tuman KJ and Ivankovich AD. Protection from coronary air embolism by a perfluorocarbon emulsion (FC-43). *J Cardiothorac Anesth* 1987; 1: 210-5

78 Tuman KJ, Spiess BD, McCarthy RJ and Ivankovich AD. Cardiorespiratory effects of venous air embolism in dogs receiving a perfluorocarbon emulsion. *J Neurosurg* 1986; 65: 238-244

79 Novotny JA, Bridgewater BJ, Himm JF and Homer LD. Quantifying the effect of intravascular perfluorocarbon on xenon elimination from canine muscle. *J Appl Physiol* 1993; 74: 1356-60

80 Spiess BD, McCarthy RJ and Tuman KJ. Treatment of decompression sickness with a perfluorocarbon emulsion (FC-43). *Undersea Biomed Res* 1988; 15: 31-37

81 Lutz J, Herrmann G. Perfluorochemicals as a treatment of decompression sickness in rats. *Pflugers Arch* 1984; 401: 174-7

82 Lynch PR, Krasner LJ, Vinciquerra T and Shaffer TH. Effects of intravenous perfluorocarbon and oxygen breathing on acute decompression sickness in the hamster. *Undersea Biomed Res* 1989; 16: 275-281

83 Elger B, Hornberger W, Schwarz M and Seega J. MRI study on delayed ancrod therapy of focal cerebral ischaemia in rats. *Eur J Pharmacol* 1997; 336: 7-14

84 Olinger CP, Brott TG, Barsan WG et al. Use of ancrod in acute or progressing ischemic cerebral infarction. *Ann Emerg Med* 1988; 17: 1208-9

85 Anonymous. Ancrod for the treatment of acute ischemic brain infarction. The Ancrod Stroke Study Investigators. *Stroke* 1994; 25: 1755-9

86 Fructus X. Treatment of serious decompression sickness. In: *Treatment of Serious Decompression Illness and Arterial Gas Embolism: Proceedings of the 20th Undersea Medical Society Workshop.* Davis JC. Ed. Bethesda, Maryland: Undersea Medical Society, 1979: 37-43

87 Snape MF, Baldwin HA, Cross AJ and Green AR. The effects of chlormethiazole and nimodipine on cortical infarct area after focal cerebral ischaemia in the rat. *Neuroscience* 1993; 53: 837-44

88 Farooque M, Isaksson J, Jackson DM and Olsson Y. Clomethiazole (ZENDRA, CMZ) improves hind limb motor function and reduces neuronal damage after severe spinal cord injury in rat. *Acta Neuropathol* 1999; 98: 22-30

89 Wahlgren NG, Ranasinha KW, Rosolacci T et al. Clomethiazole acute stroke study (CLASS): results of a randomized, controlled trial of clomethiazole versus placebo in 1360 acute stroke patients. *Stroke* 1999; 30: 21-8

90 Bowes MP, Burhop KE and Zivin JA. Diaspirin cross-linked hemoglobin improves neurological outcome following reversible but not irreversible CNS ischemia in rabbits. *Stroke* 1994; 25: 2253-7

91 Cole DJ, Drummond JC, Patel PM, Nary JC and Applegate RL 2nd. Effect of oncotic pressure of diaspirin cross-linked hemoglobin (DCLHb) on brain injury after temporary focal cerebral ischemia in rats. *Anesth Analg* 1996; 83: 342-7

92 Reasoner DK, Hindman BJ, Dexter F, Subieta A, Cutkomp J and Smith T. Doxycycline reduces early neurologic impairment after cerebral arterial air embolism in the rabbit. *Anesthesiology* 1997; 87: 569-576

93 Weber JR, Angstwurm K, Rosenkranz T et al. Heparin inhibits leukocyte rolling in pial vessels and attenuates inflammatory changes in a rat model of experimental bacterial meningitis. *J Cerebral Blood Flow & Metabolism* 1997; 17: 1221-9

94 Huang KL and Lin YC. Pharmacologic modulation of pulmonary vascular permeability during air embolism. *Undersea Hyperbaric Med* 1997; 24: 315-321

95 McDermott JJ, Dutka AJ, Evans DE and Flynn ET. Treatment of experimental cerebral air embolism with lidocaine and hyperbaric oxygen. *Undersea Biomed Res* 1990; 17: 525-534

96 Mitchell SJ, Pellett O and Gorman DF. Cerebral protection by lidocaine during cardiac operations. *Ann Thorac Surg* 1999; 67: 1117-1124

