Editorials

Recruiting without over-stretching

Acute lung injury remains a significant cause of morbidity and mortality in neonatal, paediatric and adult intensive care. Recent efforts to improve the treatment of respiratory failure have focused on techniques that avoid over distension of the lung while at the same time recruiting areas of collapse and consolidation. A number of methods of achieving these two goals have been investigated including sustained inflations, conventional ventilation with small tidal volumes and PEEP above the inflection point, high frequency oscillatory ventilation (HFOV) and partial liquid ventilation (PLV).

With each new therapeutic strategy a series of questions arise. Is the therapy effective in minimising progression of lung injury compared to 'conventional' techniques? How does efficacy compare with other therapies that have a similar aim? Are combinations rather than single therapies more effective? With the development of an increasing number of lung volume recruitment strategies there are many permutations of these questions.

In this issue of the journal Davies *et al* [1] report that the combination of partial liquid ventilation and high frequency oscillation, (PL-HFOV) does not augment the 'lung protective' effect of HFOV used as a single therapy if a sustained inflation and a high volume strategy is used with HFOV. The sustained inflation and high volume strategy are key components of the finding. If either had been omitted it is likely that a different result would have been obtained.[2]

A clinical scenario in which a combination of therapies might be considered is when the first treatment is failing. Davies *et al* used a model in which HFOV is quite effective at reversing hypoxia and minimising the progression of injury. Perhaps the place of PL-HFOV will be in more severe disease where volume recruitment and reversal of hypoxia cannot be achieved with HFOV alone. This remains to be investigated.

In the current study the mortality in the PL-HFOV group was 30% in contrast to zero mortality in the HFOV group. Mortality was not a primary outcome and the number of deaths (2) insufficient for definitive conclusion. Nevertheless the finding should be considered in the context of the literature. Gauger and colleagues,[3] reported that two of six children treated with perfluorocarbon developed pneumothoraces during perfluorocarbon administration. Cox *et al*,[4] in a laboratory study of PLV using conventional ventilation, carefully examined for air leak both radiologically and at post mortem. They found that a commonly advocated PLV strategy (i.e. large tidal volume and large dose of perfluorocarbon) was associated with a very significant increase in the risk of death and pneumothorax. Davis *et al* did not examine for this complication. Although they suspected 'liquid leak' had occurred, gas leak from the anterior regions of the lung is probably more likely. [5]

The study of Cox *et al* [4] demonstrates that, depending on the volume strategy used, it is possible to cause harm with PLV. Future studies of PLV must be designed so that adverse effects, particularly gas leak, are detected.

Dr. A. Slater
Intensive Care Unit,
Women's and Children's Hospital,
SOUTH AUSTRALIA 5006

REFERENCES

1. Davies MW, Stewart MJ, Souriel M, Chavasse R, Butt W. Oxygenation is not improved by partial liquid high frequency ventilation using a high lung volume strategy. An experimental study. Critical Care and Resuscitation 1999;1: 339-343.
2. Sukumar M, Bommaraju M, Fisher JE, Morin FC, Papo MC, Fuhrman BP, Hernan LJ, Leach CL. High-frequency partial liquid ventilation in respiratory distress syndrome: hemodynamics and gas exchange. J Appl Physiol 1998;84:327-334.
3. Gauger PG, Pranikoff T, Schreiner R J, Moler FW, Hirshi RB. Initial experience with partial liquid ventilation in pediatric patients with the acute respiratory distress syndrome. Crit Care Med 1996;24:16-22.
4. Cox PN, Frndova H, Tan PSK, Nakamura T, Miyasaka K, Sakurai Y, Middleton W, Mazer D, Bryan AC. Concealed air leak associated with large tidal volumes in partial liquid ventilation. Am J Respir Crit Care Med 1997;156:992-997.
5. Smith K, Mrozek JD, Simonton SC, Bing DR, Meyers PA, Connett JE, Mammel MC: Prolonged partial liquid ventilation using conventional and high-frequency ventilatory techniques. Gas exchange and lung pathology in an animal model of respiratory distress syndrome. Crit Care Med 1997;25:1888-1897.

