Improving the medical management of organophosphorus pesticide poisoning through health services research and training

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The work presented in this thesis describes the results of research carried out in 2 Sri Lankan hospitals from 2006 to 2010.

The results presented in this thesis are my own work accomplished under the supervision of Professor Nick Buckley and Professor Andrew Dawson. This material has not been submitted either in whole or in part at this or any other university.

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Abstract

Organophosphorus (OP) self-poisoning is a major global public health problem resulting in over 200,000 deaths each year with a case fatality of 15-30%. Early medical management consists of effective resuscitation and targeted antidote therapy.

This thesis argued that health services research and rural doctor training could be used to improve the medical management of OP poisoning in a resource limited rural Sri Lankan setting, where the delivery of critical care is limited by a lack of diagnostic tests and resuscitation skills. Research investigating the use of AChE in guiding clinical management, and research that measured the effectiveness of rural resuscitation training, were the two streams of research that were the founding pillars of the thesis. These two elements were linked together through a conceptual framework of knowledge translation, each operating at different points in the continuum of evidence being translated into practice.

An AChE POC test (Test-mate ChE) was demonstrated to provide accurate and reliable results in acute OP poisoning when compared with a reference laboratory. A survey based analysis of clinician’s knowledge, attitudes and practices found that most doctors valued the test, but also surprisingly found that doctors who were more experienced with AChE valued the test less. Low proportions valued the test in guidance of acute poisoning management (e.g. to direct oxime therapy and early discharge).

A systematic review highlighted a lack of supporting primary evidence for the use of AChE in relation to oxime use and discharge decisions. Advice on interpretation of AChE and caution about pitfalls in measurement were also lacking. These areas need to be addressed to optimise provision of AChE POC devices.
A train-the-trainer (TTT) model of resuscitation education was effective in improving resuscitation knowledge and skills in rural peripheral hospital doctors, and improvements in most components were sustained for 12 weeks. This demonstrated the effectiveness of using non-specialist doctors to conduct peer-led advanced life support (ALS) training in a low resource peripheral hospital setting, using objective knowledge and skills endpoints according to standardized metrics.

A systematic review of resuscitation of OP poisoning found no texts solely focused on acute initial management. An ‘OP specific’ ALS guideline was proposed based on consistent literature recommendations highlighting the importance of rapid atropinisation (doubling dose regimen) to be delivered simultaneous with immediate airway, breathing and circulation management. Other antidotes such as oximes should not be in the ALS guidelines.

A participatory action research approach was used to address practical problems through close engagement with health services and local training systems. The experience from both streams of research showed that such strategies were integral to the completion of the studies employed in the low resource rural setting. The thesis demonstrated health services research and training could be used to close the evidence-practice gap, and may have a role in the improvement of the medical management of OP poisoning. Future research should investigate clinical endpoints associated with the use of AChE in guiding OP poisoning management, the development of decision rules offering practical guidance in measurement and interpretation of AChE, the evaluation of OP specific ALS guidelines, and the sustainability rural resuscitation training programs.
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<th>Abbreviation</th>
<th>Full Form</th>
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<tbody>
<tr>
<td>AChE</td>
<td>Acetylcholinesterase</td>
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<tr>
<td>ACLS</td>
<td>Advanced cardiac life support</td>
</tr>
<tr>
<td>ALS</td>
<td>Advanced life support</td>
</tr>
<tr>
<td>ANOVA</td>
<td>Analysis of variance</td>
</tr>
<tr>
<td>BLS</td>
<td>Basic life support</td>
</tr>
<tr>
<td>CBPR</td>
<td>Community-based participatory research</td>
</tr>
<tr>
<td>CPR</td>
<td>Cardiopulmonary resuscitation</td>
</tr>
<tr>
<td>DVD</td>
<td>Digital video disc</td>
</tr>
<tr>
<td>ETU</td>
<td>Emergency treatment unit</td>
</tr>
<tr>
<td>ECG</td>
<td>Electrocardiogram</td>
</tr>
<tr>
<td>ER</td>
<td>Emergency Room</td>
</tr>
<tr>
<td>GEE</td>
<td>Generalised estimating equations</td>
</tr>
<tr>
<td>HO</td>
<td>House officer</td>
</tr>
<tr>
<td>ILCOR</td>
<td>International liaisons committee on resuscitation</td>
</tr>
<tr>
<td>ICU</td>
<td>Intensive care unit</td>
</tr>
<tr>
<td>KT</td>
<td>Knowledge translation</td>
</tr>
<tr>
<td>LOQ</td>
<td>Limits of quantification</td>
</tr>
<tr>
<td>MCQ</td>
<td>Multiple choice question</td>
</tr>
<tr>
<td>MO</td>
<td>Medical officer</td>
</tr>
<tr>
<td>OP</td>
<td>Organophosphorus pesticide</td>
</tr>
<tr>
<td>OPD</td>
<td>Outpatient department</td>
</tr>
<tr>
<td>PAR</td>
<td>Participatory action research</td>
</tr>
<tr>
<td>PChE</td>
<td>Plasma cholinesterase, pseudocholinesterase or butyrylcholinesterase</td>
</tr>
<tr>
<td>PEFR</td>
<td>Peak expiratory flow rate</td>
</tr>
<tr>
<td>PGIM</td>
<td>Post graduate institute of medicine</td>
</tr>
<tr>
<td>POC</td>
<td>Point-of-care</td>
</tr>
<tr>
<td>RBC-AChE</td>
<td>Red blood cell acetylcholinesterase</td>
</tr>
<tr>
<td>RCT</td>
<td>Randomised controlled trial</td>
</tr>
<tr>
<td>SACTRC</td>
<td>South Asian clinical toxicology research collaboration</td>
</tr>
<tr>
<td>SHO</td>
<td>Senior House Officer</td>
</tr>
<tr>
<td>TTT</td>
<td>Train-the-trainer</td>
</tr>
<tr>
<td>WHO</td>
<td>World health organisation</td>
</tr>
</tbody>
</table>
Publications and Presentations

Papers embodied in this thesis: contributions and acknowledgements

Chapter 1


Contributions:
BR and NB conceived and designed the study together. BR performed the literature review, and drafted the manuscript. NB provided guidance and edited the manuscript.

Chapter 4


Contributions:
BR and NB conceived the study and designed the protocol. NB and AD obtained research funding. BR and AD undertook recruitment of participating centres. BR contributed to the collection of the clinical data, and BR, HR, FW contributed to collection of the laboratory data. All authors were involved in the data analysis and interpretation. SB provided statistical advice regarding the study design and data analysis. BR drafted the manuscript and all authors contributed substantially in its revision. BR takes responsibility for the paper as a whole.

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Contributions:

BR and NB jointly designed the study. BR carried out the methodology, analysis and drafted the manuscript. NB helped with the analysis and revised manuscript drafts. TN advised on statistical aspects of the analysis and manuscript drafts. All authors read and approved the final manuscript.

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Chapter 6


Contributions:

BR Conceived and designed the study, performed the experiments, analyzed the data and wrote the manuscript.

AHD also contributed towards the analysis by facilitating the research assistants and other infrastructure. He also made intellectual contributions and revised the Manuscript

TN provided statistical advice and revised the manuscript.

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Other publications during PhD candidature

Published in indexed journals


Other publications


Presentations International and National conferences during PhD candidature

Oral presentations (by invitation)


**Oral presentations**


**Poster presentations**


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Conflicts of interest

None declared
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I am very grateful for all my trusty research assistants; including Voleena, Amal, Sameera, Sanjeeva, Manori and Prabash; and Vinothan and Manjula in the AChE project, and all the others who I worked with over the fieldwork period. Thank you also to the lead clinicians such as Dr Shaluka Jayamanna in Polonnaruwa, and Dr Dhammika De Silva, Dr P Bandara and Dr W Attapattu from the PD office in Anuradhapura, and to my friend Dr Ayanthi Karunaratne. My gratitude goes out especially to all the trainers who worked in the train-the-trainer project, and to all the doctors who were involved in my two research projects carried out in the NCP.

Thank you to the other special people whom I met along the way, and who inspired me, and helped me in the journey; Kent Olson, Chuck Pozner, Lakshman Karaliedde, Rezvi Sherrif, Mudyanse Rasnayake, Kamani Wanigasuriya, Nilmini Wjesuriya, Dushyanthi Jayasekera, Christie Weeramantry, Mr Lionel Sirisena, Venerable Mahinda, Bhikkuni Kusuma, Nayomi Munaweera, Suresh David, Darren Roberts, Romesh Singam, Indika Gawarammana, Michael Eddleston, Quinton Temby, Trevor Vickers, Sean Perera, Teresa Neeman, Mihirini De Soyza, Jarad Martin, Steve Bowe, Melita Long, Zoe Rodgers, Sue Hertzberg, Chris Curry, Gerard O'Reilly, Serena Ayers and Alison Jones. Thanks also to Sanjay Bhagia, who guided me in simulation training, and Julianne Hammond, who helped me focus on the positive whilst persevering with my goals!

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Last, but not least, a heartfelt thank you goes to my partner, Sanna, who supported me through difficult years of combined PhD study and emergency medicine training. Thanks for your understanding and for being a source of light in my life.

Despite this extensive summary, there are countless others whom I would like to thank and acknowledge, but they must sadly remain “nameless” in this exposition.

The final acknowledgement, and perhaps most important one, is to the patients themselves and the doctors who looked after them. Many of these hospital doctors let me study them despite their busy schedules, whilst working hard to improve the lives of pesticide poisoned patients. The following story is dedicated to the patients and the doctors of rural Sri Lanka.
It was quarter past midnight, when I was standing in the intensive care unit (ICU) for a 400-bed secondary referral hospital enjoying some momentary air-conditioned respite from the outside tropical heat. After an evening of trawling the medical wards checking on patients in clinical studies, and supervising research assistants who carried out the data collection, the ICU was my last stop before retiring for the night. Out of the 6 ventilated beds in the unit, 3 were occupied by intubated and mechanically ventilated organophosphorus (OP) poisoned patients who had ingested pesticides through a variety of impulsive acts.

The first patient was a 40 year-old female who had recovered from 3 cardiac arrests within the preceding 2 hours, and was on an infusion of inotropes (cardiovascular drugs) that seemed to be helping her maintain a blood pressure enough to keep her alive. I asked the doctor, who was about 3 years out of medical school in seniority, whether this particular patient would be receiving oxime therapy. Oximes are an antidote whose use is controversial in the management of OP poisoning. His answer was that it depended upon the Consultant who was looking after the patient because there were no clear protocols on its use, and no means to measure its effectiveness.

This patient had been admitted on a day where she would get oximes, and I wondered to myself, “was it going to be important in this patient? Would it make a difference? Will the inotrope infusion make a difference to her survival? Or will she arrest again no matter what we do?”

“Perhaps an acetylcholinesterase (AChE) level, if available, could be helpful in guiding this difficult decision”, I quietly thought to myself as I watched this motionless lady lie helplessly connected to an artificial ventilator through a breathing tube. AChE is a biomarker that can
give an indication of both the levels of poisoning and the effectiveness of oxime therapy, and the portable field kit that I had chosen to study could measure it.

In the next bed lay another intubated patient, a 26 year-old male, who was bare-chested, and donning a sarong for cover of his bottom half. His attire was entirely appropriate as ICU was still not “cold” despite being cooler due to the air conditioned, a welcome change from the humid heat that was present outside and in the regular ward setting. This man had been in the ICU for 2 weeks and was being treated for aspiration pneumonia rather than the direct toxic effect of the poison, which had long since left his body.

I found out about the circumstance of this patient’s admission, upon further inquiry from my ICU night doctor friend, and learned that he was transferred from a peripheral hospital with an unprotected airway, despite having a stomach full of pesticides and alcohol. He was close to having a respiratory arrest upon arrival in the secondary referral hospital. This junior ICU doctor was quite frustrated when explaining this scenario to me. He said he often received patients from peripheral hospitals, who had travelled for up to 2 hours in the back of an ambulance without nurse or paramedic, and that it was common for the patients to have not received the adequate initial advanced life support and airway protection prior to transfer.

It was easy to be critical of the doctors in the periphery but I wondered if the problem was more complex than it seemed on the surface? I had learned from a colleague’s local research that primary care doctors in the peripheral hospitals were professionally isolated and found it hard to access training. I had observed a lack of training in resuscitation for junior doctors even in the larger referral centres, and thought resuscitation education must be even more scarce in the periphery.

“Surely, there must be something that can be done to address this problem?” I reflected, wondering about a research intervention that could provide resuscitation training to the
peripheral hospital doctor population, but that hopeful thought would have to wait for another day as at that moment I still had a ward round to complete.

Finally, the last patient whose observations were collected on my routine ICU visit, was a 20 year-old female who had been distressed about a relationship that had ended, providing her with an additional stressor that contributed to her drinking poison that night. She was resuscitated in the ward and had come to ICU intubated like the other two patients.

“What would be her fate?” I wondered, whilst my mind slowed a little, already full of a heap of unanswered clinical questions about improving health care systems that could perhaps lead to improved care in these critically ill poisoned patients. “Would she also receive oxime therapy?” I continued to ponder, “And if so, is there evidence to distinguish whether this was the best therapy for her right now?” “If she arrested again, what would be the best treatment for her in that moment – do we even know?”

Such questions kept rapidly appearing, but the strategies to find some of the answers would form much more slowly, over the months, and even years to come. All I knew at that moment was that this patient was too young to die; and if something was possible make a positive difference in some small way, then we had to at least try…

The following thesis is dedicated to the pesticide poisoned patients and their families, and to the medical staff that have been entrusted with their care.
Preface – Introduction and aims of thesis

Self-poisoning is a major worldwide public health problem, resulting in over 300,000 deaths annually. Organophosphorus (OP) pesticides are the most common agents accounting for approximately 200,000 deaths each year in Asia (1-3). Case fatality is between 15-30% with current best practice, but there has been limited research dedicated to reducing the mortality and morbidity of this condition.

The high case fatality is multifactorial and has been linked to several factors including the toxicity of the pesticide, the quality of medical treatment and a lack of resources in the region where the practice of self poisoning is prevalent (4). Early medical management that includes effective resuscitation and targeted antidote therapy is often lacking (5). My research aimed to demonstrate that health services research and training were two important vehicles that could act to close the evidence to practice gap and thereby improve the medical management of OP poisoning.

I used the conceptual framework of translational research, also known as “knowledge translation” (6), to link together two streams of research that addressed the topic of OP poisoning management, which may otherwise appear unrelated. These streams consisted of research investigating the use of AChE in guiding clinical management, and research that measured the effectiveness of resuscitation training in a rural setting. Both streams tested strategies focused on improving medical management of a single condition, OP poisoning, with an overarching goal of reducing mortality and morbidity.

The different studies operate at different stages of the continuum in the translation of evidence into practice, as summarized in Figure 1. This diagram also highlights how both research topics, AChE and Resuscitation, represent more than one of the three component’s that have been described as integral to the process of knowledge
Figure 1 Schema of a translational research model for closing the evidence-to-practice gap.

Shows the contribution of individual chapters to different steps in the process of evidence being translated into practice. Schema based on a figure by Lang et al. (8) and adapted according to Arnold et al. (6).
Translation; knowledge synthesis, exchange and application (6, 7).

Peripheral hospitals are frequently the first point of contact with health services for OP poisoned patients. Half of my research focused on exploring an educational strategy in this setting, and the other half addressed a deficiency in laboratory facilities at secondary referral hospitals by providing biomarkers of OP poisoning through point-of-care (POC) testing. Specifically, I evaluated the effectiveness of a train-the-trainer (TTT) model of resuscitation education for peripheral hospital doctors, and I studied the validity of an acetylcholinesterase (AChE) POC test in acute OP poisoning, as well as the effect its results have on the knowledge, attitudes and practice of treating clinicians at secondary referral hospitals.

Both projects address a gap in the translation of existing knowledge, and recommendations into practice, and each targets aspects of an underdeveloped emergency and critical care service for acutely poisoned OP patients in resource limited rural hospital settings.

**Origin of research projects and details of fieldwork**

Before I embarked on the path of higher degree research through the Australian National University, I was an Emergency Medicine specialist-in-training working in an urban emergency department in Wellington, New Zealand. I had an interest in medical education and research, and this background combined with my discovery of specific on-the-ground deficiencies in the Sri Lankan rural health services led me to the current research projects. The South Asian Clinical Toxicology Research Collaboration (SACTRC; [www.sactrc.org](http://www.sactrc.org)) is a research collaboration whose objective is to reduce mortality from poisoning through capacity building research that utilises a range of strategies. Working through SACTRC’s infrastructure I conducted my research entirely
in Sri Lanka owing to the high prevalence of OP poisoning and consequent burden of disease.

The clinical research was conducted at hospitals in the North Central Province, the largest province in Sri Lanka. Employment is largely in agriculture and consequently agrochemicals such as OP pesticides are widely available. The POC testing research was based at the two larger referral hospitals located in the cities of Anuradhapura and town of Polonnaruwa, (Figure 2), and the resuscitation training work was conducted at smaller peripheral hospitals throughout the province. For the purpose of the argument presented in this thesis, these two referral hospitals were both considered as central “rural” hospitals because their health services shared similar resource constraints, in terms of resuscitation and laboratory facilities, when compared to the larger cities located in Sri Lanka’s commercial centres such as Kandy or Colombo. The research office was in a collaborating local university, University of Peradeniya, which was located close to Kandy, the second largest city in Sri Lanka.

My aim whilst working with SACTRC in Sri Lanka was to find practical ways of addressing the challenge of improving the medical management of OP poisoning and to participate in organizational change whilst conducting research. Thus the research strategy I employed could be considered a form of participatory action research(9, 10).

At the same time both the introduction of the POC test, and study of the TTT education model had characteristics of complex interventions(11); such as engagement with the local health service, and having more than one phase of development and evaluation for some interventions.

The research methodology I used was adapted to the health care setting where my fieldwork took place. At these hospitals there was a general lack of research culture, a paucity of methodical note taking or audit, and lack of familiarity or acceptance of the benefits of coordinated research such as randomized studies. These rural hospitals are
Sri Lanka is an Island nation of 64,000 square kilometers, and a population of 21 million people.

It is a low to middle income country with an annual income of USD $5,500 per capita, and life expectancy of 71 years for men and 78 years for women\(^{(13)}\). The figure highlights the North Central Province, and the inset shows the distribution of central and peripheral hospitals. The two central referral hospitals are marked with shaded circles and inner dot. The remaining hospitals vary in size from larger peripheral hospitals (marked with a shaded circle), to small peripheral hospitals and peripheral units (shown as black dots).
focused on delivering clinical care to very high volumes of patients with limited infrastructure.

**Gap in emergency and critical care training in rural hospitals**

The Postgraduate Institute of Medicine (PGIM) coordinates postgraduate training in all accredited specialties in Sri Lanka (including medicine, surgery, paediatrics and obstetrics and gynaecology). At the time I embarked on my fieldwork in 2006 there were no dedicated qualifications for intensivists or emergency physicians. This left a void in the provision of critical care, and particularly in the realm of resuscitation training and supervision. This situation is compounded by the fact that only a low proportion (less than 20%) of medical graduates undertake any postgraduate training, and these people are concentrated in urban hospitals. There are very few, or no, doctors undergoing postgraduate specialist training in peripheral rural hospitals where pesticide poisoned patients generally first present. From 2006 to 2010, during which time my fieldwork was conducted, no national resuscitation training programs or ad hoc resuscitation training was available in the peripheral hospitals. Since then Sri Lanka has experienced advances in the nationwide Emergency Medicine strategy that includes an active Emergency Medicine specialist training program, which was launched in 2013(14). These developments would suggest an increased access to resuscitation training for the small number of doctors who were training in Emergency Medicine, in the large urban centres where specialist training occurs. However, despite such advances in the large urban centres where specialist training occurs, a national resuscitation training program was still absent for the peripheral hospitals at the time this thesis was published.