97 Haseldonckx M, Van Reempts J, Van de Ven M, Wouters L and Borgers M. Protection with lubeluzole against delayed ischemic brain damage in rats. A quantitative histopathologic study. *Stroke* 1997; 28: 428-32

98 Aronowski J, Strong R and Grotta JC. Combined

neuroprotection and reperfusion therapy for stroke. Effect of lubeluzole and diaspirin cross-linked hemoglobin in experimental focal ischemia. *Stroke* 1996; 27: 1571-6

99 Grotta J. Lubeluzole treatment of acute ischemic stroke. The US and Canadian Lubeluzole Ischemic Stroke Study Group. *Stroke* 1997; 28: 2338-46

100 Laschinger JC, Cunningham JN Jr, Cooper MM, Krieger K, Nathan IM and Spencer FC. Prevention of ischemic spinal cord injury following aortic cross-clamping: use of corticosteroids. *Ann Thorac Surg* 1984; 38: 500-507

101 Simpson JI, Eide TR, Schiff GA et al. Intrathecal magnesium sulfate protects the spinal cord from ischemic injury during thoracic aortic cross-clamping. *Anesthesiology* 1994; 81: 1493-9

102 Suzer T, Coskun E, Islekel H and Tahta K. Neuroprotective effect of magnesium on lipid peroxidation and axonal function after experimental spinal cord injury. *Spinal Cord* 1999; 37: 480-4

103 Iwatsuki N, Takahashi M, Ono K and Tajima T. Hyperbaric oxygen combined with nicardipine administration accelerates neurologic recovery after cerebral ischemia in a canine model. *Crit Care Med* 1994; 22: 858-63

104 Haghighi SS, Stiens T, Oro JJ and Madsen R. Evaluation of the calcium channel antagonist nimodipine after experimental spinal cord injury. *Surg Neurol* 1993; 39: 403-8

105 Pointillart V, Gense D, Gross C et al. Effects of nimodipine on posttraumatic spinal cord ischemia in baboons. *J Neurotrauma* 1993; 10: 201-13

106 Imamura H and Tator CH. Effect of intrathecal nimodipine on spinal cord blood flow and evoked potentials in the normal or injured cord. *Spinal Cord* 1998; 36: 497-506

107 Anonymous. Clinical trial of nimodipine in acute ischemic stroke. The American Nimodipine Study Group. *Stroke* 1992; 23: 3-8 [published erratum appears in *Stroke* 1992; 23 (4): 615]

108 Simon RP, Swan JH, Griffiths T and Meldrum BS. Blockade of N-methyl-D-aspartate receptors may protect against ischemic damage in the brain. *Science* 1984; 226: 850-2

109 Albers GW, Goldberg MP and Choi DW. Do NMDA antagonists prevent neuronal injury? Yes. *Arch Neurol* 1992; 49: 418-20

110 Lee JM, Zipfel GJ and Choi DW. The changing landscape of ischaemic brain injury mechanisms. *Nature* 1999; 399: A7-A14

111 Spiess BD, McCarthy R, Piotrowski D and Ivankovich AD. Protection from venous air embolism with fluorocarbon emulsion FC-43 *J Surg Res* 1986; 41: 439-444

112 Anderson DK, Hall ED, Braughler JM, McCall JM and Means ED. Effect of delayed administration of U74006F (tirilazad mesylate) on recovery of locomotor function after experimental spinal cord injury. *J Neurotrauma* 1991; 8: 187-92

113 Holtz A and Gerdin B. Efficacy of the 21-aminosteroid U74006F in improving neurological recovery after spinal cord injury in rats. *Neurological Research* 1992; 14: 49-52

114 Francel PC, Long BA, Malik JM, Tribble C, Jane JA and Kron IL. Limiting ischemic spinal cord injury using a free radical scavenger 21-aminosteroid and/or cerebrospinal fluid drainage. *J Neurosurg* 1993; 79: 742-51

115 Osborn TM, LaMonte MP and Gaasch WR. Intravenous thrombolytic therapy for stroke: a review of recent studies and controversies. *Ann Emerg Med* 1999; 34: 244-55

AUDIENCE PARTICIPATION

John Knight, Melbourne.

As another anaesthetist, my only quibble with the positioning of the airway at the end of the list. I think the airway should be first, because it is the easiest one to do. Intravenous fluid requires skills that most divers do not have, and you do get people in the general community who can position people on their sides so that they can breathe again. I think we ought to be concentrating, when we talk about early treatment, not on what doctors can offer, but what the other people on the dive boat, the dive guides and the other divers, can offer.