"If you don't look for Canaries you won't find them"

'Canaries', (a name sometimes given to rare and unusual medical conditions) are often the lifeblood of

the enthusiastic postgraduate trainee. With every new patient who confronts the clinical team with a puzzling condition, a barrage of differential diagnoses (most of which can be found as footnotes in medical texts or isolated journal case reports) are suggested by the willing pre-specialist. None can be easily disregarded but most are highly unlikely as a cause of the patient's condition, and are often proposed without due consideration being given to the unusual presentation of common conditions. Nonetheless, sometimes the jackpot is hit (usually to the chagrin of the senior medical staff) and the 'Canary' is found, reinforcing the activity of the novice trainee who states gleefully "If you don't look for Canaries you won't find them".

Two case reports are published in this edition of Critical Care and Resuscitation that illustrate the need for 'Canary hunting'. Faunce *et al*,[1] by 'sleuthing' the problem of an unusually severe coagulopathy in a patient who presented with a history of intravenous amphetamine self administration, just prior to being found face down in an outside 'spa', describe the detection of snake envenomation. However, the conditions of near drowning, amphetamine overdose and now, snake envenomation, make for some difficulty in adhering to the common wisdom of Ockham's razor[2] (i.e. one should choose fewest possible aetiologies to explain multiple clinical problems).[3] Without the presence of pyrexia or rhabdomyolysis, one wonders whether amphetamines played any part in this patient's condition. Could the condition be explained more simply by a primary envenomation (e.g. snake bite or intravenous injection of snake venom - inadvertently or otherwise) followed by immersion? With almost no possibility of a false positive being present with the common brown snake envenomation test,[4] the detection of envenomation was a pleasing result. However, as with any diagnosis, the history is paramount, and I can't help feeling that one should re-interview the deceased's acquaintances (and perhaps test the contents of the syringe used for the amphetamine injection) to sleuth more of the truth.

The other case, described by Teague *et al*,[5] involves a patient with acetylcholinesterase poisoning who presents as an unknown collapse and cardiac arrest. Due to the acute presentation and requirement for standard resuscitation measures, the diagnosis of acetyl-cholinesterase poisoning and subsequent atropine therapy was delayed. It is interesting to note that pralidoxime was not used, with one of the reasons being "it may increase mortality".[5] However, it is often difficult to argue from this point of view when presenting a case that died (although I do acknowledge that using the 'what do we have to loose' reasoning, one could probably justify intravenous crushed granite). Nevertheless, particularly in a patient presenting as an acute acetylcholinesterase poisoning, a cholinesterase reactivator should be considered.

Pralidoxime (PAM) is a cholinesterase reactivator that appears to be effective if it is administered within 24 hours of the poisoning, as the organophosphate-cholinesterase bond becomes relatively permanent after 48 - 72 hours. The chloride salt of pralidoxime is usually recommended, as it has less side-effects than the iodide salt (repeated asystole has been reported with the administration of pralidoxime iodide[6]), is just as effective, and can be used in patients who have iodide sensitivity.[7] However, it is most effective in treating the nicotinic symptoms (e.g. muscular fasciculations and paralysis) of certain organophosphate poisonings, and appears to be relatively ineffective against dimefox, dimethoate, methyl diazinon, mipafox and schradan and against carbamates (it may even increase carbamate toxicity because PAM has a weak anticholinesterase activity).[8] It does not cross the blood brain barrier and therefore has no beneficial effects for central nervous system symptoms.