**Resource limitations in emergency and critical care service provision**

Resource limitations in rural areas have a strong impact on the emergency care of OP poisoned patients. In referral hospitals, laboratory tests are not commonly used. Patients are diagnosed and managed largely based on clinical findings. Access to
basic tests (biochemistry, haematology) is very limited. There is no laboratory accreditation enforcement so the quality of results can be unreliable.

There are limited numbers of intensive care beds, with the largest (1600 bed) secondary referral hospitals only having 8-10 ventilated beds within their medical intensive care unit (ICU).

Nurse and doctor to patient ratios are much lower than in western countries. It is not uncommon for a large referral hospital to only have two consultant physicians managing up to 200 patients each. Furthermore, the same consultant physicians are in charge of the medical ICU and the care of ventilated patients. Most of the middle tier doctors, senior house officers (SHO’s), who are responsible for delivery of patient care and supervising intern doctors are between 3-4 years post graduation. They also all have heavy clinical loads. Primary hospitals range in size from central dispensary units without inpatient facilities that are manned by a single doctor, to larger base hospitals with more than ten doctors. Such hospitals do not have specialist-trained doctors, and there is a limited infrastructure for training. Often the nearest training may occur several hours away and an inability for doctors at these locations to obtain leave from clinical duties leads to professional isolation(15).

‘Participatory action research’ - framework for methods used

This research also has many features of participatory action research (PAR) which involves collective, self reflective inquiry that researchers and participants undertake, so that they can understand and improve upon the practices in which they participate (9, 16). The reflective process is directly linked to action, influenced by the understanding of history, culture, and local context and is embedded in social relationships. The process of PAR should be empowering and lead to people having increased control over their lives(9). PAR is a growing field that is noted to be of
particular value in the problems affecting low income countries, and in addressing the 10:90 gap, a term highlighting that only 10% of research funds are addressing 90% of the global disease burden (9, 16-18). Another term for PAR that is seen in the literature is community based participatory research (CBPR) (16).

The studies I carried out were reflective of this approach on many levels including the conduct of research through collaboration and development of partnerships with local authorities, development of sustaining and trusting community-researcher relationships, the assessment of barriers to achieving better health, and the dissemination of findings to practice and policy. Reflections on the use of these type of methods will be addressed in the final chapter.
Chapter outline

The challenge of improving the medical management of OP poisoning in a resource limited rural setting is evaluated through interventional studies, and systematic reviews that form the chapters of this thesis. The chapters have been conventionally ordered with the background and systematic reviews at the beginning, followed by the description of experimental work. However, the research was undertaken in a different order, which is outlined below.

The thesis starts with a review of the management of OP poisoning (Chapter 1) which describes how effective resuscitation, and targeted antidote therapy, are the accepted cornerstones of acute management in the incidence of severe OP poisoning. Improvements in these two aspects of medical management are the basis for the two streams of intervention, acetylcholinesterase (AChE) POC testing, and rural resuscitation training, which is the focus of the remainder of the thesis.

The first half of the research assesses the introduction of an acetylcholinesterase POC test (Test-mate ChE 460) designed in North America for occupational use in the surveillance of agricultural workers rather than for use in the setting of severe OP self-poisoning. The POC Test-mate machine is first validated in this population (Chapter 4). Thereafter the change in knowledge, attitude and practice of clinicians with exposure to seeing AChE test results was studied, with the expectation that the introduction of this widely recommended test may improve all three (Chapter 5). It became clear after the analysis of this study that interpretation of AChE results was not straightforward. Thus, I conducted a detailed systematic review of the literature on the range of specific recommendations for the use of AChE in the management of OP poisoning, and the degree such recommendations were backed up by evidence (Chapter 2).
The second stream of research was related to advance life support (ALS). I observed preventable poor outcomes in OP poisoned patients that were largely due to poor resuscitation. Frequently such results were observed in transferred patients who had been inadequately resuscitated at the peripheral hospitals where they first presented. I also observed a lack of practical training and supervision in resuscitation. This motivated me to carry out some pilot training work using mannequins, video technology and scenarios that led to shifts in ALS knowledge and skills. This pilot work is what inspired my study that evaluated the effectiveness of a train-the-trainer (TTT) model of resuscitation in peripheral hospital doctors (Chapter 6). It also addressed the shortage of specialist trainers through the use of peripheral hospital doctors to run peer-led resuscitation education workshops.

In the context of doing general advanced life support training, it became apparent that specific OP ALS guidelines might more directly address the challenge of resuscitation in the context of OP poisoning. Thus, I conducted a systematic review (Chapter 3) that identifies which components are broadly accepted, and the sequence in which antidotes should be recommended, and this was incorporated into an OP specific ALS guideline. The TTT study described in Chapter 6 did not test the proposed guideline because the first step was to find out whether a "model" of training for rural hospitals was feasible and effective in teaching a previously validated guideline such as standard ALS.

Chapter 7 summarizes the contributions, strengths and weaknesses of the thesis and outlines suggestions for future research and policy changes relating to AChE POC testing, and resuscitation training for OP poisoned patients.
Chapter 1: Overview of organophosphorus pesticide poisoning

Published: This chapter has been published as a book chapter in an emergency medicine instructional text.

1) Anticholinesterase pesticides including organophosphorus (OP) compounds and carbamates are highly toxic insecticides requiring emergency management.

2) They are responsible for over 200,000 deaths annually worldwide. Most follow deliberate self-poisoning and occur in the developing world.

3) The primary toxic mechanism is inhibition of neuronal acetylcholinesterase that causes an acute cholinergic crisis and results in parasympathetic effects such as diarrhoea, urination, miosis, bronchorrhoea, emesis, lacrimation and salivation (DUMBELS). It can also cause cardiac effects such as brady- or tachycardia, and hyper- or hypotension, neuromuscular junction blockade and coma.

4) Initial management includes resuscitation (airway, breathing and circulation), oxygen, IV fluids, large doses of atropine, and oximes.

5) Measurement of biomarkers such as red blood cell acetylcholinesterase (RBC-AChE) and plasma cholinesterase (PChE) may guide management including when to start, continue and stop oxime therapy.

6) Ongoing reassessment of respiratory status including the need for endotracheal intubation, and for atropine is essential to avoid morbidity.

7) The delayed onset of respiratory failure due to the ‘intermediate syndrome’ up to 5 days later mandates prolonged careful observation.

8) Carbamates are similar to OPs but have a more rapid onset and the inhibition of AChE is reversible. There is thus no benefit from the use of oximes.

9) There is a large variation in case-fatality for OP from <2% to >30% and with carbamates from 2% to 10%.
**Introduction**

Organophosphorus (OP) compounds and carbamates belong to the group of anticholinesterase drugs and are amongst the most widely used insecticides. Organophosphates are esters of phosphoric acid and are the active ingredients of many insecticides. Examples include parathion, malathion, chlorpyrifos, dichlorvos, etc. Accidental or suicidal exposure can cause life-threatening poisoning (19). The management of severe toxicity is the focus of this chapter because of its relevance to the field of emergency medicine.

OPs are extremely toxic chemicals that present with a myriad of clinical problems in poisoning which lead to difficulties in management. Oral ingestion in cases of deliberate self harm may involve doses 100-1000 fold greater than occupational exposure.

Anticholinesterase pesticides are a heterogenous class of agents with over 100 OP compounds and over 20 carbamates in use. There is marked variation in toxicological manifestations and severity, which makes risk assessment and management more complex(3, 19). It is best to consider all oral poisonings with anticholinesterase agents as being potentially life threatening (20).

Certain OP anticholinesterases have been developed as chemical warfare agents such as GA [tabun], GB [sarin], and GD [soman]. These are extremely toxic to humans and have a rapid onset of effects with more severe CNS manifestations. They have occasionally been used in recent times in warfare and terrorist attacks, but clinical experience and research are limited(19, 21).

Carbamates are similar to OP in mechanism, presentation and treatment. They feature the carbamate ester functional group. Examples include aldicarb, carbofuran, fenoxycarb, carbaryl, ethienocarb, and fenobucarb. Carbamates have been regarded
as less toxic because of their reversible binding to acetylcholinesterase (AChE). Although the duration of toxicity is thus shorter, the onset is rapid and many have a comparable case-fatality to OP compounds(22).

**Epidemiology**

Anticholinesterase poisoning is most common in rural areas of the developing world, where as per the WHO estimates, millions of people are affected annually(1). In Asia alone 200,000 deaths per year result from intentional ingestion of OP compounds, with an estimated case fatality of 15-30%(1-3, 5). While much less common in the developed world, OP poisoning remains significant and still accounts for a substantial proportion of severe poisonings, with comparable case fatality rates(23).

**Pathophysiology**

*Toxicodynamics*

Anticholinesterase pesticides inhibit esterase enzymes, especially acetylcholinesterase in synapses (AChE) and on red blood cell membranes (RBC-AChE), and butyrylcholinesterase in plasma, which is sometimes referred to as ‘plasma cholinesterase’ (PChE).

Inhibition of neuronal AChE prevents hydrolysis of the neurotransmitter acetylcholine (ACh) leading to its accumulation in both sympathetic and parasympathetic synapses (Figure 1-1). The initial effects predominate in the parasympathetic nervous system producing a range of clinical features known as the “acute cholinergic crisis”. These cholinergic features generally respond to high-dose atropine as they are due to action at the muscarinic Ach receptor. ACh accumulation also leads to central nervous system effects, sympathetic nervous system effects and neuromuscular junction blockade that are due to action on the nicotinic Ach receptor and these effects do not respond to atropine treatment. The exact combination of these different clinical features varies greatly depending on the particular OP compound.
Figure 1-1 Mechanism of organophosphorus (OP) poisoning- showing the three main reactions that occur; 1) reversible inhibition 2) reactivation and 3) irreversible inhibition (‘ageing’).

*Modified and reproduced with permission from Emergency Medicine Australasia 2000;12:22-37(24)*

OP-inhibited neuronal AChE sometimes undergoes reactivation restoring normal function. This occurs at a slow rate spontaneously, or it can be catalysed by oximes (see Figure 1-1). However a proportion of inhibited AChE also undergoes irreversible inhibition, a process known as ‘ageing’. Aged AChE cannot be regenerated even with oxime therapy. New enzyme needs to be synthesised to restore function if a significant proportion of the AChE becomes aged. The extent to which induced or spontaneous reactivation occurs is determined by the chemical structure of the OP. The half-life of ageing also depends on this and ranges from minutes to 33 hours(25).
**Toxicokinetics**

**Absorption**

All organophosphates are rapidly absorbed from the small intestine. Peak concentrations occur within a few hours after oral ingestion. Absorption after dermal exposure is slower and highly dependent on formulation.

**Distribution**

Organophosphates are a diverse group of compounds with a wide range of lipid/water solubility characteristics and have variable, but usually large, volumes of distribution (Vd).

**Metabolism-Elimination**

Most OP are metabolised in the liver to more active metabolites (–thions are converted to –oxons). These “pro–” poisons such as parathion, fenthion and chlorpyrifos are usually highly lipid soluble and are eliminated slowly from fat. The slow conversion of these substances may lead to delayed and/or prolonged cholinesterase inhibition. A range of enzymes may be involved in detoxifying reactions such as Cytochrome P450 (CYP450). A major route of elimination of the active oxon is through OP hydrolases such as paraoxonase(26).

**Clinical Features**

Four clinical syndromes are described in OP poisoning(26)

1) Acute cholinergic crisis (the most common) – see Table 1-1
2) Subacute proximal muscle weakness (‘Intermediate syndrome’)
3) OP induced delayed neuropathy (OPIDN)
4) Chronic OP induced neuropsychiatric disorder (COPIND)
## Table 1-1 Clinical syndromes and manifestations of anticholinesterase poisoning

(Table modified from (20, 27-30).

<table>
<thead>
<tr>
<th>Clinical syndrome</th>
<th>Onset of symptoms</th>
<th>Clinical Manifestations</th>
<th>Lab investigations or special tests</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Spectrum of features</td>
<td>Muscarinic features</td>
<td>Nicotinic features</td>
</tr>
<tr>
<td>Acute cholinergic syndrome</td>
<td>Immediately (peak onset usually by 6 hours)*</td>
<td>Parasympathetic activity</td>
<td>Fasciculations</td>
</tr>
<tr>
<td>(severity)</td>
<td></td>
<td>Diarrhoea</td>
<td>Muscle weakness</td>
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<td></td>
<td></td>
<td>Urination</td>
<td>Paralysis</td>
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<td></td>
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<td>Miosis</td>
<td>Respiratory failure</td>
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<td></td>
<td></td>
<td>Bronchorrhea</td>
<td>Sympathetic activity</td>
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<td></td>
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<td>Emesis</td>
<td>Mydriasis</td>
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<td></td>
<td></td>
<td>Lacrimation</td>
<td>Tachycardia and Hypertension</td>
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<td></td>
<td></td>
<td>Salivation</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>(also bradycardia and bronchospasm)</td>
<td></td>
</tr>
<tr>
<td>Severe Features</td>
<td>Hypotension and bradycardia (or less commonly tachycardia)</td>
<td>Hypotension and bradycardia (or less commonly tachycardia)</td>
<td>Hypotension and bradycardia (or less commonly tachycardia)</td>
</tr>
<tr>
<td>Intermediate Syndrome (IMS)</td>
<td>24-96 hours</td>
<td>Resolving</td>
<td>Classically presents with respiratory muscle weakness often requiring intubation and mechanical ventilation for a period of time. Neck muscle, bulbar and proximal limb muscle weakness.</td>
</tr>
</tbody>
</table>

* Exception is highly fat soluble OPs such as fenthion which initially present with mild features abut have severe features after the first 24 hours(32)
**Acute Cholinergic Crisis**

This crisis consists of muscarinic, nicotinic and central nervous system (CNS) features of anticholinesterase poisoning as shown in Table 1-1. Symptoms occur rapidly usually within 4-6 hours of exposure. In severe cases, life threatening respiratory failure develops rapidly due to excessive lung secretions and bronchospasm (muscarinic receptors); decreased level of consciousness (CNS effect involving both muscarinic and nicotinic receptors), and respiratory muscle paralysis (nicotinic receptors).

Cardiovascular effects include bradycardia or tachycardia, hypotension or hypertension, ventricular arrhythmias, and cardiac arrest. Gastrointestinal tract (GIT) effects include vomiting and diarrhoea.

**Intermediate Syndrome**

This was described in 1987 as the delayed onset of severe muscle weakness (including respiratory muscle paralysis) occurring from day 2 onwards after patients had made an initial recovery(33). It is characterized by proximal truncal muscle weakness, neck weakness and sometimes bulbar palsy, classically occurring 1-4 days after poisoning and after resolution of the initial cholinergic crisis(34).

This delayed onset of weakness can catch inexperienced clinical staff unawares and is a major cause of preventable death from OP poisoning. While the classical description is recognised, it is clear that the syndrome of delayed muscle weakness has a wide spectrum of severity ranging from sub-clinical to severe, and may occur with or without recovery from cholinergic effects, earlier or later than 24-96 hours(31).
Differential Diagnosis
The classical presentation of OP poisoning with muscle fasciculation, pinpoint pupils, decreased level of consciousness and respiratory signs poses few diagnostic challenges, with the most pathognomic sign being muscle fasciculations, most easily observed on the tongue. A decreased PChE or RBC-AChE confirms the diagnosis.

When there is no clear exposure history to anticholinesterase pesticides and the presentation is less than typical, the differential diagnosis is wide and will depend on the main symptom complex being exhibited. A patient with predominant dyspnoea, bronchorrhoea and wheeze may be mistaken as having cardiogenic pulmonary oedema or asthma(35). A patient with predominant CNS features and respiratory complications may be assumed to have a primary CNS problem and aspiration. Patients with profuse diarrhoea and vomiting may be mistaken to have gastrointestinal pathology. Other substances with overlapping manifestations such as clonidine, opioids, antipsychotic drugs, and chlorphenoxy herbicides should also be considered in a patient with an unknown poisoning.

Investigations

Biomarkers of exposure
When available PChE and RBC-AChE measurements are useful in clinical management. Both RBC-AChE and PChE have a wide normal range, and approximately 1:2000 normal individuals have no detectable PChE. PChE activity does not relate to the severity of poisoning, but is used as a sensitive marker of exposure to OP and to confirm the diagnosis. RBC-AChE correlates well with synaptic AChE function and is therefore a reasonably good marker of severity (see Figure 1-2). A major issue regarding the use of both RBC-AChE and PChE in clinical management of OP is the lack of availability of the tests. Bedside AChE detection kits are likely to become more widely available in the future management of acute poisoning.
Figure 1-2 Interpretation of biomarkers used in the management of anticholinesterase poisoned patients.

(a) and (b) An increase in red blood cell acetylcholinesterase (RBC-AChE) activity after each bolus dose of pralidoxime. Continued ongoing response suggests that ongoing therapy may have been beneficial in the patient shown in (b). The late decline in activity in both cases is likely to be due to ‘aging’. (c) Rapid spontaneous reactivation of RBC-AChE in acute carbamate poisoning, where no oxime were given. A more gradual regeneration of plasma cholinesterase (PChE) is also noted (data from author (36)).
**RBC-AChe**

RBC-AChe activity may be a useful guide to therapy in a number of different ways. Reduced activity (<75% of the lower limit of normal range) confirms the diagnosis of anticholinesterase poisoning. The extent of depression roughly correlates with clinical severity (RBC AChe only) and less than 10% of normal activity is usually associated with severe toxicity (27). RBC-AChe activity may be used to monitor the therapeutic effects of pralidoxime, as the RBC-AChe activity should increase if the oximes are effective (see Figure 1-2a).

Monitoring RBC-AChe activity can also suggest whether it is reasonable to stop oximes as RBC-AChe activity will fall rapidly over 6 to 12 hours once the oximes are stopped if there are still anticholinesterases present. If this is observed oximes can then be restarted as long as reactivation is continuing to occur (see Figure 1-2b).

**PChE**

PChE levels can indicate when there is no more anticholinesterase present as the PChE will steadily rise back to normal at the rate of 5-10% per day after the OP is eliminated (37). More rapid rates of recovery of both RBC-AChe and PChE activity suggests reversible inhibition that is seen with carbamate poisoning (see Figure 1-2c).

Despite the above notes there are many pitfalls in the use of biomarkers (3, 38). Whilst they can be helpful, the use of atropine and oximes in the management of anticholinesterase pesticide poisoning should be based primarily on clinical features. Investigations should play a secondary role in aiding clinical decision making.
Other useful investigations and measurements

ECG—QT prolongation may occur, and both brady and tachyarrhythmia may be present. All patients with moderate to severe poisoning should be monitored on a cardiac monitor.

Chest Radiograph—This should be done in all severe poisonings, as aspiration pneumonia, possibly due to the hydrocarbons in the formulation, is common.

Arterial Blood Gas Analysis—It is indicated in severe poisoning to monitor respiratory function and to check for respiratory failure.

Spirometry—Serial measurements of forced vital capacity or tidal volume are a method of detecting early respiratory muscle dysfunction.