Richard Moon.

Yes. I absolutely agree; the point is well taken and thank you.

Ian Seppelt, Sydney.

When you are advising non-medical people who are treating an accident, do you ask them to give air breaks, or do you say continuous surface oxygen as long as possible? How long do you accept if it is going to be a few hours until they get to you?

Richard Moon.

Since oxygen toxicity is unlikely during administration of surface O_2 for a few hours, I do not recommend scheduled air breaks.

Mike Loxton, Royal Australian Navy.

Just an observation on the surface oxygen. We did a retrospective study of about 260 cases treated at the School of Underwater Medicine from 1983 to 1993, and certainly we found in the univariate analysis a very significant advantage in using surface oxygen, but when we allowed for confounders, we did not find a statistically significant advantage. The main confounder appeared to be treatment delay. Those patients given surface oxygen were treated a lot earlier, and after allowing for that, we did not find a statistically significant advantage. Just an observation, and

perhaps the number of cases would not allow me not to advise surface oxygen.

Richard Moon.

Your point, that confounding variables may explain what appears to be a beneficial effect of surface oxygen, is a good one. For example, someone prepared with the kit necessary to administer surface oxygen might be more likely to transport an injured diver expeditiously to a treatment facility, and therefore obtain a better outcome because of speedy treatment. I think it is possible that our data underestimate the effect of surface oxygen, because it is often administered in a less than intensive manner. It is often given for only a few minutes at a time; in nearly a third of cases reported to DAN in 1998 it was administered for less than an hour.

Gordon Bentley, Brisbane.

Faced with a long journey and a limited supply of oxygen, would you recommend giving a high concentration for a short time, or a lower concentration throughout the entire journey?

Richard Moon.

That is an excellent question, to which I do not know the answer.

Fiona Sharp, Perth.

Tirilazad been shown to be a benefit in males for spinal cord injury and trauma. Have there been any studies done on tirilazad being used in decompression injuries involving the spinal cord?

Richard Moon.

As far as I know, it has not.

Tony Lee, Malaysia.

There used to be some interest in lignocaine. Has it gone numb?

Richard Moon.

Although there is experimental evidence, and some anecdotal clinical evidence, that lignocaine is effective in decompression illness, in this setting I would still consider it an experimental drug.

Brian Casey, Sydney.

You made reference to plasma in one of your studies in terms of intravenous fluid use. I wondered what particular intravenous fluids you would use if you had got everything available, plasma, Ringer's lactate, saline?

Richard Moon.

I support Alf Brubakk's point, that hypotonic fluids are not good choices. Whether isotonic colloid or crystalloid fluids are preferred is not yet established. In anesthetic practice in the US we tend to be concerned about cost, so in the absence of evidence in favor of using colloids, we tend to favor crystalloids. Whether there is any difference in effectiveness between Ringer's lactate and normal saline in DCI, I do not know, but I would suspect not.

Akin Toklu, Turkey.

Is there any experimental study which suggests not to use aspirin?

Richard Moon.

There are anecdotal stories about improvement after using aspirin in neurological bends, but I think we do not really know. Dr Mike Bennett in Sydney is doing a study on a non-steroidal anti-inflammatory drug, which may have a similar effect to aspirin, and I look forward to his presentation in a few months or a year to give us the answer on that.

Alf Brubakk.

I do not think there are any studies on aspirin. But one point is that the aggregation of thrombocytes that one sees caused by gas bubbles does not seem to be influenced by aspirin. It seems to be due to a different mechanism. Another point is that there are some older studies which seem to indicate that several non-steroidal anti-inflammatory drugs seem to have a dramatic effect on decompression sickness. There are several mice studies which have not been repeated for 30 or 40 years, which would be very interesting to repeat. There is other data to indicate that it might do some good. That is all I know about it.

There was a question about oxygen, how much should you use? Do you give a high concentration for a short time, or a lower concentration over a longer period? I think the answer depends on when you start to give it. Do you start giving it immediately? It is obvious that the higher the oxygen concentration, the faster the bubbles will shrink. If you are after an immediate treatment effect to get rid of the bubbles, then I would say use as much oxygen as you can, as early as you can. When it comes to secondary effects, it is much more complicated, and I cannot answer that.

Richard Moon.

It is interesting that patients will often tell you that they breathed oxygen for a while, and there was improvement, but when they stopped breathing it, the symptoms came back.