Pralidoxime chloride is relatively non toxic, although rapid intravenous administration may be associated with nausea, tachycardia, disturbances of vision, headache, dizziness and weakness due to transient neuromuscular blockade. It has an elimination half-life of 1.2 hours and is normally excreted by the kidneys.[9]

However, (as acknowledged by Teague *et al*[5]) some reports have questioned its effectiveness,[10,11] with one stating that 'PAM has no place' in the current management of organophosphate poisoning.[6] In one study, no clinical evidence of reactivation of the phosphorylated cholinesterase was observed,[12] and in another study, the use of PAM (4 gm in the first 24 hr followed by 1 gm daily for 5 days) was not associated with an improvement in outcome.[13] Nevertheless, the doses used in these studies may have been insufficient,[14] as other studies have reported beneficial effects from high dose PAM administration.[15,16,17]

To reach the suggested effective plasma concentration of 4 mg/L, PAM should be administered as a 1 g intravenous bolus, followed by an infusion of 0.5 g/hr (i.e. 12 g/day).[18] Some have even recommended higher doses (e.g. 30 mg/kg, followed by 8 mg/kg/hr,[16] and in children 25 - 50 mg/kg followed by a continuous infusion of 10 - 20 mg/kg/hr[17]), following the report that a plasma concentration of 4 mg/L does not permit the full exploitation of the therapeutic potential of pralidoxime.[19]

In the case presented by Teague *et al*,[5] PAM would probably have made little difference to the final outcome (indeed if it was used, we may now be discussing another case where PAM was associated with a cardiac arrest), and, as Teague *et al* acknowledge,

the outcome may have more likely been different if a rapid diagnosis (i.e. an earlier look for the 'Canary') and an earlier administration of atropine had occurred.

Dr. L. I. G. Worthley
Department of Critical Care Medicine
Flinders Medical Centre
SOUTH AUSTRALIA 5042

REFERENCES

1. Faunce TA, Bidstrup H, Nickells JS. Brown snake envenomation complicating near drowning and amphetamine overdose. Critical Care and Resuscitation 1999;1:360-361.
2. William of Ockham (or Occam) c. 1285-1349.
3. Ewing M. Occam's razor. Med J Aust 1975;2:443-444.
4. Cox JC, Moisidis AV, Shepherd JM, Drane DP, Jones SL. A novel format for a rapid sandwich EIA and its application to the identification of snake venoms.J Immunol Methods 1992;146:213-218.
5. Teague B, Peter JV, O'Fathartaigh M, Peisach AR. An unusual cause for cardiac arrest. Critical Care and Resuscitation 1999;1:362-365.
6. Scott RJ. Repeated asystole following PAM in organophosphate self-poisoning. Anaesth Intens Care 1986;14:458-460.
7. Ellin RI, Wills JH. Oximes antagonistic to inhibitors of cholinesterase II. J Pharm Sci 1964;53:1143-1150.
8. Taylor P. Anticholinesterase agents. In: Gilman AG, Goodman LS, Rall TW, Murad F, eds. The pharmacological basis of therapeutics. New York: MacMillan, 1985;110-129.
9. Karalliedde L. Organophosphorus poisoning and anaesthesia. Anaesthesia 1999;54:1073-1088.
10. Johnson S, Peter JV, Thomas K, Jeyaseelan L, Cherian AM. Evaluation of two treatment regimens of pralidoxime (1gm single bolus dose vs. 12 gm infusion) in the management of organophosphorus poisoning. J Assoc Physicians India 1996;44:529-531.
11. Cherian AM, Peter JV, Samuel J, Jaydevan R, Peter S, Joel S et al. Effectiveness of P2AM in the treatment of organophosphorus poisoning. A randomised, double blind placebo controlled clinical trial. J Assoc Physicians India 1997;45:22-24.
12. Genandran A. Organophosphate insecticide poisoning and its management. Anaesth Intens Care 1974;4:361-368.
13. de Silva HJ, Wijewickrema R, Senanayake N. Does pralidoxime affect outcome of management in acute organophosphorus poisoning. Lancet 1992;339:1136-1138.
14. Johnson MK, Vale JA, Marrs TC, Meredith TJ. Pralidoxime for organophosphorous poisoning. Lancet 1992;340:64.
15. Tush GM, Anstead MI. Pralidoxime continuous infusion in the treatment of organophosphate poisoning. Ann Pharmacother 1997;31:441-444.
16. Balali-Mood M, Shariat M. Treatment of organophosphate poisoning. Experience of nerve agents and acute pesticide poisoning on the effects of oximes. J Physiol Paris 1998;92:375-378.
17. Schexnayder S, James LP, Kearns GL, Farrar HC. The pharmacokinetics of continuous infusion pralidoxime in children with organophosphate poisoning. J Toxicol Clin Toxicol 1998;36:549-555.
18. Thompson DF, Thompson GD, Greenwood RB, Trammel HL. Therapeutic dosing of pralidoxime chloride. Drug Intell Clin Pharm 1987;21:590-593.
19. Worek F, Backer M, Thiermann H, Szinicz L, Mast U, Klimmek R, Eyer P. Reappraisal of indications and limitations of oxime therapy in organophosphate poisoning. Hum Exp Toxicol 1997;16:466-472.