Nerve conduction studies—Repetitive nerve stimulation studies are of most value in monitoring for the Intermediate Syndrome, as they show parallel changes with progressive muscle weakness(31). A change from a decrement–increment pattern to progressive or severe decrements indicates severe weakness and that respiratory failure is usually imminent(31, 34).
Criteria for Diagnosis

The finding of pinpoint pupils following agricultural exposure or a history of pesticide ingestion should raise suspicions of anticholinesterase poisoning. Widespread muscle fasciculation is pathognomonic in this setting. There is often a strong odour which may be due to hydrocarbon solvents. Other features of an acute cholinergic crisis DUMBELS (see Table 1-1) also aid in the diagnosis. Where doubt exists, the diagnosis may be confirmed by either a decreased RBC-AChE or PChE activity, although early emergency management must not wait for these tests.

Treatment

Principles of Therapy

Therapy involves rapid resuscitation of the patient with oxygen, IV fluids, atropine, and sometimes an oxime acetylcholinesterase reactivator. See Table 1-2 for a summary of antidote use in treating anticholinesterase poisoning.

Summary of Management (see also Table 1-2) (3, 5, 19, 22, 26, 35, 37, 39, 40)

- Check airway, breathing and circulation. Place the patient in the lateral position with the head down. Provide high flow oxygen and perform endotracheal intubation if the patient’s airway or breathing is compromised.

- Obtain IV access and give
  - 1-3 mg of atropine IV as a bolus, increase as required using a ‘doubling dose’ regime followed by an infusion (41) (see Table 1-2)
  - IV infusion of 0.9% normal saline to keep the systolic blood pressure above 80 mmHg and urine output > 0.5 mL/kg/h
If severe signs of poisoning are still present then give pralidoxime chloride 1-2g (or obidoxime 250 mg) intravenously over 20-30 min through a second IV cannula. Follow with pralidoxime of 0.5 g/h, (or obidoxime 30 mg/hr).

Re-assess atropine requirement
- Continue with a doubling dose regimen if further boluses of atropine are required and titrate therapy to clinical response (improvement of bradycardia, hypotension, secretions and bronchorrhoea) (41). Assess for atropine toxicity which commonly present as delirium and tachycardia (42).
- Where only some of the endpoints of atropinisation are achieved then the potential benefits should be weighed against the risks of giving further atropine boluses. Eg: A patient with resolved bradycardia who still had bronchorrhoea after atropine therapy may reach a point where further atropine doesn’t improve lung signs further (here other causes of bronchorrhoea such as aspiration must be considered) (5).
- Severe hypotension may benefit from vasopressors, providing adequate fluid resuscitation has been given.

The need for, and duration of, continuing oxime infusions are controversial. Consider stopping oximes if atropine requirements are low and the patient is not intubated; or if there is an increase in PChE. The RBC-AChE can be monitored after stopping oximes. If there is a fall in activity and worsening of symptoms, then the oximes may be recommenced (see Figure 1-2).

Treat agitation with adequate sedation using IV benzodiazepines such as diazepam 0.1-0.2 mg/kg, or midazolam 0.05-0.1 mg/kg.
- Physical restraints should be avoided for agitation as severe, life-threatening hyperthermia may be provoked.
Seizures should be treated with IV benzodiazepines such as diazepam 0.1-0.2 mg/kg, or midazolam 0.05-0.1 mg/kg.

Benzodiazepines may also improve the central control of respiration, paradoxically improving respiratory function preventing the need for endotracheal intubation.

Ongoing frequent monitoring to:

- Assess for a recurrence of an acute cholinergic crisis requiring further atropine. Such recurrences are most common with highly fat-soluble OP such as fenthion, where acute symptoms may occur up to 2-3 days following ingestion.

- Review respiratory function. Intubation and mechanical ventilation are indicated if a patient’s tidal volume is below 5 mL/kg or vital capacity is below 15 mL/kg; if there are paradoxical or disordered diaphragmatic movements, or if apnoeic spells occur; or if the PaO$_2$ <60 mmHg despite supplemental oxygen.

- Monitor strength of muscle power, particularly neck flexion. The Intermediate Syndrome may develop 1-4 days after resolution of the acute cholinergic crisis, and manifest with proximal muscle weakness, neck weakness, and bulbar palsy. These indicate a high risk of respiratory failure, which may require intubation and ongoing ventilation in ICU.
### Table 1-2 Antidotes for poisoning with anticholinesterase insecticides

*(Table modified from (5, 22))*

<table>
<thead>
<tr>
<th>Class of antidote</th>
<th>Specific antidote</th>
<th>Dose and administration</th>
<th>Goal of Antidote</th>
<th>Endpoints to titrate antidote</th>
<th>Toxicity of Antidote</th>
<th>Levels of evidence* for use</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Anti-muscarinic</strong></td>
<td>Atropine (others include glycopyronium bromide and hyoscine methobromide – not discussed)</td>
<td>Initially 1-3mg IV for adults. Re-assess in 5 min and double dose if endpoints have not been achieved. Continue doubling the dose every 3-5 min until endpoints of atropinisation are achieved. Large total doses may be necessary but usually not more than 25 to 75 mg. Follow on with 10-20% of the loading dose per hour as an infusion</td>
<td>To reverse features of muscarinic overactivity.</td>
<td>HR &gt; 80/min Systolic BP &gt; 80 mmHg Clear chest Dry axillae</td>
<td>Delirium Hyperthermia</td>
<td>Likely to be of benefit</td>
</tr>
<tr>
<td><strong>Oximes (acetylcholinesterase re-activator)</strong></td>
<td>Pralidoxime chloride</td>
<td>IV loading dose 30 mg/kg over 20-30 min, followed by an infusion of 8 mg/kg/hr Thus in 60-70 kg adult = 2g followed by 500 mg/hr infusion</td>
<td>To prevent muscle weakness and respiratory failure (nicotinic features)</td>
<td>Administer oxime infusion until either:- Clinical recovery (decreased or negligible atropine requirement) PChE starts to increase Serial RBC-AChE shows a lack of increase in response to oximes, or maintenance of RBC-AChE level after stopping oximes</td>
<td>Vomiting Tachycardia &amp; diastolic Hypertension (noted particularly when bolus given too rapidly)(39)</td>
<td>Unknown effectiveness</td>
</tr>
<tr>
<td><strong>Obidoxime</strong></td>
<td>IV loading dose of 4mg/kg (followed by infusion of 750mg/day)</td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td><strong>Benzodiazepines</strong></td>
<td>Diazepam, lorazepam, or midazolam</td>
<td>0.1-0.2 mg/kg (increments of 5-10 mg) to achieve endpoints. Or lorazepam 0.07 mg/kg up to 4 mg, or midazolam 0.05-0.1 mg/kg (increments of 2.5-5 mg)</td>
<td>To treat seizure activity and offer moderate sedation</td>
<td>Control of seizures and sedation</td>
<td>Decreased level of consciousness and respiratory depression. However paradoxically improved respiratory status has been noted in recommended doses of antidote</td>
<td>Likely to be beneficial</td>
</tr>
</tbody>
</table>
**Intubation and ICU Management**

There should be a low threshold for early endotracheal intubation in OP poisoning (see above guidelines), as a high proportion of patients will need definitive airway management (43). In a series of 376 OP poisoned patients treated in a rural hospital in Sri Lanka, 24% of patients were intubated. Of these, 58% were intubated within the first 2 hours of admission, however, these patients usually did not require extended ventilation (32). In contrast those patients who were intubated after 24 hours usually required prolonged ventilation.

In low resource settings, factors such as lack of ICU beds make the management of severe cases of poisoning challenging, including the decision if and when to intubate. However, delayed intubation in the patient with a compromised airway results in greater morbidity from airway complications. Failure to protect the airway early may also result in hypoxic brain injury and aspiration pneumonitis, with a longer stay in the ICU and greater secondary morbidity and mortality.

Extubation can be difficult in OP poisoned patients owing to slow recovery of respiratory muscle function. Re-intubation is frequently required so patients should be closely monitored for the first 12 hours after extubation. Ideally before extubation, patients should no longer require atropine or oxygen, be conscious and the tidal volume and neck muscle power should be improving.

**Carbamates**

The management for carbamates is the same as above except that oximes are not indicated. The clinical course is usually shorter; and delayed or prolonged respiratory failure is much less common.
Other antidotes

A number of other antidotes have been suggested largely based on small research series to improve the mortality and morbidity in OP poisoning. These include the use of fresh frozen plasma, magnesium, clonidine, and bicarbonate. Current data on these antidotes does not support their routine use.

Decontamination

Decontamination should only be performed after initial resuscitation is underway, including the use of atropine. Contaminated clothing should be removed, but should not compromise care.

Gastric lavage is not supported by good evidence. It should not be performed until patients have been stabilised and the airway is protected with an endotracheal tube. Forced emesis also has no evidence supporting its use and has a high risk of increasing respiratory complications(44). It should be abandoned. Activated charcoal is not indicated. A recent large randomised controlled trial including 1310 patients with anticholinesterase poisoning showed no benefit on mortality or any other outcome from use of activated charcoal(45).

Nosocomial Poisoning

Hundreds of thousands of patients with severe OP poisoning are seen by health care workers across Asia. Most workers use no special precautions other than gloves and gowns, and no cases of nosocomial (or secondary) poisoning with significantly reduced RBC-AChE activity have been reported anywhere in the world. A recent consensus statement for Australian emergency departments concluded there was negligible risk of nosocomial poisoning in those treating OP poisoned patients if universal precautions such as the wearing of gloves, gowns and masks are used(46).
**Prognosis**
The overall in-hospital case-fatality for OP poisoning is around 15%(3). However, the prognosis varies considerably with different OP, with case-fatality ranging from <2% to >30%. For example, in one large series the case-fatality for poisoning by chlorpyrifos, fenthion and dimethoate was 8%, 16% and 23% respectively(47). The case-fatality for each agent is approximately double when patients are symptomatic. There is less data on the case-fatality for the carbamates, however, one large cohort study showed similarly contrasting rates for carbofuran (2%) and carbosulfan (10%).

**Prevention**
Restriction of pesticides is important as self-poisoning is associated with ease of access to pesticides, particularly in rural parts of many developing countries in Asia. Significant decreases in mortality from pesticide poisoning have resulted following bans on the most highly toxic OP pesticides(48).

**Controversies**
The use of pralidoxime in OP poisoning

- Oximes were discovered in the 1950s and consistently showed benefit with pre-treatment (single dose) in animal studies.
- Cohort and RCT studies however have shown contradictory results(25, 49, 50).
- It is likely that oximes will benefit some patients at some dose and duration, but that they may also sometimes cause significant and serious adverse effects(50).
- The 2000 WHO recommendations on dosing pre-date the most recent trials (see Treatment)(24). Further studies are therefore required to identify which patients will benefit, and what is the optimal dosing regimen.
- Serial measurements of RBC-AChE may be useful to better titrate oximes dose to response.
Chapter 2: A systematic comparison of recommendations for the measurement of acetylcholinesterase in acute organophosphorus pesticide poisoning
Abstract

Context: The measurement of the AChE biomarker has been suggested to be able to potentially assist in management of organophosphorus pesticide (OP) poisoning through confirmation of diagnosis and severity, guidance of oxime therapy (through provision of a titrateable endpoint to therapy), and patient discharge decisions. Despite improvements in access to the test in the last decade, there is still no published consensus statement giving unequivocal guidance on the use of AChE in the management of acute OP poisoning.

Objective: The study aim was to answer to what extent there is a consensus on where AChE is recommended in the management of OP poisoning, and what specific parameters have been provided to guide AChE, through a review the literature using a systematic approach.

Methods:

Data sources - Review articles, book chapters and electronic resources were included in our source list.

Study selection - Google scholar and Pubmed search engines were used to identify texts that focused on management recommendations for acute OP pesticide poisoning published between 2008 and 2013. Articles with an environmental focus on environmental poisoning, nerve agents, or chronic exposure were excluded. The source list was supplemented by other relevant toxicological and emergency medicine texts that have been used in similar published reviews.

Data extraction: We asked the literature 59 questions relating to recommendations for AChE in a range of situations and also recorded whether texts were citing literature in covering these topics.
Results: 27 texts (6 review articles, 15 book chapters, 6 monographs from online resources) providing recommendations for the management of acute OP poisoning were identified. 26/27 recommended the measurement of AChE in OP poisoning, and the majority of these recommendations were in the context of confirmation of diagnosis (23/27). The test was less widely recommended in the context of guiding oxime therapy (14/27), and patient discharge (6/27). Potential pitfalls were not covered widely (6/27) despite original evidence existing and being cited in a minority of this group. Specific cut-off points or reference values for AChE were lacking across the range of topics explored.

Conclusions: This review identified two key gaps in the recommendations for AChE in the management of OP poisoning. The first gap surrounds a lack of primary evidence reporting specific guidelines for the use of AChE in relation to oxime use and discharge decisions, and the impact of the use of AChE on clinical outcomes. Better evidence, may help to reduce variation in guidelines, and improve the management of OP poisoning.

The second was that existing evidence on pitfalls in measurement and interpretations are not widely covered in texts. Such preventable errors need to be highlighted routinely.
Background

Organophosphorus pesticide (OP) self-poisoning is a significant global public health problem leading to 200,000 deaths each year in South Asia alone (1, 2, 51).

Acetylcholinesterase (AChE) is an intermediate biomarker of OP poisoning that has been studied from the time that OP poisoning was first reported. The measurement of this enzyme to assist in management of OP poisoning is often recommended in both Emergency Medicine and Toxicology textbooks (37, 52-55). Its potential roles have been discussed in the following broad areas:

1) confirmation of diagnosis and severity
2) guidance of oxime therapy, and
3) patient discharge decisions.

However, some texts also note that there are many pitfalls to the measurement of AChE in practice, and that interpretation of AChE can be complex. Laboratory facilities are often unable to provide clinicians with results in a timely fashion, particularly in low-income Asian countries where there is a high incidence of poisoning. Point-of-care AChE testing may partially solve this problem (56).

There is no published consensus statement giving clear unequivocal guidance to clinicians on the use of AChE in the management of acute OP poisoning. The purpose of the current review, using a systematic approach, is to answer to what extent there is a consensus on a) where AChE is recommended in the management of OP poisoning, and b) what specific parameters have been provided to guide AChE.

We are specifically interested in the strength and breadth of recommendation, and practical guidance that the literature provides regarding its use in the areas of confirmation of diagnosis and severity, guidance of oxime therapy, and patient
discharge decisions. Secondarily we are interested how the pitfalls of measurement, and the challenges with interpretation of AChE results are described in the literature when recommendations are present.

**Methods**

We performed a systematic literature review using google scholar searching for articles published between 2008 and 2013 that focused on the management of acute OP poisoning using the following search terms:-

- (organophosphate OR organophosphorus OR anticholinesterase) AND
- (poisoning OR toxicology) AND (treatment or management) AND (review OR book)

A secondary search was made using PubMed searching for the same keywords but limited to review articles only.

We were interested in management of patients who had been poisoned as a result of pesticide ingestion, so we specifically excluded texts that focused on nerve agents or chemical warfare, environmental exposures or animals, or that did not have any recommendations toward “management”.

We limited the search to the last 5 years (2008 – 2013), and references that had a minimum citation index of 2 citations per year for review articles (for articles published before 2013), or at least 1 citation per year for book chapters (published before 2011), and we set this distinction on the rationale that text book chapters are less likely to be cited than articles.

Major texts of Toxicology and Emergency medicine, handbooks and electronic resources were added to the source list as such resources have the potential to
significantly impact on medical care. The electronic resources included commonly accessed internet based resources such as UpToDate, and eMedicine. We followed a similar methodological approach that used in a comparative review of recommendations for a different component of OP poisoning management(41).
**Figure 2-1** Search strategy for inclusion of texts in this review

**Google Scholar**
- **Search Terms**
  (organophosphorus or organophosphate or anticholinesterase) and (poisoning or toxicology) and (treatment or management)
- **Limitations**
  Human, English, Review, Last 5 years publication (2008 - 2013)
- 653 hits, 14 relevant
- Title review and/or text review
- 6 articles meet criteria;-
  • 3 book chapter
  • 3 review articles

**Pubmed**
- **Search Terms**
  (organophosphorus or organophosphate or anticholinesterase) and (poisoning or toxicology) and (treatment or management)
- **Limitations**
  Human, English, Review, Last 5 years publication (2008-2013)
- 77 results
- Title review and/or abstract review
- 5 Review articles identified
  (3 already identified from google search)

**Related OP poisoning management reviews**
- 33 texts in source list from Eddleston et al. (2004)
  List updated and expanded to 28 current texts by Conner et al. (2013)
  Source list limited to study criteria. Excluded following:-
  > 5 years - 3
  not focus - 7
  can’t access - 3
- 15 texts remaining from Connor et al. source list
  1 updated version from Eddleston et al. (not included in Conner et al.)

**Selection criteria**

**Inclusion**
- Clinical management focus
- Acute poisoning
- Pesticide (not nerve gas)
- Current literature (Publication last 5 years)

**Exclusion**
- Non clinically focussed
- No management instruction
- Environmental focus
- Chronic exposure focus
- Nerve agent texts
- Publication < 2008
- Non English language

**Other supplementary texts**
- Other Book Chapters and Online resources that meet inclusion criteria

27 Texts
- 6 Reviews
- 15 Book chapters
- 6 Online resources
The list of supplementary texts was guided by previously published literature reviews on aspects of OP poisoning management (41, 57). A diagram outlining the search strategy is shown in Figure 2-1.

We asked the literature 59 specific questions relating to information about 5 domains covering a range of issues relevant to AChE recommendations in OP poisoning. These questions were constructed by a consensus amongst experts in the field. The broad domains of inquiry included recommendations for AChE in confirming diagnosis and assessing severity of OP poisoning, guiding oxime therapy and patient discharge, and pitfalls in measurement and collection, as well as difficulties in interpretation of assay results (Table 2-1). We also recorded for each specific point that was covered, whether the various texts cited the scientific literature, and the number of citations quoted if more than one source was referenced.

**Results**

Table 2-1 lists 27 texts (3, 58-83) that were analysed to answer the research questions. This includes of 15 book chapters, 6 review articles, and 6 monographs from online databases.

Our search strategy identified a total of 304 hits on Google Scholar, 59 review articles from a Pubmed search, and 36 texts from other published clinical reviews on OP poisoning from the search terms used, but the list was refined to the final 27 texts based on selection criteria outlined in Figure 2-1. The majority of texts were excluded because of their focus on basic science or non-clinical aspects of the pharmacology of OP poisoning, environmental poisoning or poisoning by nerve agents.

Almost all the texts (26/27) recommended the measurement of AChE for some aspect of OP poisoning management. Most recommended measurement of the assay in the
Figure 2.2 Coverage of topics on AChE recommendations for guiding clinical management
context of confirmation of diagnosis (23/27), and it was less frequently mentioned in the context of guidance of oxime therapy (14/27), and patient discharge (6/27) (Figure 2-2). The potential pitfalls of measurement of AChE were not widely covered, for example, caution about incorrect collection technique was only mention in 6/27 texts (Figure 2-3).

Specific cut-off points or reference values were lacking across the range of topics explored. Specific values were provided in less than half (11/23) the texts that recommended AChE for diagnosis, and in 1 out of the 6 texts that recommended it for discharge. Of the 13 texts that suggested AChE could be used to guide oxime therapy none provided specific values to guide clinical decisions (Figure 2-2).

AChE biochemistry was variably covered. Some points, such as the distinction between RBC-AChE and PChE (25/27) were made by nearly all the texts. However, other details that were more focused on the clinical application of these biomarkers, such as PChE being a less specific marker of poisoning (6/27), were only covered in a minority of texts (Figure 2-3).