Chris Acott, Adelaide.

A couple of years ago I was looking up about oxygen, intravenous fluids, steroids, the French regime that Fructus invented, and aspirin. There were only 40 or 50 patients, not very many, but the ones who actually received aspirin as well as steroids, and oxygen, and fluids actually probably did a little bit worse that those who did not, in the long term.

Robyn Walker, Royal Australian Navy.

Getting back to oxygen and fluids. I think while we are telling everyone to use them, we have to encourage people to talk to the treating unit. Just this week, we received a patient, evacuated from Vanuatu by a private company. We were not asked to comment on how she should be transported. She had 15 hours of 100% oxygen without an air break. Although she arrived asymptomatic she had significant pulmonary oxygen toxicity. Those who arranged the evacuation had not realised that oxygen toxicity could be a problem for us if we then had to treat that person in the chamber. Secondly, she was given five litres of intravenous fluid in five hours. However, she was asymptomatic when that fluid treatment was commenced. Certainly while fluids and oxygen are very important, I think we need to give people some advice before patients are transported. I would urge them to talk to the treating unit before transport.

Professor Richard E Moon has been a Guest Speaker at the 1997 and 1999 Annual Scientific Meetings. His address is Department of Anesthesiology, Duke University Medical Center, PO Box 3049, Durham, North Carolina 27710, USA. Phone +1-919-681-5805. Fax +1-919-681-4698. E-mail <moon0002@mc.duke.edu>.

DECOMPRESSION ILLNESS SEQUELAE IN TUNA FARM DIVERS

Chris Acott

Key Words

Decompression illness, hyperbaric oxygen, occupational diving, sequelae, training, treatment.

Introduction

Fisherman divers, the abalone divers of south and south-eastern Australia, salmon farm divers of Tasmania and the pearl divers of the tropical north, are part of the fishing culture of Australia. Some Australian coastal towns are dependent on such fishing.

Tuna fish are one of South Australia's natural resources. The majority of tuna fishing is conducted in the Southern Ocean by vessels based in Port Lincoln.

Port Lincoln, near the tip of the Eyre Peninsula, was first settled in 1834. It was to have been the capital of the new colony of South Australia because of its deep natural harbour. However, lack of an adequate fresh water supply and the low rainfall inland saw that Adelaide, 250 km (156 miles) east as the seagull flies, became the capital. Port Lincoln, with a population of 12,000 and over 600 km (375 miles) by road from Adelaide, is the centre of the South Australian Tuna industry. Its main industries are fishing (tuna and abalone), grain exporting, tourism and wine production.

Tuna fishing

Until the 1990s the Tuna industry used single vessel techniques, baited lines, often attached to poles which enabled strong men to swing the heavy fish inboard. Tuna schools are now co-operatively netted in the open sea and then the nets are towed back to Port Lincoln. Here the tuna are kept in netted enclosures, near the shore, for fattening before harvesting. The main export market for the tuna is Japan. Divers are employed for net maintenance, clearing the dead tuna from the enclosures and in the tuna harvest. In the early years harvesting was by swimming each fish to the surface, which involved many extremely rapid ascents, from depths of up to 18 m, in each "dive". This practice contributed to the high incidence of decompression illness (DCI) and was stopped by regulations introduced in 1995.[1]

The tuna are kept inside an inner net while an outer net prevents any intrusion by sharks. Sharks have been found between the nets but to date (May 1999) no diver has been attacked by a shark, however, this may reflect a lack of reporting of any such attack.

Government marine biologists have expressed concern about the impact the nets have on the environment. All the debris from feeding and fish excrement are deposited below the nets, and no attempt has been made to clear this rubbish away. Already one storm has stirred up this debris and suffocated millions of dollars worth of fish. Furthermore the presence of the tuna has lured sharks, in particular Great Whites, to the area where the nets are sited. These areas are close to the local beaches.

The divers

Between August 1993 and January 1995, 17 divers employed in the tuna industry were treated for decompression illness by the Hyperbaric Medicine Unit at the Royal Adelaide Hospital [RAH HMU]. Many of these 17 divers had continued to dive while symptomatic. In all but one case there was a delay before medical treatment was obtained. From January 1995 a further four divers have been treated, making a total, to May 1999, of 21 divers.

Amazingly, the initial response by the South Australian Government and Medicare, the Australian Federal Government's national health insurance system, to this cohort of 17 divers with DCS was that the RAH HMU's