Hyperbaric oxygen therapy: time for change

Therapies based upon sound scientific principal and favourable observational experience have in the past readily become entrenched in medical practise. Hyperbaric oxygen for carbon monoxide poisoning is one such therapy. For researchers to have sought to challenge these traditional practises or therapeutic dogma by applying the methods of the prospective randomised controlled trial, says much about the scientific rigour of modern medicine.

Scheinkestel *et al*[1] are the latest group to test the traditional role of hyperbaric oxygen in the treatment of carbon monoxide poisoning and the Journal welcomes a further commentary by this group on this important issue.[2] These authors have been acknowledged as providing one of the largest and most thorough investigations to date on this question.[3]

Moon and Delong in their editorial accompanying the report would have us believe that this latest work changes nothing.[4] Surely the weight of prospective randomised trials not favouring hyperbaric oxygen use in patients with carbon monoxide poisoning now places the burden of proof on those who have the alternative view. Scheinkestel *et al*, must be congratulated for their work, and one must agree with them that it is time for change.

On current evidence, the best treatment for severe acute carbon monoxide poisoning is normobaric high flow oxygen (14 L per minute) by non-occlusive facemask (100% oxygen for ventilated patients) for at least 3 days (or up to 6 days in patients who remain symptomatic). Hyperbaric units that continue to use hyperbaric oxygen for carbon monoxide poisoning should do so within the bounds of a randomised controlled trial, to explore whether remaining subtleties, such as faster application or different hyperbaric recipes, improve the result compared with high concentration normobaric oxygen.

Dr. A. W. Holt
Department of Critical Care Medicine
Flinders Medical Centre
SOUTH AUSTRALIA 5042

REFERENCES
1. Scheinkestel CD, Bailey M, Myles PS, Jones K, Cooper DJ, Millar IL, Tuxen DV. Hyperbaric or normobaric oxygen for acute carbon monoxide poisoning: a randomised controlled clinical trial. Med J Aust 1999;170:203-210.
2. Scheinkestel CD, Millar IL Let's leave behind dogma!. Critical Care and Resuscitation 1999;1:400-403.
3. Hyperbaric oxygen did not reduce persistent neurologic sequelae of carbon monoxide poisoning. Evidence-Based Medicine 1999;4:124.
4. Moon RE, DeLong E. Hyperbaric oxygen for carbon monoxide poisoning. Med J Aust 1999;170:197-198.

The logo

In September 1996 the Australasian Academy of Critical Care Medicine (AACCM) considered that a logo would be useful to promote its message. An advertising agency was consulted with the request that the image for the logo should be 'simple, stylised and conservative' and one representative of 'scholarly and academic activity - yet not ornate, ancient or ostentatious'.

The logo (as shown) was presented to the Board of the AACCM with the explanation that it 'takes the form of a shield, typical of universities and academic institutions. The shield is comprised of the elements of hands, book and heart, literally suggesting care, knowledge, and quality of life. It is believed that these attributes are relevant to Critical Care and the aims of the Academy. The hands are cupped, embracing the lower half of the shield and the knowledge symbolised by the open book; together they support the heart, itself a symbol of care but also depicting the sustaining of life.'

The logo was accepted as the logo for the Australasian Academy of Critical Care Medicine at a meeting of the board in November 1997.

The Australasian Academy of Critical Care Medicine