**Citation of scientific literature**
There was a large variation amongst texts in how often information was supported by citation. The total number of citations per text varied from 0 to 37 in relation to the 59 review questions (Figure 2-4a). On average the review articles were more likely to cite the literature having a median of 4.5 citations per text, than book reviews or online resources where there was median of 1 citations per text (see Figure 2-4b). However, variation was also noted within all subgroups of review articles, textbook chapters and online monographs, where there were 1 or 2 outliers who quoted much more literature than average. It was also noted that citations for recommendations varied by topic. The proportion of recommendations with citations supporting pitfalls of measurement of AChE was almost double (33%) that for use of AChE in diagnosis, oxime therapy and discharge (17% each) (Figure 2-4c).
### AChE biochemistry
- Distinction between AChE and PChE made
- RBC-AChE and PChE markers of OP poisoning
- PChE more sensitive marker of exposure
- PChE is less specific for exposure
- PChE doesn’t give information about poisoning severity
- Increasing PChE can indicate no more OP is present
- *PChE test can be used to provide prognostic information
- RBC-AChE more reflects nervous tissue AChE
- RBC-AChE more reflects severity
- RBC-AChE is a less useful marker after aging
- RBC-AChE levels take longer to return to baseline than PChE

### Pitfalls: collection and measurement
- Caution about incorrect collection technique
- Temperature is a factor - PChE activity
- Ex-vivo mentioned for RBC-AChE
- Room temperature can influence ex-vivo reactions
- Cooling and dilution decreasing ex-vivo reactivation
- Normal range in PChE is &quot;assay dependent&quot;

### Pitfalls: Interpretation
- Mention specific pitfall(s) of interpretation (AChE)
- Specifies pitfall for RBC-AChE
- Specifies pitfall for PChE
- False negative due to high baseline
- False positive in RBC-AChE (not 100% specific)
- Describe the variability of different OP agents

### Variation in normal ranges
- Advice about normal ranges for RBC-AChE
- Actual values for normal ranges for RBC-AChE
- Advice about normal ranges for PChE
- Actual values for normal ranges for PChE
- Other factors affect normal range of RBC-AChE
- Other factors normal range of PChE

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**Figure 2-3** Coverage of topics on AChE biochemistry and pitfalls in measurement and interpretation of assays
Figure 2-4 Evaluation of citations quoted in chapter on OP poisoning, showing a) the total number of citations per text, b) the number of citations by type of text, and c) the proportion of recommendations for different domains of OP poisoning that refer to evidence.
### Table 2-1 Coverage of topics related to recommendations of AChE measurement in OP poisoning management and frequency of citations to literature by different texts.

<table>
<thead>
<tr>
<th>Review</th>
<th>Book Chapter</th>
<th>Online Resource</th>
</tr>
</thead>
<tbody>
<tr>
<td>AChE recommended for confirming Diagnosis</td>
<td>26</td>
<td>2</td>
</tr>
<tr>
<td>Specific cut-off values</td>
<td>25</td>
<td>3</td>
</tr>
<tr>
<td>AChE ranges for poisoning severity</td>
<td>24</td>
<td>4</td>
</tr>
<tr>
<td>Severity of poisoning correlated with symptoms</td>
<td>23</td>
<td>5</td>
</tr>
<tr>
<td>Distance between AChE and PCHE made</td>
<td>22</td>
<td>6</td>
</tr>
<tr>
<td>RBC-AChE and PCHE are only &quot;markers&quot; of OP poisoning</td>
<td>21</td>
<td>7</td>
</tr>
<tr>
<td>PCHE more sensitive marker of exposure</td>
<td>20</td>
<td>8</td>
</tr>
<tr>
<td>PCHE is less specific for exposure</td>
<td>19</td>
<td>9</td>
</tr>
<tr>
<td>PCHE doesn't give information about poisoning severity</td>
<td>18</td>
<td>10</td>
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<tr>
<td>Increasing PCHE can indicate no more OP is present</td>
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<tr>
<td>PCHE level can be used to provide prognostic information</td>
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<tr>
<td>RBC-AChE more reflects nervous tissue AChE</td>
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<td>13</td>
</tr>
<tr>
<td>RBC-AChE more reflects severity</td>
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<td>14</td>
</tr>
<tr>
<td>RBC-AChE is a less useful marker after ageing</td>
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<td>15</td>
</tr>
<tr>
<td>RBC-AChE levels take longer to return to baseline than PCHE</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>Caution about incorrect collection technique</td>
<td>11</td>
<td>17</td>
</tr>
<tr>
<td>Temperature is a &quot;test&quot; - PCHE stability</td>
<td>10</td>
<td>18</td>
</tr>
<tr>
<td>Toxins measured for RBC-AChE</td>
<td>9</td>
<td>19</td>
</tr>
<tr>
<td>Room temperature can influence in-vivo reactions</td>
<td>8</td>
<td>20</td>
</tr>
<tr>
<td>Cooling and dilution decreasing in-vivo resolution</td>
<td>7</td>
<td>21</td>
</tr>
<tr>
<td>Normal range in PCHE is &quot;age-dependent&quot;</td>
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<td>22</td>
</tr>
<tr>
<td>Values above normal ranges for RBC-AChE</td>
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<td>23</td>
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<tr>
<td>Values above normal ranges for PCHE</td>
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<tr>
<td>RBC-AChE more obvious markers of OP-AChE</td>
<td>3</td>
<td>25</td>
</tr>
<tr>
<td>Other factors affect normal range of RBC-AChE</td>
<td>2</td>
<td>26</td>
</tr>
<tr>
<td>Other factors affect normal range of PCHE</td>
<td>1</td>
<td>27</td>
</tr>
<tr>
<td>Mention specific path of interpretation (AChE)</td>
<td>10</td>
<td>28</td>
</tr>
<tr>
<td>Specifics path for RBC-AChE</td>
<td>9</td>
<td>29</td>
</tr>
<tr>
<td>Specifics path for PCHE</td>
<td>8</td>
<td>30</td>
</tr>
<tr>
<td>False negative due to high baseline</td>
<td>7</td>
<td>31</td>
</tr>
<tr>
<td>False positive in RBC-AChE (not 100% specific)</td>
<td>6</td>
<td>32</td>
</tr>
<tr>
<td>Describe the variability of different OP agents</td>
<td>5</td>
<td>33</td>
</tr>
<tr>
<td>ACHE can guide some therapy</td>
<td>4</td>
<td>34</td>
</tr>
<tr>
<td>AChE should be measured if on some therapy</td>
<td>3</td>
<td>35</td>
</tr>
<tr>
<td>Specifics RBC-AChE</td>
<td>2</td>
<td>36</td>
</tr>
<tr>
<td>Specifics PCHE</td>
<td>1</td>
<td>37</td>
</tr>
<tr>
<td>Resuscitation with zones provides a guide to ageing</td>
<td>10</td>
<td>38</td>
</tr>
<tr>
<td>AChE used to decide on starting some therapy</td>
<td>9</td>
<td>39</td>
</tr>
<tr>
<td>AChE measurement to be taken before starting PMM</td>
<td>8</td>
<td>40</td>
</tr>
<tr>
<td>AChE before and after toxin-dosing</td>
<td>7</td>
<td>41</td>
</tr>
<tr>
<td>AChE measurement during some Rx</td>
<td>6</td>
<td>42</td>
</tr>
<tr>
<td>AChE after stopping some</td>
<td>5</td>
<td>43</td>
</tr>
<tr>
<td>Guide to frequency of checking AChE in some therapy</td>
<td>4</td>
<td>44</td>
</tr>
<tr>
<td>How to interpret AChE in some therapy</td>
<td>3</td>
<td>45</td>
</tr>
<tr>
<td>Required some Rx effective if RBC-AChE increases</td>
<td>2</td>
<td>46</td>
</tr>
<tr>
<td>Amountd of increase specific</td>
<td>1</td>
<td>47</td>
</tr>
<tr>
<td>RBC-AChE can indicate when opines are ineffective</td>
<td>10</td>
<td>48</td>
</tr>
<tr>
<td>AChE can indicate when to stop some</td>
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<td>49</td>
</tr>
<tr>
<td>RBC-AChE can indicate when opines are ineffective</td>
<td>8</td>
<td>50</td>
</tr>
<tr>
<td>AChE should be measured if on some therapy</td>
<td>7</td>
<td>51</td>
</tr>
<tr>
<td>AChE before and after toxin-dosing</td>
<td>6</td>
<td>52</td>
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<tr>
<td>AChE measurement to be taken before starting PMM</td>
<td>5</td>
<td>53</td>
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<tr>
<td>AChE before and after toxin-dosing</td>
<td>4</td>
<td>54</td>
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<tr>
<td>AChE during some Rx</td>
<td>3</td>
<td>55</td>
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<tr>
<td>AChE after stopping some</td>
<td>2</td>
<td>56</td>
</tr>
<tr>
<td>Guide to frequency of checking AChE in some therapy</td>
<td>1</td>
<td>57</td>
</tr>
<tr>
<td>How to interpret AChE in some therapy</td>
<td>10</td>
<td>58</td>
</tr>
<tr>
<td>Required some Rx effective if RBC-AChE increases</td>
<td>9</td>
<td>59</td>
</tr>
<tr>
<td>Amountd of increase specific</td>
<td>8</td>
<td>60</td>
</tr>
<tr>
<td>RBC-AChE can indicate when opines are ineffective</td>
<td>7</td>
<td>61</td>
</tr>
<tr>
<td>AChE can indicate when to stop some</td>
<td>6</td>
<td>62</td>
</tr>
<tr>
<td>AChE before and after toxin-dosing</td>
<td>5</td>
<td>63</td>
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<tr>
<td>AChE measurement to be taken before starting PMM</td>
<td>4</td>
<td>64</td>
</tr>
<tr>
<td>AChE before and after toxin-dosing</td>
<td>3</td>
<td>65</td>
</tr>
<tr>
<td>AChE during some Rx</td>
<td>2</td>
<td>66</td>
</tr>
<tr>
<td>AChE after stopping some</td>
<td>1</td>
<td>67</td>
</tr>
</tbody>
</table>

**Colour Key:**
- No recommendation
- Recommendation without citation
- Recommendation with "x" number of citations

- **Note:** Some citations are not provided due to the nature of the document.
Discussion

There was a general agreement that AChE assay could help with diagnosis and should be ordered if available. However, the test is less likely to be practically useful in this situation because a diagnosis of OP poisoning is most often made without difficulty on the basis of history and clinical features. AChE is only likely to be helpful when there is a diagnostic challenge\(^{(73)}\), such as with co-ingestion with other substances, or in paediatric populations when the diagnosis could be more elusive\(^{(84)}\), and even in such situations the common lengthy delay to obtain results may limit its usefulness.

Both oxime therapy, and discharge decisions are areas of OP poisoning management that can be complex, and one where a biomarker could be of great benefit. We paradoxically noted that texts much more frequently mentioned AChE’s potential to guide diagnosis and severity than mentioned its role in guiding oxime therapy or patient discharge (despite the much greater potential for improvement in clinical outcomes in the latter situations). Also only a minority (2/27) of the texts cited evidence recommending the measurement of AChE in the context of oxime therapy\(^{(59, 63)}\). This likely reflects a lack of primary literature to support such recommendations. Similarly, only 1 of the 6 recommendations for use of AChE in discharge decisions referenced literature in support of this suggestion\(^{(73)}\).

Discharge decisions can be complex in OP poisoning with a proportion of poisonings from fat soluble OP agents having a delayed onset of cholinergic symptoms\(^{(47)}\), up to 2 days following the initial presentation. Delayed respiratory failure (e.g. intermediate syndrome) may occur up to 96 hours following initial cholinergic symptoms\(^{(32, 47)}\).

There was also a lack of incorporation of evidence into recommendations noted, in particular with regard to the pitfalls of AChE collection, measurement and interpretation, where only a minority of texts provided citation for original articles. For example, an original study by Worek et al\(^{(85)}\) highlighted that ex-vivo reactions could
lead to inaccurate measurements, but was only cited by 1 text (63) out of the 5 that described this phenomenon.

Whilst some aspects of basic science of AChE were covered relatively widely amongst the texts, including the differentiation of RBC-AChE and PChE, only a few texts (6/27) highlighted the clinical relevance of some of these features, such as that increasing PChE may indicate that OP has been largely eliminated (3, 37, 63, 69, 73, 75).

A common theme that was noted across all the different domains of question was the lack of specific values of AChE that were quoted in text. The lack of a detailed explanation of interpretation the complexity is likely to limit the utility of the advice (even if the principle is sound). For example, the approach outlined above in regard to rising PChE needs to be further clinically evaluated to provide specific values that are sufficiently sensitive to exclude ongoing poisoning.

Specific values were quoted for diagnosis, and severity, however, there was some variation in the exact cut-offs suggested for diagnosis, and different levels of severity. For example, the threshold for diagnosis varied between <90% and <50% (59) of normal RBC-AChE. The format of reporting the test and values also varied between texts with some discussing only one of the two biomarkers (RBC-AChE and PChE) and even a few that were unclear as to which cholinesterase test was referred to. Correlations of values with symptoms and management implications such as “patients with less than 10% of normal red-cell AChE activity had grossly deranged muscle function and needed high doses of atropine” (3) was only occasionally provided.

No text that suggested increasing AChE indicated effectiveness of oxime therapy provided specific values or details on the extent of increase that was required. Supporting material was limited to two texts that simply showed an illustrative case of
the expected behavior of AChE levels with oximes (3, 75). This highlights the need for more research to guide the use of AChE in assessing oxime response.

Few texts covered the many pitfalls in interpretation. For example, the significant variation in normal ranges for PChE and to a lesser degree RBC-AChE was highlighted in only a minority of texts.

To our knowledge, no reviews have previously examined the literature recommendations for use of AChE in OP poisoning management. However, there are two related reviews on recommendations for initial atropinisation in OP poisoning, which have been published roughly 10 years apart (41, 57). The first review pointed out great variation in recommendations that existed in the literature, but encouragingly the more recent review showed there was an emerging consensus in recommendations supported by clinical studies. We hope this article might prompt a similar reevaluation of AChE and encourage new evidence.

We used google scholar as the main search engine to find texts that were focused upon the management of OP poisoning because it offered a broad search that included textbooks, journal articles, and online resources, and to this effect it is argued by some authors to provide a sensitive first choice search strategy (86). However, the solo use of google scholar is still controversial, and when we used PubMed to perform a secondary search, we found two extra review articles.

The key limitation of this study is that our search criteria may have missed texts that are from non-English speaking countries and that are widely used. However, we have covered a broad range of texts that are accessed by clinicians and most of our conclusions are not sensitive to small changes in the number of included texts.
The type of publication contained within our source list ranged widely in type and length of article, and it is possible word restrictions in some of the smaller publications, such as handbooks, and more concise textbook chapters, may have been a factor impacting on the wide variation in coverage of all questions and topics assessed. The list included clinical handbooks, such as the Oxford clinical handbook of Emergency Medicine(77), where the text was only a single page in length, to reports in large compendiums of clinical practice, such as Goldfranks toxicology textbook whose chapter on OP poisoning was 45 pages in length(63). We also assessed online resources(78-83) as we wanted to review all guidelines that were easily accessible to clinicians. These online monographs often had a different format and style from textbooks and review articles. However, the main finding of variation of recommendations was noted both between types of texts and within these subgroups (shown in Table 2-1, and highlighted in Figure 2-4c).

It was beyond the scope of the current study to systematically evaluate the quality of information that was being cited by the reviewed texts. However, we noted a range of sources being referred to including review articles and also original scientific papers. Most supporting citations were to other review articles/textbooks; and in some key areas such as the interpretation of AChE in oxime therapy, or the use of AChE in discharge decisions, there was a complete absence of citations to supporting original research.

**Conclusion**

This review identified two key gaps in the recommendations for AChE in the management of OP poisoning. The first gap surrounds a lack of primary evidence to support specific guidance in the use of AChE in relation to oxime use and discharge decisions, and whether this approach improves clinical outcomes. Better evidence,
may help to reduce variation in guidelines, and improve the management of OP poisoning.

The second gap was that existing evidence on pitfalls in measurement and interpretation was not widely covered in texts. Such preventable errors need to be highlighted routinely.
Chapter 3: A systematic comparison of recommendations for advanced life support (ALS) in organophosphorus poisoning
Abstract

Context: Resuscitation, including advanced life support (ALS) is the mainstay of the emergency treatment of OP self poisoning. Despite high case fatality from this condition, responsible for 200,000 annual global deaths, there are still no international guidelines that describe an ALS protocol for OP poisoning, or suggest how this would differ from standard ALS.

Objective: The study aim was to find a) whether ALS instructions are described in the literature on OP poisoning management, and b) to identify what are the recommended components of ALS, including the sequence and priority of specific antidotes, and how this differs from standard ALS.

Methods:

Data sources - Review articles, book chapters and electronic resources were included in our source list.

Study selection - Google scholar and Pubmed search engines were used to identify texts that focused on management recommendations for acute OP pesticide poisoning published between 2008 and 2013. Articles with an environmental focus on environmental poisoning, nerve agents, or chronic exposure were excluded. The source list was supplemented by other relevant toxicological and emergency medicine texts that have been used in similar published reviews.

Data extraction: Texts were analysed to see whether they met a predefined criteria for having an instructive ALS format. Questions were then asked to identify which components of resuscitation were recommended and what their relative priority was. The questions used for data extraction covered a range of options including airway, breathing, circulation, disability, antidote therapy, exposure and staff safety, gastrointestinal decontamination, and post resuscitation care.
**Results:** 27 texts (6 review articles, 15 book chapters, 6 monographs from online resources) providing recommendations for the management of acute OP poisoning were identified. Less than half 10/27 recommended were written with an instructive ALS framework, and more commonly had a narrative that provided a discussion of a range of potential treatments. The majority of texts (9/10) included antidote therapy, and atropine was included as a component ALS in 8 of these texts, and a rapid atropinisation protocol was specified in 7/8. Oxime therapy was an ALS component in 5/10 texts. Atropine was given a higher priority in 6/8 texts and an equal priority in 2/8, but was mentioned before oximes. Does of atropine specific to cardiac arrest were not available in the literature. Airway support was highlighted as a management priority in almost all texts, airway opening maneuvers (6/27) and managing the patient in a left lateral position (4/27) was only mentioned in a minority of texts.

**Conclusions:** There is no consistently described protocol for ALS in OP poisoning management. We created an ALS guideline based upon a relative consensus in the literature that emphasises the importance and priority of early rapid atropinisation such as that achieved by using a doubling dose regimen, We did not include oxime therapy in the guideline as there was a lack of clear recommendation, and oximes are unlikely to provide predictable improvement in the underlying pathophysiology that causes acute respiratory failure. Further research needs to be conducted on the specific antidote therapy that is likely to improve outcomes in active cardiac arrest. Also outcome based research on effectiveness of strategies for airway support at the bedside should be undertaken as respiratory arrest is the basis of much of OP poisoning mortality and addressing it's prevention is an important component of ALS for this condition.
Background

Organophosphorus pesticide (OP) self-poisoning is a condition that results in up to 200,000 deaths annually in Asia (1-3, 32, 51). The condition’s case fatality is estimated to be 8-15% despite current management, and this is primarily due to respiratory arrest, which progresses to cardiorespiratory arrest (32, 87). Resuscitation, including advanced cardiac life support (ALS) is the mainstay of emergency treatment in acute OP poisoning.

Currently there are no international guidelines that describe an ALS protocol for OP poisoning, or suggest how this would differ from standard ALS. However, precedent has been set in the resuscitation literature for toxicological resuscitation to be treated as a “special condition” in international guidelines on resuscitation (88) and the scientific literature (89). Modifications to standard ALS have been described for a number of toxicological presentations addressing the underlying pathophysiology of these more uncommon presentations. The international liaison’s committee on resuscitation (ILCOR) is the largest body of advice for resuscitation and in the 2010 guidelines documented special considerations in the delivery of ALS for 10 conditions ranging from digoxin overdose to carbon monoxide poisoning (90). However, such modified protocols only addressed poisoning presentations that are commonly encountered in higher income countries. OP poisoning which is primarily a condition of the developing world has not been covered, despite it being the leading cause of poisoning death globally and having a higher risk of in-hospital death than the poisonings currently covered in ALS guidelines. Development of such a guideline may have been inhibited by incomplete consensus on recommendations for the overall management for OP poisoning (3, 91-93).
Acute ALS in OP poisoning – literature recommendations

The focus of the current review was to identify whether literature recommendations for OP poisoning management can be incorporated into the existing ALS framework, to provide a specific focus on acute care delivery within the first 15 minutes to 1 hour of acute OP poisoning that requires resuscitation.

Figure 3-1 illustrates 3 commonly encountered case scenarios of OP poisoning that demonstrate a spectrum of presentations at this high end of severity, ranging from critical illness and peri-arrest, to full blown cardiorespiratory arrest. All of these cases require immediate resuscitation according to an ALS framework. These scenarios were based upon real encounters of patients who had consumed variable amounts of OP pesticide orally in a rural background, (often with co-ingestion of alcohol) presenting to secondary referral centers in Sri Lanka (48, 94). The generalizability of these scenarios, is supported by similar presentations in case series reported from developed world settings (61), with comparable case fatality (23). The aim of having a backdrop of these scenarios in such settings was to provide a frame of reference to the clinical questions we were asking from the literature.

Adequate training in skills, and knowledge of how to act, is likely to be an important aspect of reducing mortality in managing the most severely poisoned patients. Such management puts the greatest onus on the frontline doctors, who are often not well equipped to deal with such situations. A previous treatment protocol has been published targeting this group (5). This protocol dealt with severe poisoning but provided minimal advice on the management of the patient in cardiorespiratory arrest.
Case scenarios depicting a range of severity of acute OP poisoning presentations requiring acute ALS.

**Scenario A**
- 36 yo male
- Ingested 100mls of unknown OP pesticide 4 hours ago
- Presents obtunded (brought in by relatives)
- CPR started 2 minutes prior
- Time of ingestion: 4 hours

**Scenario B**
- 27 yo female
- Ingested 100mls of pesticide
- Copious amount of lung secretions, with widespread crackles and wheeze
- Emesis
- RR 40, O2 sats 86% on 6L/min
- P 45, systolic BP 80-90
- Time of ingestion: unknown

**Scenario C**
- 51 yo male
- Likely ingested unknown amount of OP pesticide, co ingestion with alcohol
- Hydrocarbon odor, wet shirt and trousers
- Vomiting in hospital, P 100, systolic BP 100, RR 24, O2 sats 96% on 6L/min
- Lung crepitations, sweating profusely
- Fasciculation’s and clonus.
- Time of ingestion: 2 hours previously

**Aim of Tox-ALS management recommendations**

1) What proportion of the OP management literature is focussed on the above spectrum of severity and is structured in an ALS framework to provide stepwise instructions in the above cases?
2) Does a toxicologically integrated ALS guideline currently exist?
3) Which antidotes would it include, and where with they be inserted in the ALS framework?
4) What would be the focus and order of other ALS components (ABCDE’s, including decontamination)?
5) How much this guideline based upon recommendation literature be in agreement with current original research on the same topic?

**Figure 3-1** Case scenarios depicting a range of severity of acute OP poisoning presentations requiring acute ALS.

Corresponding research questions for a literature review that would provide a toxicology integrated ALS guideline are also shown.
This chapter aims to investigate how well structured the literature on OP poisoning management is in the provision of ALS instruction. Specifically we are interested in which components ALS components should be included and in what order they should be carried out. We also paid particular attention to where specific antidote therapies, such as atropine, pralidoxime and diazepam, should be inserted in the sequence, and whether they belonged at all in the framework of acute ALS. We were also interested in the degree to which the unique aspects of OP poisoning pathophysiology were addressed by the components of ALS that were recommended, including muscarinic features that compromise both the cardiovascular and respiratory systems and the relative position of atropine in comparison with oxime in the ALS framework.

Practically speaking the aim of the review was to find out what a junior doctor could use within the first 15 minutes of treating an acutely poisoned patient who is either critically ill, or who had arrested, and to identify the areas of consensus and variation in components and sequence of ALS in OP poisoning, and where antidote therapies fit into this sequence.

**Methods**

We performed a systematic literature review using google scholar searching for articles published between 2008 and 2013 that focused on the management of acute OP poisoning using the following search terms:

(organophosphate OR organophosphorus OR anticholinesterase) AND (poisoning OR toxicology) AND (treatment or management) AND (review OR book)
A secondary search was made using PubMed searching for the same keywords but limited to review articles only.

Our area of interest was in management of patients who had been poisoned as a result of pesticide ingestion, so we specifically excluded texts that focused on nerve agents or chemical warfare, environmental exposures or animals, or that did not have any recommendations toward “management”.

We limited the search to the last 5 years (2008 – 2013), and references that had a minimum citation index of 2 citations per year for review articles (for articles published before 2013), or at least 1 citation per year for book chapters (published before 2011), and we set this distinction on the rationale that text book chapters are less likely to be cited than articles.

This recent time frame was chosen to allow examination of literature that had the opportunity to incorporate the most recent scientific literature. The reason for this is that there had been a significant increase in research funding examining organophosphate poisoning dating from 2002. This increase in funding reflected concerns of both the global significance of OP poisoning in self-harm and concerns about chemical warfare agents. This funded research supported large clinical observational studies, randomized controlled trials, and clinical reviews in many areas of acute management, such as efficacy of oxime therapy (49, 50, 95), atropine dosing regimen (42, 96), bedside monitoring of cholinestase (56) and peripheral nerve function (97) in acute poisoning, issues with decontamination (44, 98), reviews on alternate antidotes (99), as well as position statements for staff safety in initial management (46). Given the recent expansion literature on OP poisoning management and the lag time between original research becoming incorporated into guidelines, the current is perhaps timely.
Major texts of Toxicology and Emergency medicine, handbooks and electronic resources were added to the source list. The electronic resources included commonly accessed internet based resources such as UpToDate, and eMedicine, as such resources have the potential to significantly impact on medical care.
Figure 3-2  Search strategy for inclusion of texts in this review

**Pubmed**

*Search Terms*
(organophosphorus or organophosphate or anticholinesterase) and (poisoning or toxicology) and (treatment or management)

*Limitations*
Human, English, Review, Last 5 years publication (2008 - 2013)

77 results

Title review and/or abstract review

5 Review articles identified
(3 already identified from google search)

**Google Scholar**

*Search Terms*
(organophosphorus or organophosphate or anticholinesterase) and (poisoning or toxicology) and (treatment or management)

*Limitations*
Human, English, Review, Last 5 years publication (2008 - 2013)

653 hits, 14 relevant

Title review and/or text review

6 articles meet criteria;
- 3 book chapter
- 3 review articles

**Related OP poisoning management reviews**

33 texts in source list from Eddleston et al. (2004)

List updated and expanded to 28 current texts by Conner et al. (2013)

Source list limited to study criteria. Excluded following:-

- > 5 years - 3
- not focus - 7
- can’t access - 3

15 texts remaining from Connor et al. source list

1 updated version from Eddleston et al. (not included in Conner et al.)

**Selection criteria**

**Inclusion**
- Clinical management focus
- Acute poisoning
- Pesticide (not nerve gas)
- Current literature (Publication last 5 years)

**Exclusion**
- Non clinically focussed
- No management instruction
- Environmental focus
- Chronic exposure focus
- Nerve agent texts
- Publication < 2008
- Non English language

**Other supplementary texts**
Other Book Chapters and Online resources that meet inclusion criteria

27 Texts
- 6 Reviews
- 15 Book chapters
- 6 Online resources
The list of supplementary texts was guided by previously published literature reviews on aspects of OP poisoning management (41, 57). A diagram outlining the search strategy is shown in Figure 3-2.

**Evaluation of recommend components and sequence of ALS in OP poisoning**

69 specific questions, constructed by a consensus amongst experts in the field, were used to evaluate which components of ALS were being recommended in literature on management to OP poisoning, and what general sequence these were carried out. These questions were grouped according to a standard framework of ALS including airway, breathing, circulation, disability, with additional questions focused on post resuscitation care, antidote therapy and decontamination which related more to the toxicological context of ALS (Table 3-1).

**Recommendation style: ALS framework**

We included texts as having an ALS framework based upon characteristics of the recommendation style (see Box 3-1). For the style to be considered compatible with an ALS framework there had to be a dedicated section of text dealing with the initial resuscitation with more than single word descriptions about the steps of management. These steps had to include the management of airway, breathing and circulation, at a minimum, to be considered to cover the topic of ALS, however, they also could include other components such as antidote therapy, disability and decontamination. The section also had to be written in an instructive style, rather than a third person description to qualify as an ALS framework (Box 3-1).

The rationale for these criteria was to search for a format of recommendation that could easily be followed in an emergency without the need for deliberation between alternative therapies.
**ALS framework (instructive, ordered sequence of steps)**

1) Is there a specific section that addresses Airway, Breathing Circulation (ABCs)
2) Is section instructive → include ALS framework,
3) Are components ordered? → include ALS framework
   - Are components numbered → note “numbered steps”

---

**Box 3-1 Method for determining whether a text was considered to provide recommendations within an “ALS framework”**;

Any text that offered a discussion of possible interventions that would require further evaluation before taking action was not regarded to have an instructive ALS format.

We also recorded whether a numbered list of steps was provided which was used to further differentiate the ALS texts.

**Specific Therapies in ALS framework**

When an ALS framework was present, it was recorded whether atropine, oxime or diazepam administration was reported. When both oxime and atropine were recommended we recorded in which order and/or priority atropine therapy was given in relation to oxime therapy.

**Results**

Table 3-1 lists 27 texts (3, 58-83) that were analysed to answer the research questions. This includes of 15 book chapters, 6 review articles, and 6 monographs from online databases.
Table 3-1 Questions answered by different texts across a range of topics covering ALS recommendations in acute OP poisoning.

Darker shading indicates when questions were answered by statements that cited other literature. The number of citations for each point is also noted.
Figure 3-3  Resuscitation guidelines in OP management texts showing a) the proportion of texts written in an ALS framework, using an instructive format b) which antidotes included in ALS framework, and c) the priority and given to atropine over oximes in the ALS framework
Our search strategy identified a total of 304 hits on Google Scholar, 59 review articles from a PubMed search, and 36 texts from other published clinical reviews on OP poisoning from the search terms used, but the list was refined to the final 27 texts based on selection criteria outlined in Figure 3-2. The majority of texts were excluded because of their focus on basic science or non-clinical aspects of the pharmacology of OP poisoning, environmental poisoning or poisoning by nerve agents.

**Proportion of texts with ALS framework**

Less than half (10/27) the texts were written within an ALS framework (Figure 3-3a) whilst the majority provided recommendations through a narrative that had varying degrees of focus on the acute initial management, and often contained a discussion of more than one potential treatment. Over half (6/10) of the former group had instructions that were organized in numbered steps providing a clear sequence to the components of ALS. A subset of the texts (2/10) consisted of both a general discussion and an ALS framework that supplemented the other in the form of a table (82) or a box inset(3). One text clearly outlined in a table alternative sequences to ALS components (e.g. intubation, atropine, decontamination) based upon the severity of poisoning(68). However, this text was not considered to have an ALS framework due to the lack of detail and instruction associated with the components described, thereby not meeting the criteria of “detailed stepwise instructions that could be used in an emergency” as defined in Box 3-1.

The majority of texts written in an ALS compatible format (9/10) included antidote therapy, and atropine administration was included as a component of ALS in 8 of these texts (Figure 3-3b). Atropine was recommended for all symptomatic patients, and a rapid infusion protocol involving a doubling dose was specified for all but one of these texts (7/8). Oxime therapy was included as an ALS component in 5/10 texts and a further 2/10 texts where the instruction was either less definite or conditional (e.g. “consider giving oximes”(66), or “give oximes if symptoms are present only after
atropinisation(75)). Atropine was given a higher priority in the sequence of ALS steps than oximes in all but two texts (6/8), and in one text oximes were not mentioned in the ALS section of recommendations(79) (Figure 3-3c). In the two texts that were marked as having no distinction in priority, atropine therapy was mentioned first. However, there was insufficient explanation of the significance of this position to favour the importance of atropine over oximes in the ALS sequence. Benzodiazepines were mentioned as an antidote in 8/10 texts, being recommended for either seizures or for agitation.

**General recommendations for antidote therapy**

General recommendations for antidote therapy, sourced from the complete set of reviewed texts, which include both those texts that had an ALS framework to those texts that provided recommendations for more general situations (Figure 3-3). Atropine was linked to resuscitation in the majority of texts (22/27), whereas only 15/27 talked about oximes in the context of resuscitation and initial management. More than half the texts also highlighted the importance of atropine as core component in management of OP poisoning, compared to oxime therapy where 19/27 texts described the controversy that surrounds the efficacy of oximes. Evidence was cited in over half of these texts on that topic.

The majority of texts recommended a doubling dose of atropine (17/27) and WHO equivalent dose of oxime administration (20/27). Obidoxime was less often specified or recommended as a potential oxime agent (11/27).

When looking across all texts regardless of whether recommendations were provided in an ALS framework, atropine (22/27) was again more widely recommended in the context of resuscitation and acute care than oximes (15/27), see Figure 3-4.
### General recommendations for antidote therapy in OP poisoning

#### Atropine
- Atropine therapy mentioned
- Linked to resuscitation
- Identified as core treatment
- Doubling dose recommended
- Review frequently (every 5 mins)
- Atropine endpoints (>2/4) mentioned
- No need for oxygen before atropine
- Describe symptoms of toxicity
- Describe management of toxicity

#### Oximes
- Oxime therapy mentioned
- Linked to resuscitation
- Controversy of efficacy discussed
- Indication clearly provided
- Specifies pralidoxime (PAM)
- Specifies obidoxime
- WHO dose PAM (2g bolus, 0.5-1g/h infusion)
- Alternative dose PAM
- Titrate to provided clinical endpoint?
- Titrate to RBC-AChE endpoints?

#### Other Treatments
- lower priority than standard treatment
- Magnesium sulphate
- Alpha 2 blockers (clonidine)
- NaHCO3
- Haemodialysis
- BuChE scavengers

![Figure 3-4 Recommendations for specific therapies in OP poisoning sourced from all texts](image)

The figure above illustrates the number of texts covering each topic, with bars indicating whether there is evidence cited or no citation.
Airway, Breathing and Circulation
ALS recommendations in OP resuscitation

**Airway/Breathing**
- Respiratory support is management priority
- Oxygen
- Open airway
- Left lateral position, neck extended
- Monitor neck flexors
- Monitor ventilation volume
- Indication to intubation provided
- Avoid suxamethonium

**Circulation & IV therapy**
- IV access
- x2 IV cannulae
- IV fluids
- Rate specified to target physiologic endpoint
- Arrhythmia management
- Inotropic support indication
- Recommends specific ionotropes

**Number of texts covering topic**
- No citation
- Evidence cited

Figure 3-5 Review of literature recommendations regarding airway, breathing and circulation components of ALS in OP poisoning resuscitation
Figure 3-6  Review of literature recommendations regarding the disability, decontamination and staff safety aspects of ALS in OP poisoning resuscitation. Post resuscitation monitoring recommendations are also displayed.
In over half (19/27) of reviewed texts the controversy surrounding efficacy of oxime’s use was mentioned with just under half or these (8/19), providing references to evidence to substantiate the uncertainty of this therapy. Whilst all the text mentioned the possibility of oxime therapy, only 11/27 texts clearly stated or suggested that it was indicated. Conversely the recommendation for atropine was clear across all texts, with over half (16/27) identifying it as either a well established or core treatment in OP poisoning management.

A rapid atropinisation regimen was widely recommended, with a doubling dose strategy being described in 17/27. Approximately half of the latter group cited the research behind this strategy of atropine dosing (41).

Pralidoxime was specified as an oxime in almost all texts, with only 11/27 additionally specifying obidoxime as a possibility. The majority of texts (18/27) described the WHO recommended dose of oximes, but an alternative dose was described in 12/27 texts.

**Other therapies recommended**

A range of other treatments including magnesium sulphate, alpha 2 blocking drugs, sodium bicarbonate, and haemodialysis or haemoperfusion, and bioscavengers were mentioned in a minority of texts (between 5 and 9/27). They were also described under sections peripheral to the core management section and given a lower priority than a standard antidotal treatment of atropine plus pralidoxime when recommended. One exception was in a review article where sodium bicarbonate therapy was given a higher priority, with the citation of other supporting evidence (59).

**Airway, breathing, circulation, disability and decontamination**

Airway support was highlighted as a management priority in almost all the texts (Figure 3-5) sometimes linked to a description of the pathophysiological basis for this
impairment of this system (e.g. both central respiratory depression and bronchorrheoa from peripheral secretions). However, only a minority recommended practices or actions that would specifically address airway problems such as airway opening maneuvers (6/27), and managing the patient in the left lateral position (4/27) with the neck extended to avoid the risk of aspiration. Recommendations to open the airway, continued assessment of tidal volume, and neck flexor strength was mentioned in only 6/27 texts. Indications for intubation was provided in approximately half (14/27) of the texts, but these were for the most part an instruction, such as intubate if respiratory compromise, rather than measurable criteria such as in one text intubation was suggested based upon tidal volume and arterial oxygenation(3).

Less than half the texts highlighted recommendations that specifically prioritized aspects of managing the circulatory system (for example, stating that IV access should be established, or that 2 IV lines were required). A minority of texts highlighted how the pathophysiology of OP poisoning could give rise to hypotension and only 2/27 texts emphasized the titration of IV fluid therapy towards a clinical endpoint. Inotropic therapy was only discussed in 6/27, and only 2 texts recommending specific inotropes however, the recommendations were not accompanied by clear rationale or citations to original research.

Disability, decontamination and post-resuscitation monitoring recommendations

Benzodiazepines for seizures and agitation were recommended in 22 and 16 texts respectively (Figure 3-6). Agitation due to over atropinisation, and treatment to avoid hyperthermia in restrained agitated patients were given as indications in only 3 texts.

There was agreement amongst the texts with the importance of resuscitation and stabilization prior to any decontamination attempts (21/27 texts). The lack of evidence for gastrointestinal decontamination after 1 hour from ingestion, due to rapid absorption
from the stomach, was highlighted in a minority of texts. Protection of the airway prior
to gastrointestinal decontamination, if indicated, was recommended in half (14/27), but
only one linked this assertion to evidence such as a published review of
complications(44) following gastric lavage.

A recommendation of universal precautions for all staff was noted in 13/27 texts, with a
small subset referring to a position statement(46) that provided further evidence for
how secondary poisoning of staff was rarely if ever documented. A minority over
emphasized staff safety, and others suggested elaborate personal protective gear with
a lack of evidence supporting these recommendations.

**Patterns of citations of supporting literature**
The recommendations for airway, breathing and circulation were not supported by
citations to the literature in general, however some specific points relating to airway
recommendations such as avoiding suxamethonium (due to the risk of prolonged
respiratory paralysis) were cited in a high proportion.

A high proportion of the recommendations relating to antidote administration with
regards to atropine, oximes and other treatments were associated with more frequent
reference to supporting literature.

**Discussion**

This review highlighted that there is no consistently described formula for ALS in OP
poisoning management. Analysis of recommendations from a variety of emergency
medicine, and toxicology texts across the standard domains of ALS including airway,
breathing, circulation, disability and decontamination, and specific antidote therapy
revealed some areas of relative consensus surrounding the importance and priority
early rapid atropine administration, and some areas where there was variation such as in the recommendation of oxime therapy.

**Guideline for ALS in OP poisoning**

We created a guideline (Table 2.1 and Table 2.2) focusing specifically on ALS guidelines for two levels of severity at high end of the highest end of the critical illness spectrum. The three case scenarios gave context to these levels which ranged from managing a patient presenting with severe poisoning and critical illness (peri-arrest) to patient who has already had a cardiac arrest from OP poisoning (Figure 3-1). This guideline aimed to provide a sequence and priority to the key ALS elements in the context of what should a junior doctor do right now, in the first 15 minutes to one hour, when faced with any one of these patients.

We review a range of types of text ranging for clinical and toxicology hand books (Oxford Clinical Handbook of Medicine(77), Olson’s Poisoning and Drug Overdose(69)) to compendiums of Emergency Medicine (Tintinalli(74), Rosen(72)), and Toxicology (Goldfrank’s(63)). As such, the scope of recommendation was quite wide. The majority of texts were concerned with providing an overview of potential therapies that someone studying the topic of OP poisoning management could use, along with reasonable detail regarding controversies in treatment, and covered a range of aspects of treatment from initial management to ongoing treatment. As hypothesized no text was solely focused on the acute initial management and resuscitation of severely poisoned or arresting patients. The information concerning ALS components had to be extracted to answer our research questions outlined in Table 3-1, and was not always possible due to gaps in the provision of ALS instruction.
### Table 3.2.1 ALS guideline for acute OP poisoning – Severity level 1.1 (cardiorespiratory arrest)

<table>
<thead>
<tr>
<th>Sequence</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial priorities: CPR + Atropine</td>
<td></td>
</tr>
</tbody>
</table>
| **1. Compressions + Atropine** | Start CPR according to ALS guidelines  
- Give atropine bolus 5mg  
- Consider longer duration of CPR >30mins |
| **2. Ventilate/ Intubate** | Open airway, oropharyngeal airway, Bag-mask ventilate, intubate (without drugs) between cycle when able (consider administering via ET tube if no IV access) |
| **3. Continue IV Atropine** | IV access. Give atropine as soon as possible in conjunction with CPR / airway measures.  
IV atropine 2mg bolus initial dose, re-assess every 5 mins for achievement of endpoints of atropinisation (clearing of chest secretions, P>80, sBP>80, drying of peripheral secretions/sweating). If endpoints not achieved double the dose and continue re-assessment. |
| **3. IV Fluids** | IV fluids 20ml/kg stat Normal saline, or equivalent crystalloid, with continuous infusion -> Aim to keep systolic BP above 80mmHg, and urine output >0.5mL/kg/hr. |
| **4. Cardiac monitoring** | Apply cardiac leads to check for arrhythmia's if available. If Torsades de Points occur - give 2mg MgSO4 as rapid IV infusion |
| **5. Ongoing post-resuscitation monitoring** | After ROSC - will need ICU level monitoring for at least 24hours  
*Monitor atropine*  
Continue doubling dose of atropine until atropinisation is achieved, re-assesing every 5 mins. Follow with an atropine infusion of 10-20% the total dose used*.  
*Monitor for respiratory failure*  
Check Neck Flexion & Tidal volume (see indications for intubation – Table 3.3) |
| **6. Decontamination** | Remove excess clothing can occur in conjunction with Steps 1-4, but defer skin washing until ROSC (which can otherwise impair life saving CPR and ALS). When stable wash skin with soap and water. |
Gastric Lavage (GL) and Activated Charcoal (AC) are not indicated unless patient has been stabilised, and treated with oxygen and atropine.

Thereafter perform GL only if <1-2 hours from time of ingestion, and airway is protected; with orogastric tube ONLY after airway protection with intubation. Finish with a dose of AC.

**Table 3.2.2 ALS guideline for acute OP poisoning – Severity level 1.2 (critical illness / peri-arrest)**

<table>
<thead>
<tr>
<th>Sequence §</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial priorities: Airway management/ Atropine / +/- intubate early</td>
<td></td>
</tr>
</tbody>
</table>
| 1a. Airway management | Suck excess secretions  
Open airway (head tilt, chin lift, jaw thrust)  
FiO2 100% via non-rebreather mask  
Manage in left lateral position, head down, avoid aspiration |
| 1b. IV Atropine | IV access, IV atropine 2mg bolus initial dose, re-assess every 5 mins for achievement of endpoints of atropinisation (clearing of chest secretions, P>80, sBP>80, drying of peripheral secretions/sweating).  
If endpoints not achieved give double the IV dose and continue re-assessment. |
| +/- Intubation | If respiratory compromise intubate (see “indications for intubation” – maintain low threshold)  
**Intubation pathway**  
Induction agent: Diazepam 5mg IV  
Muscle relaxant: Rocuroneum (non depolarising muscle relaxant) |
| 2. Continue IV atropine | re-assess every 5 mins for achievement of endpoints of atropinisation. If endpoints not achieved give double the IV dose and continue re-assessment.  
If atropinisation is achieved, follow on with an atropine infusion of 10-20% the total dose used. |
| 3. IV Fluids | 20ml/kg, titrate towards sBP>80mmHg, UO >0.5ml/kg/h |
| 4. Cardiac monitoring | Apply cardiac leads to check for arrhythmia’s if available. If Torsades de Points occur - give 2mg MgSO4 as rapid IV |
5. Post resuscitation monitoring

ICU monitoring. If intubated monitor ventilator settings and oxygenation

If not intubated, continue to review respiratory function:

**Indications for intubation**
- Tidal volume < 5mL/kg
- Apnoea
- PaO2 < 60mmHg
- FiO2 > 60%

Check for
A) re-development of cholinergic signs & symptoms
B) development of peripheral respiratory failure
   1) Flexor neck strength (ask to lift head off bed)
   2) Continue to check Tidal volume every 4 hours

6. Decontamination

Remove excess clothing can occur in conjunction initial resuscitation. When stable wash skin with soap and water. (discard contaminated clothing)

Gastric Lavage (GL) and Activated Charcoal (AC) are not indicated unless patient has been stabilised, and treated with oxygen and atropine

Thereafter perform GL only if <1-2 hours from time of ingestion, and airway is protected; with orogastric tube ONLY after airway protection with intubation. Finish with a dose of AC

---

**Key to ALS guideline**

ROSC - return of spontaneous circulation
GL - gastric lavage
AC - activated charcoal
sBP - systolic blood pressure
P - Pulse, HR - Heart rate, bpm - beats per minute

§ Staff Safety - Universal precautions (gloves and gown) for all patient contact. Use facemask if treating patient in closed environment, and rotate staff to minimise exposure to hydrocarbon solvent.

Nosocomial poisoning is not a significant threat (46). Avoid delays to resuscitation of patient (NB - sealed whole body suite is not indicated).
### Table 3-3.1 Guidelines for atropine ALS of OP poisoning

<table>
<thead>
<tr>
<th>Atropine in ALS</th>
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<tbody>
<tr>
<td><strong>Indication</strong></td>
</tr>
<tr>
<td><strong>Rationale</strong></td>
</tr>
<tr>
<td><strong>Evidence</strong></td>
</tr>
</tbody>
</table>
| **Standard dose** | **Adult:** 2mg IV bolus, (Child: 0.05 mg/kg IV bolus)  
Re-assess every 5 mins for achievement of endpoints of atropinisation  
Once parameters have begun to improve, cease doubling dose. Similar or smaller doses can be used. Once patient is stable start atropine infusion of 10-20% of total dose need to stabilise patient over 1 hour. (3, 5, 41) |
| **Endpoints** | Give atropine until  
- Chest is clearing (with clinical judgment as  
- HR > 80 bpm  
- sBP > 80  
(Sweating stops, Pupils dilate)  
Keep giving atropine, doubling dose every 5 minutes until endpoints achieved  
Sweating stops in most cases. Pupils will commonly dilate and not a useful sign of endpoint of initial atropine treatment because a delay exists before maximal effect. However, very dilated pupils are an indicator of atropine toxicity. (3, 5, 41) |
| **Adverse effects** | Confusion, urinary retention, hyperthermia, bowel ileus and tachycardia (70) |
Treatment: Stop infusion. Can give diazepam if agitation. Restart atropine later.

Do not restrain patient for toxicity as can develop life threatening hyperthermia.

Guideline to dosage

Cohort of 22 severely poisoned patients required total mean of 23.4mg of atropine, and maximum of 75(41)

Hundreds of milligrams of atropine by bolus and continuous infusion may be required over the course of several days (82). A maximum daily dosage as high as 3.5g has been reported(68).

Arrest dose (increased IV bolus)

In the context of cardiorespiratory arrest, the most efficacious dose has not been established through clinical trials.

In Asia an initial dose of 5-10mg of atropine is commonly used, and there is no evidence to suggest that such a dose would be detrimental in an arrested patient.

Table 3.3.2 Guidelines for benzodiazepines ALS of OP poisoning

<table>
<thead>
<tr>
<th>Benzodiazepines in ALS</th>
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<tbody>
<tr>
<td>Indication</td>
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</tbody>
</table>

Endpoints

Mild sedation
Maintains safe level of consciousness

Adverse effects
Over-sedation, decreased level of consciousness

Table 3.3.3 Indications for intubation as part of ALS in OP poisoning

<table>
<thead>
<tr>
<th>Intubation in ALS</th>
</tr>
</thead>
<tbody>
<tr>
<td>Acute assessment</td>
</tr>
<tr>
<td></td>
</tr>
</tbody>
</table>
Ongoing assessment

Assess neck flexor strength regularly in conscious patients
(Ask patient to lift head off the bed and hold it in that position whilst pressure is applied to the forehead)

Tidal volume should be measured every 4 hours in these patients

Indications for intubation (3)

Intubate and ventilate patients if either:-
- tidal volume is below 5mL/kg
- vital capacity is below 15mL/kg,
- apnoeic spells are present
- PaO2 < 8kPa (60mmHg) on FiO2 >60%

Considerations in OP poisoning

Avoid suxamethonium as prolonged respiratory muscle paralysis may occur due to inhibition of pseudocholinesterase

Instead a competitive neuromuscular blocker such as rocuroneum can be used

Diazepam should be given to all patients after intubation as animal studies have shown a neuroprotective effect, and paradoxical improvement in respiratory function

Table 3-3.4 Guidelines for oximes in OP poisoning

<table>
<thead>
<tr>
<th>Oximes in OP poisoning (not indicated in acute ALS)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Indication</strong></td>
</tr>
<tr>
<td>In symptomatic patients who are not responding to atropine therapy.</td>
</tr>
<tr>
<td>PAM is most likely to be effective early, however, do not delay active resuscitation (ie Airway, Breathing, Circulation and Atropine) to administer PAM. <strong>There is a lack of evidence to suggest it’s befit in the ALS framework for OP poisoning.</strong></td>
</tr>
</tbody>
</table>
| Considered if there are nicotinic symptoms for certain OP within certain time limits;
  - dimethyl - 4 hours
  - diethyl - 24 hours |
| **Endpoints** |
| Clinical |
| • no clear established endpoints (effects may be delayed).
  • may see improvement in muscle power or decrease in fasciculation
  • NMJ function using RNS or “train of 4” |
| Biochemical |
| • Increase in RBC-AChE in response to bolus may indicate effectiveness of oxime therapy |
• Decline of RBC-AChE within 6 hours post stopping oximes may indicate OP still active in system and benefit of re-starting oximes

Adverse effects
Rapid administration can lead to hypertension, vomiting and a transient reversible neuromuscular blockade(72)

The question of what sequence antidotes should be inserted or integrated into an ALS framework could only be accurately answered from the 11 texts reported in a format that allowed interpretation of a sequence of components. Comparing recommendations across both this subset of ALS framework texts and the entire collection, the message of atropine being an integral component of OP poisoning treatment and oximes being secondary was clear. Many of the texts acknowledged the controversy of oxime efficacy; many without explicitly stating whether they were advocating its use or not(63). Oximes are unlikely to provide a predictable improvement in the underlying pathophysiology that causes acute respiratory failure. In addition given the overall lack of evidence for efficacy, in any phase of OP toxicity, we have left oximes out of the ALS algorithm. This is in keeping with the majority of texts that were reviewed.

Use of guidelines to manage case scenarios
Scenario A in the depicted in Figure 3-1 is relevant to OP ALS algorithm, severity level 1.1 which outlines a cardiac arrest algorithm where there is muscarinic hyperactivity. Scenarios B and C pertain to the severity level 1.2. In both these ALS guidelines the key feature that is emphasized, and only covered in a minority of the reviewed texts, is the integration of ongoing rapid atropine infusion during the delivery of other components of ALS. In both cases establishing an initial intravenous bolus of atropine, followed on by doubling doses and frequent reassessment is present in conjunction with cardiopulmonary resuscitation in the level 1.1 algorithm, and in conjunction with airway opening and intubation in the level 1.2. There is a sound rationale for the use of an antimuscarinic in OP poisoning, and particularly in resuscitation as the majority of cardiac arrests are as result of an initial respiratory arrest, that progresses to cardiorespiratory arrest. As many as 25% of acute OP presentations require ventilation and intubation, and this is likely to occur within the first 24 hours(32). Early respiratory
failure develops because of central respiratory failure due to the CNS effects of OP of poisoning, and peripheral respiratory failure due cholinergic activity leading to increased lung secretions and bronchospasm; atropine in adequate doses reverses these processes. The highly cited paper that has promoted this treatment protocol (5), has led to extensive adoption of this approach by other texts (57). However, the position of atropine early in the sequence of ALS was only promoted or emphasized in a few texts and this gap in ALS recommendations is a key finding in the current review that has been addressed within the proposed ALS guideline. The lack of emphasis for early atropine is compounded by the fact that the position of antidotes in a sequence of management steps is less clear or not possible in texts that don’t provide instructions in an ALS framework or some other kind of ordered format.

A further difference in the proposed guideline to the reviewed texts is the removal of oximes from the ALS guideline. Only one text that had recommendations in a ALS format omitted oximes as we are suggesting (79). However, all 8 texts that recommended antidotes as part of their ALS framework suggested a lower priority of oxime therapy compared with atropine in the sequence or ALS components. The evidence base for controversy surrounding oxime therapy is wide and some of these articles were cited in over half (11/19) the texts that mentioned the controversy. However, two studies that are important in the debate were only cited by a minority of texts that describe the controversy, these being Cochrane review published in 2011, which showed a lack of evidence to determine whether oximes were harmful or beneficial (95), and an RCT that examined the WHO dosing regimen of pralidoxime published in 2008, that showing no evidence of benefit in clinical outcomes (50). These add further support for not including oximes in ALS framework. Having said that, we are not making any comment with regards to the use of oximes in the non ALS / resuscitation setting, and it may be reasonable to administer oximes under the discretion of the treating clinicians after initial stabilisation has occurred, particularly if there is a poor response to atropine, as mentioned in one text (75).
Diazepam is an adjunctive therapy that was widely recommended for agitation and seizures, and has been suggested through animal studies to have neuroprotective effect\(^{(100)}\), and cause a paradoxical improvement in respiratory function\(^{(101, 102)}\), and therefore could be given to all patients. However, this role was not reflected in the reviewed texts.

**OP management’s influence on aspects of standard ALS**

Airway support as a management priority was highlighted in nearly all the texts. However, less than half the texts provided any specific instructions in this regard, such as open airway, or manage in a left lateral position to decrease the chance of aspiration. Also the link between early and rapid atropinisation and improvement of respiratory function was not always described. Monitoring of tidal volume, and neck flexion strength was stated to be useful by some texts, and one included this as a basis for indications for intubation, which we have adopted in the ALS guideline we have proposed. However, it was also noted that the description of these measures were not supported by citations to clinical research and the effectiveness of such an approach remains to be demonstrated.

**Circulation**

Only a minority of texts mentioned insertion of two IV cannulae, and with good rationale (e.g. one for giving antidotes, another for fluids, particularly if intubation is contemplated). This could be better highlighted as in our experience it is a common error in Sri Lanka for severely poisoned patients to have only a small single cannula at the time of arrest.

There was some variation regarding cardiovascular elements of ALS, where less than half the texts mentioned arrhythmia management. This ranged from stating that cardiac monitoring should be carried out to suggesting specific treatment strategies, such as
the use of magnesium in the management of Torsades de Pointes. Also only a minority (6/27) described or recommended the use of inotropes, and only 2 mentioned specific inotropes which suggest there may be a gap in the literature with regard to evidence for an approach to hypotension in OP poisoning.

Decontamination

The priority of ‘ABC’ over decontamination is agreed by most texts and has been reiterated in the ALS guideline. Similarly, that GI decontamination should occur only after airway protection was stated in over half the texts, however, a corresponding paper on the hazards of gastric lavage(44) was rarely cited.

Staff Safety and Personal protection

Universal precautions is all that is suggested by a nosocomial poisoning position statement(46), and most recommendations reflected this, although there was some variation as to whether this meant gloves and gown, or glove gown and mask.

There was further variation in recommendations, with a number of texts pointing out that nitrile gloves are more impervious to chemical such as OP than latex and rubber gloves. However, access to these gloves is limited in Asia and there are no reports of nosocomial poisoning in such settings despite high patient loads and the use of standard universal precautions. Specialized full body suits with charcoal masks (as suggested by one text) are not necessary for the hospital setting described in our scenarios, however the text in question was more focused on providing information in the pre hospital context.
Future clinical studies

This process of carrying out this review uncovered a number of unanswered questions to do with guidance in cardiac arrest management in the specific context of OP poisoning. Whilst there has been a reasonable amount of research on the clinical effectiveness of atropine regimens, such as the doubling dose regimen, in severely poisoned patients, we found no research investigating the ideal doses of atropine in a cardiac or cardiorespiratory arrest. On the ground observations of practice in Sri Lanka peripheral hospitals was that 5mg or 10mg doses of atropine were frequently administered via infusion or bolus (sometimes before transferring the patient to a secondary referral center) and there did not appear to be any serious problems from this practice. A ceiling on the total dose of atropine, or targets of a minimum achievable therapy in arrests has not been established. Thus, it may be reasonable to give even up to 20mg as bolus in a cardiac arrest situation, considering that an average dose of atropine of 23.4mg was given in one case series, and administration of this dose over 8 to 30 minutes, and has been the basis for of the doubling dose protocol that has been widely adopted in recommendations for non arrested patients(41, 57).

The measurement of details regarding characteristics of arrests due to OP poisoning would provide valuable information that could aid protocols for CPR and resuscitation. Collection of data on type of arrest (e.g. pulseless electrical activity versus ventricular fibrillation) and average duration of CPR performed where there are good neurological outcomes, would help inform which algorithm is optimal (e.g. pathways that either involve or don’t involve defibrillation), and what should be the maximum duration of CPR before making a decision to withdraw CPR. In general a convention of 30 minutes is used for fear of poor prognosis with prolonged CPR, but in the general toxicology literature good neurological outcome has been reported in cases arrest where CPR has been carried out for long periods of time (e.g. 3 to 5 hours), which led to guidelines that suggested that more prolonged CPR and resuscitation may be warranted in patients with overdose(103).
Standardised cardiac arrest registries that are already in use in many parts of the world, allow for collection and analysis of cardiac arrest outcomes providing valuable information on the abovementioned matters. These may provide valuable information if conducted in settings where there are frequent cardiac arrests due to OP poisoning(104). A recent retrospective study that collected detailed data on 33 OP poisoned patients in a western hospital showed that CPR was conducted on 6 occasions where 5 were asystolic arrests and 1 was a VF arrest. There was one survivor but it is not clear how long CPR was conducted before return of spontaneous circulation occurred. Similar observational studies with greater numbers could help better guide cardiac arrest protocols such as the one being suggested in Table 3-2. This is a feasible future research idea that may more easily be carried out in developing countries where there are high volumes of poisoned patients and high case fatality.

Translation of ALS guidelines in Developed and Underdeveloped EM systems – impressions from the field

Having experience of working in Emergency Medicine systems that can be classified as mature, such as in Australasian Emergency Departments(105), and Sri Lankan secondary referral centers which have a more developing Emergency Medicine systems (106), it is likely that a guideline such as proposed will translate differently in these two settings, according to background practice. Doctors in western countries with highly developed critical care systems have a clinical practice more focused on advanced life support. In contrast, rural developing country doctors are highly reliant on and rehearsed in providing acute medical therapies. We anticipate they will persist with escalating atropinisation protocols, whereas Western doctors may move more rapidly to intubation and ventilation. A further practical issue for OP resuscitation in Western countries is the absence of a stockpile of atropine that is required in
abnormally high quantities in acute OP poisoning. Even a single severely ill patient may exhaust the hospital supply of atropine. Thus implementation of these draft guidelines may require logistical and knowledge deficits to be addressed.

**Limitations**

One limitation of this study is that our search criteria may have missed texts that are from non-English speaking countries and that are widely used. However, we have covered a broad range of texts that are accessed by clinicians and most of our conclusions are not sensitive to small changes in the number of included texts.

Whilst the guideline for ALS in OP poisoning was informed by a systematic review of existing recommendations, it could be strengthened further by additional systematic reviews of original evidence. Each component of ALS as listed in the summary Table 3-1, deserves its own systematic review in order appraise the evidence for each recommendation, but this was beyond the scope of the current study. The guideline described in the present study aimed more to be a working model in which to capture key recommendations, that were congruent with strategies to address the unique characteristics of OP poisoning management, and this can be developed and modified further in the future after clinical testing, rather than providing a definitive guide.

**Further development of the ALS guideline**

Demonstrating its impact in clinical practice would strengthen the support for an ALS guideline. Such research should also examine any translational blocks and the face validity of the recommendations. Research could also assess the understanding of proposed protocol by the target audience, as well as what strategies can be used to promote its integration into practice.

There is evidence to suggest that adoption of different guidelines is quite variable, even guidelines based on widespread consensus such as the guideline recommendation of
the ILCOR guidelines on resuscitation. The guideline we have proposed is based on an instructive format that outlines clearly the sequence of resuscitation steps. This format has been devised in accordance with clinical experience of treating many cases of severe OP poisonings, where it has been recognised that both the provision of detail surrounding the steps of resuscitation and the sequence in which they are carried out are likely to be important factors in addressing the unique pathophysiology of this poisoning. However, as with all guidelines, there should be some evaluation process to assess the uptake of policy as well as whether it makes a difference in clinical outcomes. Tools are available to aid with guideline development\(^{(107, 108)}\), however, there is some debate about even some commonly used tools in this arena\(^{(109)}\).

Finally, original basic science research and clinical studies are indicated to explore the numerous components of resuscitation that have been uncovered with variable recommendations in this review (e.g. what is the clinical impact of more careful monitoring of respiratory function in preventing respiratory failure, or delayed intubation).

**Conclusions**

Despite high proportions of patients requiring CPR for cardiac arrest, and a there being a reversible component to the pathophysiology of OP poisoning existing, no ALS guideline exists in international recommendations to guide the management of this frequent global presentation. There is a gap in the literature in the provision of management guidelines at this acute end of the spectrum. Furthermore, the majority of OP poisoning management texts have not been written with an ALS framework in mind.

We have created an instructive ALS guideline tailored for the severely poisoned, ranging from the arrested patient to the critically ill and severely poisoned patient,
based largely upon what is already being recommended, but taking into account advances in the scientific literature during the past 5 years.

There is consensus over the beneficial role of atropine in the ALS of OP poisoning, and early rapid aggressive atropinisation in all critically ill, or arrested patients, and this is a key feature of the ALS guideline.

Oxime therapy is controversial even in standard management and has no role in the acute initial care focus of the ALS guideline, but may be consider after resuscitation and stabilization of the patient.

The sequence of CPR components would place atropine as top priority that can be considered as running in parallel to the more conventional therapies for ‘ABC’; as it is expected to improve both the cardiovascular and respiratory physiology. Respiratory failure and a low threshold for early intubation is also a feature of the guideline, and we recommend some of the guidelines involving tidal volume highlighted in a minority of the reviewed texts.

Future research is needed to validate the use of an ALS guideline such as the one provided, and it is likely that a process of further development and modification may necessary. Research is also recommended to further address gaps in evidence that evaluate the efficacy of aspects of clinical practice in advanced cardiac life support such as antidotal efficacy during cardiac arrests, indications for intubation, and assessment of benefits of monitory respiratory function.
Chapter 4: Evaluation of the Test-mate ChE (cholinesterase) field kit in acute organophosphorus poisoning

Published: This chapter has been published as a journal article.

Abstract

Study Objective: Measurement of acetylcholinesterase (AChE) is recommended in the management of organophosphorus (OP) poisoning, which results in 200,000 deaths annually. The Test-mate ChE 400 is a portable field kit designed for detecting occupational OP exposure that measures red blood cell acetylcholinesterase (RBC-AChE) and plasma-cholinesterase (PChE) within 4 minutes. This study evaluates the Test-mate ChE field kit against a reference laboratory test in the context of acute OP self-poisoning.

Methods: A prospective comparison study of 14 patients with acute OP poisoning was carried out between November 2007 and June 2008. RBC-AChE and PChE was measured in 96 and 91 samples using the Test-mate ChE field kit and compared with a reference laboratory. The limits of agreement method (Bland and Altman), kappa statistics, and correlation coefficients (Pearson) were used to evaluate the agreement between the two test methods.

Results: There was good agreement between the Test-mate ChE and the reference laboratory for RBC-AChE. The mean difference (Test-mate - reference) was -0.62 U/gm Hb, 95% limits of agreement -10.84 to 9.59 U/gm Hb. Good agreement was also observed between the different clinical categories; (weighted kappa 0.85). Measurement of PChE also showed good agreement with a mean difference (Test-mate – reference) of +0.06 U/ml blood, 95% limits of agreement -0.41 to 0.53 U/ml blood. Pearson’s correlation coefficients were 0.88 (95% CI 0.83 to 0.92) for RBC-AChE and 0.87 (95% CI 0.81 to 0.91) for PChE.

Conclusion: The Test-mate ChE field kit reliably provides rapid measurement of RBC-AChE in acute OP poisoning.
**Introduction**

**Background**

OP pesticide self-poisoning is a serious public health problem resulting in approximately 200,000 annual deaths worldwide (3, 48). The case fatality is as high as 15-30% depending on the type and amount of OP agent consumed and the delay in the initiation of treatment (47). Respiratory failure is common leading to intubation rates as high as 25% of all cases of acute OP poisoning(32). Poisoning is due to the inhibition of acetylcholinesterase (AChE; EC 3.1.1.7) in nerve tissue leading to the accumulation of synaptic acetylcholine. However, because neuronal AChE cannot be directly measured in patients, AChE in red blood cells (RBC-AChE) and plasma cholinesterase (PChE; EC 3.1.1.8) are used as biomarkers of exposure to OP compounds(110, 111). The measurement of these biomarkers is recommended in the management of OP poisoning(3), as they can be used to confirm the diagnosis, grade the severity of poisoning, guide antidote therapy, and they may also help in facilitating early discharge in cases of mild poisoning. However, the test is not available in most parts of the developing world, where the highest number of cases are seen.

One of the greatest challenges in carrying out RBC-AChE assays in OP poisoned patients is the need for special measures during blood collection, such as immediate dilution and cooling of samples, in order to prevent ex-vivo reactions occurring in cases of acute poisoning². These measures are particularly important in patients who are receiving oxime antidote therapy, as results may be inaccurate when omitted(3, 85, 112). However these precautions are not taken in many settings where cholinesterase monitoring is required clinically, including in the developed world. Therefore a rapid and accurate system of AChE testing is not available for acute OP poisoning in most parts of the world. Improved methods to rapidly monitor severe OP poisoning, would also be relevant to the treatment of anticholinesterase nerve agents used in chemical warfare(113).
**Importance**
The Test-mate ChE™ is a portable field kit, which measures RBC-AChE and PChE within 4 minutes per test, and was designed for determining exposure to anticholinesterase pesticides in agricultural workers. There have been 4 studies published on the evaluation of this field kit, but only two of these involved direct measurements from patients (114-117). We have concerns about the generalisability of results from these studies to the setting of acute OP self-poisoning because the field kit was designed for occupational use and to be more accurate when measuring higher levels of AChE (personal communication with the manufacturer), and may be less accurate in acute poisoning where the poison load is much higher.

**Goals of this investigation**
The aim of our study was to evaluate the performance of the Test-mate ChE field kit in acute OP poisoning by measuring the agreement between results from the field kit and results from a reference laboratory test in cases of OP self-poisoning.

**Materials and Methods**

**Study Design & Setting**
A prospective comparison study was carried out at a secondary referral hospital in rural Sri Lanka.

**Selection of participants**
Consecutive patients admitted with a history of OP self-poisoning between November 2007 and June 2008 were eligible for inclusion. This study was investigating the impact of bedside cholinesterase testing on decisions made by physicians. Local internal medicine physicians were responsible for the management of patients. Symptomatic OP poisoned patients were initially resuscitated with intravenous atropine using bolus doses and infusions titrated to clinical response. Pralidoxime was
sometimes prescribed depending on the preference of the treating physician (usual
dose of 1g pralidoxime chloride IV every 6 hours for 48 hours).

At the time of patient selection we already had 12 months experience in using the Test-
mate ChE field kit for the measurement of cholinesterase levels in pesticide poisoned
patients. Fourteen patients were selected in whom we expected the ‘reference test’ to
be most accurate because of a lower likelihood of ex-vivo reactions.

These patient’s samples were all collected within the 6 months before the shipment to
the reference laboratory and had a documented cold chain. Carbamate poisoning was
excluded from the comparative sample because of the authors’ experience of rapid ex-
vivo reactivation in such cases, which could render the reference test results unreliable
(unpublished data).

**Interventions**

The protocol was approved by the ethics review committee of Peradeniya University
(Sri Lanka). All OP poisoned patients were tested for RBC-AChE and PChE using the
Test-mate ChE field kit. Duplicate samples were prepared at the same time to be
tested at a later date in a reference laboratory. The frequency of blood tests depended
upon the severity of poisoning, and whether oximes were being used (see Figure 4-1).
**Figure 4-1** Study protocol showing frequency of blood testing for acetylcholinesterase.

*Symptomatic patients were tested more frequently than asymptomatic patients. Patients who were receiving oxime therapy were tested pre and post pralidoxime dose.*

**Methods of Measurement**

Cholinesterase measurements using the Test-mate ChE field kit

This study used a Test-mate ChE field kit [model 400, EQM research] designed for use over an extended temperature range (10-50 degrees centigrade)(118). The field kit consisted of a battery operated portable cholinesterase testing system that used the modified Ellman method. The amount of yellow colour produced as a result of the Ellman reaction is measured using a photo spectrometer indicating the quantity of cholinesterase present (see online appendix for further details). RBC-AChE and PChE were measured within 4 minutes per test using venous blood.
The precision of the Test-mate ChE field kit had previously been established by the manufacturer with analysis of 100 replicate samples of blood to which OP agents had been added (119).

10 microlitres of venous blood was transferred from the EDTA anticoagulated tube and mixed with the buffer solution. The acetylthiocholine or butyrylthiocholine within the buffer solution hydrolyses the RBC-AChE or PChE respectively, producing carboxylic acid and thiocholine, which reacts with the Ellman reagent (dithionitrobenzoic acid) to form a yellow colour. The rate of production of the yellow colour was measured on the photometer at 450nm, and this value indicated the activity of cholinesterase (114). RBC-AChE activity was determined in the presence of a specific inhibitor of PChE and the value is corrected for the amount of haemoglobin by dividing the measured AChE by the haemoglobin concentration (also measured photometrically). The machine was operated in an air-conditioned research room (temperatures between 19C to 22C) within the hospital premises.

The measurement of PChE was similar, also utilising 10 microlitres of whole blood. It simply requires a “mode change” button to be pushed on the Test-mate ChE device, prior to testing.

In cases of very low cholinesterase levels the Test-mate ChE field kit displayed the warning “No Reaction” followed by the level of enzyme activity. In some instances a negative integer (close to zero) was obtained. We converted these values to zero for the purpose of data analysis, as negative enzyme activity is not possible.

Standard deviations of 0.82 (U/g Hb) and 0.15 (U/ml blood) were observed for repeated RBC-AChE and PChE measurements respectively, and from this we calculated the limits of quantification (LOQ) to be 4.1 U/g Hb for RBC-AChE and 0.75 U/ml blood for PChE. Testing above these limits, we verified the precision of the Test-
mate ChE in our setting by testing replicate cholinesterase measurements in 10 patients with OP self-poisoning. The mean coefficient of variance (CV) was 4.5% for RBC-AChE (range 1.3% to 8.4%) and 6.0% for PChE (range 2.0% to 11.6%). Using regression to extrapolate values where we would expect the CV to be greater than 20%, we re-estimated the LOQ for Test-mate ChE in our setting to be 1.3 U/g Hb (4.1% of normal) for RBC-AChE and 0.26 U/ml blood for PChE.

Cholinesterase measurements using the reference test
Duplicate samples were tested for RBC-AChE and PChE at the Bundeswehr Institute of Pharmacology and Toxicology, in Munich, Germany, and the modified Ellman method was used as previously described(85). The reference laboratory sample was prepared at the same time as testing with the Test-mate field kit. Sample preparation for RBC-AChE measurement consisted of transferring 200 microlitres of whole blood to another collection tube. This sample was immediately diluted and mixed with ice-cold distilled water in a 1:20 dilution, and frozen soon afterwards in order to minimise ex-vivo reactions.

The mean coefficient of variance (CV) measured at the reference laboratory was 2.75% for RBC-AChE (range 0.50% to 4.26%) and 4.00% for PChE (range 2.23% to 5.54%). The limits of quantification were 0.2 U/g Hb and 0.026 U/ml for RBC-AChE and PChE respectively(85).

Samples for PChE measurement were prepared by centrifuging the anticoagulated blood and transferring 1ml of plasma into a separate tube.
All samples were stored in a minus 20 degree centigrade freezer before being transported to the reference laboratory in Germany. The cold chain was strictly maintained during transport.

**Data Collection and Processing**

All blood samples were collected by research assistants who were junior doctors trained in venipuncture. They were also trained in the operation of the Test-mate ChE field kit according to the users manual (supplied by EQM research), and with additional power point presentations and a training video specifically created for education of the research protocol. As a quality control measure the principle investigator supervised the performance of each research assistant during the collection, processing and storage of samples in 5 test cases.

Results for RBC-AChE and PChE measurements obtained from the Test-mate ChE field kit were recorded on a datasheet and transferred to a computer spreadsheet program (Microsoft Excel). The results from the reference laboratory were also entered into an Excel spreadsheet. The reference laboratory staff did not have access to the Test-mate results.

**Outcome measure**

Primary outcome measures were the RBC-AChE and PChE levels measured at the bedside using Test-mate ChE field kit, and in the reference laboratory.

**Primary data analysis**

The ‘limits of agreement’ method (described by Bland and Altman(120, 121)) was used to assess agreement. The differences between the two methods were plotted against their mean for each individual blood sample. This plot is bounded by the 95% limits of agreement (which is equivalent to +/- 1.96 SDs above and below the mean difference) [calculated using GraphPad Prism v5]. The agreement for the different clinical categories of RBC-AChE inhibition was analysed using the weighted Cohen’s kappa statistic [using STATA 10].
Regarding the clinical categories of RBC-AChE inhibition, we based the cut-off points upon literature findings for the degree of symptoms associated with different levels of RBC-AChE activity, which were as follows: 'normal' >75% ( >23.6 U/g Hb), 'mild inhibition' 30-74% (9.4-23.5 U/g Hb), 'moderate inhibition' 10-29% (3.1-9.4 U/g Hb) and 'severe inhibition' <10% (<3.1 U/g Hb) (Table 4-1)(27, 28, 39, 122, 123).

**Table 4-1 Clinical categories of RBC-AChE activity.**
The cut-off points were based on animal and clinical research that correlated expected symptoms with levels of RBC-AChE activity.

<table>
<thead>
<tr>
<th>Clinical category of AChE inhibition</th>
<th>% Normal AChE (Normal taken at 31.4 U/g Hb)</th>
<th>AChE level (U/g Hb)</th>
<th>Expected symptoms based on Evidence</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>≥ 75%</td>
<td>≥ 23.6</td>
<td>Asymptomatic&lt;sup&gt;(26)&lt;/sup&gt;. Occupational guidelines suggest &gt;77% signifies 'no exposure'&lt;sup&gt;(122, 123)&lt;/sup&gt;</td>
</tr>
<tr>
<td>Mild inhibition</td>
<td>30-74%</td>
<td>9.4-23.5</td>
<td>Clinical symptoms with normal muscle function (Based upon animal studies&lt;sup&gt;(39)&lt;/sup&gt; and neuromuscular transmission data from clinical cases&lt;sup&gt;(27, 113)&lt;/sup&gt;)</td>
</tr>
<tr>
<td>Moderate inhibition</td>
<td>10-29%</td>
<td>3.1-9.4</td>
<td>Diaphragmatic Muscle paralysis expected&lt;sup&gt;(26, 39)&lt;/sup&gt;</td>
</tr>
<tr>
<td>Severe inhibition</td>
<td>&lt;10%</td>
<td>&lt;3.1</td>
<td>Strongly impaired neuromuscular transmission and diaphragmatic paralysis expected&lt;sup&gt;(27, 39)&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

For the purpose of comparing test methods the reference test PChE results were multiplied by (1- packed cell volume) to adjust units from ‘U/ml plasma’ to ‘U/ml blood’.
The fractional packed cell volume was estimated by multiplying the haemoglobin concentration (g Hb/100 mL) by 3 and dividing by 100(124).
Results

Characteristics of Study Subjects
A total of 14 OP poisoned patients were studied and 96 pairs of test results for RBC-AChE and 91 pairs for PChE were compared. The patient characteristics and types of OP agents responsible for poisoning are shown in Table 4-2. The median age was 35 years, and there were a greater proportion of male patients (79%, 11/14). The most commonly ingested OP agent was chlorpyrifos (50%, 7/14). All but 3 patients received pralidoxime therapy. The average number of tests per patient was 6.6, collected over a mean of 4 days in hospital. The delay to reference test analysis after blood sampling ranged from 2-8 months. Two patients (14%) were intubated during the course of admission and no patient deaths were observed in the study group.

Table 4-2 Patient characteristics of study group, number of cholinesterase tests, and specific OP agents ingested.

<table>
<thead>
<tr>
<th>Sample characteristics</th>
<th>No. (%)*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Median age, y</td>
<td>35 (range 19-52)</td>
</tr>
<tr>
<td>Male sex</td>
<td>11 (79)</td>
</tr>
<tr>
<td>Median length of stay, days</td>
<td>3 (range 1-11)</td>
</tr>
<tr>
<td>Patients intubated</td>
<td>2 (14)</td>
</tr>
<tr>
<td>Patients receiving pralidoxime</td>
<td>11 (79)</td>
</tr>
<tr>
<td>Deaths</td>
<td>0</td>
</tr>
<tr>
<td>Median no of RBC-AChE tests/ patient</td>
<td>6.5 (range 2-13)</td>
</tr>
<tr>
<td>Median no of PChE tests/ patient</td>
<td>7 (range 0-13)</td>
</tr>
</tbody>
</table>

Type of organophosphorus ingested

<table>
<thead>
<tr>
<th></th>
<th>No. (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chlorpyrifos</td>
<td>7 (50)</td>
</tr>
<tr>
<td>Diazinon</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Quinalphos</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Phenthoate</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Dimethoate</td>
<td>1 (7)</td>
</tr>
<tr>
<td>Unknown organophosphorus</td>
<td>3 (21)</td>
</tr>
</tbody>
</table>

*Data are provided as No. (%) unless otherwise indicated
**Main Results**

**Agreement of RBC-AChE measurements**

There was good agreement between the Test-mate ChE and the reference test for RBC-AChE and the Pearson correlation coefficient was 0.88, (95% CI 0.83 to 0.92). Figure 4-2 displays the levels of RBC-AChE recorded by each test method and shows that the majority of points lie within the same clinical category, indicated by dotted lines. The agreement between the clinical categories of normal, mild, moderate and severe inhibition is shown numerically in Table 4-3 (weighted Cohen’s kappa 0.85).

![Figure 4-2 Scatter diagram showing RBC-AChE activity determined by the Test-mate ChE field kit plotted against activity determined by the reference test.](image)

*The different clinical categories for levels of RBC-AChE inhibition; - normal, mild, moderate and severe inhibition is indicated by dotted lines.*
Table 4-3  Distribution of RBC-AChE results according to clinical category.

Shaded cells show where the same category was observed by both test methods. Overall there was a good agreement observed between the two tests (weighted Kappa=0.85).

<table>
<thead>
<tr>
<th>Test-mate ChE results (U/g Hb) by clinical category</th>
<th>Reference Test results (U/g Hb) by clinical category</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (≥ 23.6)</td>
<td>Normal (≥ 23.6)</td>
</tr>
<tr>
<td>Mild inhibition (9.4-23.5)</td>
<td>Mild inhibition (9.4-23.5)</td>
</tr>
<tr>
<td>Moderate inhibition (3.1-9.4)</td>
<td>Moderate inhibition (3.1-9.4)</td>
</tr>
<tr>
<td>Severe inhibition (&lt;3.14)</td>
<td>Severe inhibition (&lt;3.14)</td>
</tr>
<tr>
<td>Totals</td>
<td>Totals</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>Normal (≥ 23.6)</td>
<td>30 (31.2%)</td>
</tr>
<tr>
<td>Mild inhibition (9.4-23.5)</td>
<td>5 (5.2%)</td>
</tr>
<tr>
<td>Moderate inhibition (3.1-9.4)</td>
<td>1 (1.0%)</td>
</tr>
<tr>
<td>Severe inhibition (&lt;3.14)</td>
<td>1 (1.0%)</td>
</tr>
<tr>
<td>Totals</td>
<td>37 (38.5%)</td>
</tr>
</tbody>
</table>

The Bland Altman plot (Test-mate – reference) shows the mean bias was -0.62 U/g Hb and the 95% limits of agreement were from -10.84 to 9.59 U/g Hb (Figure 4-3a).

Agreement of PChE measurements

Good agreement was also demonstrated for PChE (Figure 4-4), but there was less evidence for this as 64% (58/91) of the measured values were below the limits of quantification (LOQ) for the Test-mate ChE. However, when results were categorised into being either above or below the LOQ there was good agreement (kappa = 0.69).

The Bland Altman plot (Test-mate-Reference) shows a positive bias of 0.06 U/ml for Test-mate ChE. The 95% limits of agreement were from -0.41 to 0.53 U/ml (Figure 4-3b). The Pearson correlation coefficient was 0.87 (95% CI 0.81 to 0.91).
Figure 4-3 Bland Altman plots showing the difference measurement between the Test-mate ChE and reference test results plotted against the mean of both methods for a) RBC-AChE and b) PChE (*after adjustment to U/ml of whole blood).

Horizontal lines represent the mean bias and 95% limits of agreement, and associated 95% CI’s. The limit of quantification for PChE measurement by Test-mate ChE (0.26 U/ml) is marked by a vertical dotted line.
Figure 4-4 Scatter diagram showing the Test-mate PChE activity are plotted against the reference test PChE activity (*after adjustment to U/ml of whole blood). The line of equality is represented by a dotted line. The limit of quantification (LOQ) for the Test-mate ChE (0.26 U/ml) is marked on the Y axis.

Discussion

Our study found good agreement between the Test-mate ChE field kit and a reference test in the measurement of RBC-AChE. The good agreement (weighted kappa 0.85) between the different clinical categories of RBC-AChE inhibition suggests this test is sufficiently accurate to guide clinical decisions in the management of OP poisoning.

Our findings were different to that of a previous study, which found a large upward bias in Test-mate RBC-AChE results (+8.2 to 9.9 U/g Hb), contrasting the small negative bias (-0.62 U/g Hb) that we found(115). Variation in the temperature at time of testing
in the field was subsequently raised as a possible source of error to explain this bias(117). This was not a significant consideration in our study as we used the latest model (Model 400) of the Test-mate ChE field kit, which contains a temperature compensation algorithm allowing its use over an extended temperature range.

A second more recent study also contrasted our findings by noting a systematic positive bias of 42-48% in RBC-AChE measurement when compared with a reference test, and this was thought to be related to differences in haemoglobin estimation by the different test methods(114). The use of dilution or cooling to avoid ex-vivo reactions by their reference laboratory method was not documented, and it is possible that the discrepancy in RBC-AChE results related to problems with their reference test(3).

Previous studies of PChE measurement by the Test-mate ChE in an occupational setting have had conflicting results(114, 115). One study contrasted our results for PChE by finding poor agreement with a large negative bias and wider 95% limits of agreement(115), and the second more recent study supported our findings of good agreement(114). However, it is worth noting that the units of PChE in reference tests (U/ml plasma) have to be adjusted to match the Test-mate ChE (U/ml blood), and only one of these studies clearly documented this. Conversion adds another potential inaccuracy caused by the use of another measured variable, Hb concentration. Our findings suggest PChE measurement can be used to detect inhibition in a qualitative sense, as might be the case with confirmation of diagnosis in cases of suspected OP or carbamate poisoning. However, in practice the interpretation of PChE is difficult, due to its large variation in the normal population, and comparison against a baseline level is recommended(122). This may be possible in an occupational setting but it is impractical in acute poisoning. RBC-AChE is a more clinically useful biomarker due to its closer resemblance to neuronal AChE and its capacity for reactivation from an inhibited state after oxime therapy(3).
Limitations

Junior doctors carried out the outcome measure of Test-mate ChE cholinesterase results instead of trained lab personnel contrary to the manufacturer’s recommendations. Thus it is possible that operator error could have been a factor accounting for some of the observed discrepancies when comparing the two test methods, and this was not controlled for. Previous studies evaluating the use of Test-mate ChE in both a laboratory and “field setting” by non-laboratory staff have concluded reduced accuracy and precision in the field setting (114, 115). In contrast to these finding, our data showed that there was acceptable agreement between the Test-mate ChE field kit and the reference test despite this limitation of the field kit being operated by non-laboratory personnel.

Future research directions

We also observed that in some cases the patterns of AChE activity over time matched the patient’s clinical features more closely for measurements made by the Test-mate ChE compared with those by the reference test (data not shown). This raised the possibility that the Test-mate could have been more accurate than the reference test in the current study setting. The reference test in this case could not be considered as a ‘gold standard’ because of possible inaccuracy related to the speed of freezing, quality of cold chain during storage and shipment, as well as time delay between sampling and testing, despite the stringent measures that were taken to minimise these factors during the study. These factors could have been avoided if the reference test consisted of simultaneous measurement in a local laboratory that has experience in cholinesterase testing (a facility that was not available at the time of the current study). Future research could aim to achieve this and further investigate the discrepancy observed in some test results in more detail.

The measurement of AChE in carbamate poisoning (the other major group of anticholinesterase agents responsible for high numbers of poisonings) should also be carefully planned in future studies. This type of poisoning was excluded from our
sample because of the high potential for ex-vivo reactions in carbamate poisoning that would result in unreliable reference laboratory values.

**Conclusions**

Based on the findings of our study we can recommend the measurement of RBC-AChE when using the Test-mate ChE in acute poisoning because of its good agreement with reference test from a laboratory experienced in cholinesterase determination. A key strength of our study is that a much wider range of RBC-AChE inhibition (from 0 – 100%) was studied, whereas previous clinical studies had not studied inhibition exceeding 50% (e.g.(114)). Also, our results were novel in that they demonstrated that this agreement was present amongst OP poisonings by 5 different agents and in patients receiving pralidoxime.

The Test-mate ChE field kit appears a reliable method to rapidly measure RBC-AChE in OP poisoned patients, and can be used to confirm the diagnosis and indicate the severity of poisoning. Further research is required to see if serial AChE measurements aid the management of OP poisoning, and whether the test is also reliable in patients with carbamate poisoning.
Chapter 5: Effect of acetylcholinesterase (AChE) point-of-care testing in OP poisoning on knowledge, attitudes and practices of treating physicians in Sri Lanka

Published: This chapter has been published as a journal article.

Citation: Rajapakse BN, Neeman T, Buckley NA. Effect of acetylcholinesterase (AChE) point-of-care testing in OP poisoning on knowledge, attitudes and practices of treating physicians in Sri Lanka. BMC Health Serv Res. 2014;14:104.
Abstract

**Background:** Toxicology and Emergency medicine textbooks recommend measurement of acetylcholinesterase (AChE) in all symptomatic cases of organophosphorus (OP) poisoning but laboratory facilities are limited in rural Asia. The accuracy of point-of-care (POC) acetylcholinesterase testing has been demonstrated in acute OP poisoning but no study has investigated how it would be valued in a practical setting. This study aims to assess the effect of seeing AChE POC test results on the knowledge, attitudes and practices of doctors who frequently manage OP poisoning.

**Methods:** We surveyed 23 clinicians, who had different levels of exposure to seeing AChE levels in OP poisoned patients, on a) knowledge about the management of OP poisoning and biomarker interpretation, b) attitudes towards the value of AChE in guiding poison management, oxime therapy and discharge decisions, and c) practices of ordering AChE in scenarios of mild and severe self-poisoning.

**Results:** An overall high proportion of doctors valued the test (68-89%). However, we paradoxically found that doctors who were more experienced in seeing AChE results valued the test less. Lower proportions valued the test in the guidance of acute poisoning management (50%, p=0.015) and the guidance of oxime therapy (25%, p=0.008), and it was apparent the test would not generally be used to facilitate early discharge. The time at which AChE was measured influenced the perceived value of the test (p<0.001), and the highest proportion of respondents valued it on admission. A lack of correlation of test results with the clinical picture, and a perception that the test was a waste of money when compared to clinical observation alone were comments raised by some of the respondents who did not value the test.

Greater experience with seeing AChE test results was associated with increased knowledge (p=0.034). However, a disproportionate lack of knowledge on interpretation
of biomarkers and the pharmacology of oxime therapy (12-50%) was noted, when compared with general knowledge on the mechanism of OP poisoning and management (78-90%).

**Conclusions:** Our findings suggest an AChE POC test may not be valued by rural doctors. The practical use of AChE in OP poisoning management is complex, and a poor understanding of how to interpret test results may have affected its perceived utility. Future research should evaluate the impact of providing both AChE and training in interpretation on clinicians’ attitudes and practice.
Background

Organophosphorus (OP) insecticide poisoning is responsible for significant mortality and morbidity. The case-fatality of OP self poisoning is high and there are over 200,000 annual deaths worldwide(3).

Toxicology and Emergency medicine textbooks recommend that acetylcholinesterase (AChE) measurement should be performed in all symptomatic cases of OP poisoning where the test is available, as this biomarker may help confirm diagnosis and severity, guide the starting and stopping of oximes by titrating the dose to changing enzyme levels, and may help in guiding patient disposition(37, 52-55). Some text books recommend checking AChE every 12-24 hours in symptomatic patients(54). However, accurate laboratory tests require complex collection methods and a lack of availability of reliable point-of-care (POC) laboratory services makes these recommendations difficult to follow(55). Recent research has validated the use of a POC acetylcholinesterase testing device (Test-mate ChE) for acute OP self-poisoning in rural Sri Lanka, but to date there are no studies to indicate how clinicians would value, and use, such a test should it become available(56). We were not able to find studies that evaluated the benefit of POC devices in Asian countries, and a deficiency in research surrounding the role of POC testing in a rural hospital setting has also been identified by other researchers(125).

We designed a study, which surveyed the knowledge, attitudes and practices of clinicians in a secondary referral centre who are frequently treating OP poisoning. We looked at what effect exposure to seeing AChE test results had on these parameters. We specifically asked whether clinicians would order such a test if it were available, and how useful it would be in their management of OP poisoning (if at all). Our study intervention was to make AChE results available to clinicians in acute OP poisoning.
through POC testing, without specific training or education on how to interpret the test results.

Our hypothesis, based upon textbook recommendations, was that AChE tests would be widely ordered and regarded as useful if they were made available. We also hypothesised that doctors with greater experience of the test would report a higher perceived benefit from the test in terms of showing improved knowledge about OP poisoning, guidance of oxime therapy, and the facilitation of early discharge of patients with mild symptoms.

This study aimed to assess the knowledge, attitudes, and practices amongst a range of treating clinicians who manage high volumes of OP poisoned patient, and who did not generally have access to AChE results. We also aimed to report changes that occurred in relation to the introduction of a point-of-care AChE device(56).

**Methods**

The University of Peradeniya Ethical Review committee approved the study, and consent was implied by participation in a paper survey.

**Selection of Doctors**

The study targeted the practicing doctors who worked in the General Medical ward and intensive care ward of a secondary referral centre (with approximately 800 hospital beds) in a rural Sri Lankan setting. All levels of the medical hierarchy including Consultants, Senior House officers (SHO’s), Medical officers (MO’s), and house officers (HO’s) were included in the study.
**Intervention**

The intervention consisted of the provision of AChE results from OP poisoned patients, over a 13 month period, to treating clinicians. Clinicians were surveyed at beginning and end in order to capture respondents with a range of experience of the seeing AChE test results (see Figure 5-1).

**Measurement of AChE results**

Blood samples were taken from all consenting OP poisoned patients admitted to the medical wards and intensive care unit by trained research assistants according to a study protocol and the results were added to the patient record so that clinicians could use this information if they desired.

The RBC-AChE and PChE levels were measured, using the Test-mate ChE point-of-care device, before and after doses of oxime in patients who were on this therapy. These results were graphed to highlight any relationship to doses given (Figure 5-2), in a similar fashion to what has been recommended in the literature(52).

**AChE testing protocol**

A specific protocol guided the frequency and timing of blood tests in relation to oxime doses (Appendix B1). Symptomatic patients who were treated with oximes had blood tests taken pre and post doses of oxime during the first 48 hours, and a pre and post dose test were taken on a daily basis thereafter. Symptomatic OP poisoned patients who weren’t treated with oximes were tested at the same time points, omitting the post oxime measurement.

Asymptomatic patients had an initial blood test followed by a daily blood test thereafter. Patients with unknown poisoning were treated as described depending on whether they were symptomatic or not, and whether they were being treated with oximes or not. After 5 days of admission the frequency of blood testing was reduced to alternate day testing.
**Figure 5-1** Flowchart showing distribution of surveys and response rate.
Figure 5-2 Shows the method of making AChE levels from OP poisoned patients available to treating clinicians (study intervention).

Red blood cell acetylcholinesterase (AChE) and plasma cholinesterase (PChE) results were presented to clinicians via results sheet consisting of a table and graph, which was added to patient record.
Management of OP poisoned patients on whom tests were performed

Internal medicine physicians were responsible for the management of all pesticide poisoned patients who were treated according to local practice. Symptomatic OP poisoned patients were generally resuscitated with atropine via an intravenous bolus followed by infusion, with the dose titrated to clinical response. Oximes were sometimes prescribed depending on the preference of the treating physician.

Study endpoints:

Survey of treating doctors

A self reported survey (Appendix C2) was distributed to all the doctors including an information sheet explaining the confidentiality of the data that would be obtained.

The survey had 3 components:-

1) 25 True/false statements (worth 1 mark each) organized into 5 questions on knowledge of OP poisoning, use of oximes and AChE testing
2) Short answer questions assessing attitudes towards AChE testing and choice of oxime therapy
3) Scenario based questions assessing clinical practice regarding ordering AChE tests, oxime therapy, and patient discharge.

The principal investigator delivered the questionnaire personally to each doctor in the sampling frame of 40 doctors responsible for treating poisoned patients. They were instructed to complete and return the questionnaire as soon as possible.

True/False knowledge questions

The knowledge component comprised 5 areas each covered with 5 true/false statements. Each correct answer was given one mark and each incorrect answer a negative mark resulting in a maximum score of 5 and a minimum score of -5 for each of the 5 areas, which was then converted into a percentage. The questions tested
knowledge on the mechanism of OP pesticides toxicity, the inhibition of AChE, types of biomarker in OP poisoning, the clinical correlation of biomarker levels in poisoned patients and the response of AChE to oximes (Appendix B.1). The level of difficulty was aimed at ‘expert’ level (ie. a level that a toxicologist could be expected to know).

Short answer questions on experience and attitudes

A short answer question format was used to assess the doctors’ prior experience with treating OP poisoned patients, number of AChE test results seen, and perceived usefulness of the AChE test (Appendix B.2). The doctor’s usual practice regarding the dose and duration of oximes therapy in mild, moderate and severe OP poisoning was recorded in this section.

Scenario evaluation of attitudes and practice in cases of OP poisoning

The last part of the survey consisted of four commonly encountered patient scenarios: two scenarios with severe poisoning, and florid cholinergic signs, and two scenarios with mild poisoning, either receiving or not receiving oximes (Appendix B.3). These scenarios were based upon commonly encountered patients. The scenarios assessed whether oximes would be prescribed, and whether an AChE test would be ordered (and thus considered beneficial OP poisoning management) at different time points in course of the patient admission. Survey questions also explored the willingness to discharge a mildly poisoned patient earlier than the standard 4 days of inpatient observation.

Clarifying statements as an adjunct to survey data

We provided respondents with the opportunity to clarify their choices with free text. Headings such as “Comments…”, or prompts like “Why/Why not?” would follow questions that required either a binary or categorical answer such as “Do you think an acetylcholinesterase level (AChE) will be useful in helping guide treatment with oximes?"
Survey analysis

The study was initially designed to compare survey responses before and after exposure to the intervention (which was participation in an observational study providing doctors with bedside AChE results). Because some doctors reported prior experience with AChE tests, and some respondents reported having no experience of seeing AChE levels after the intervention we decided to analyse the survey respondents as a cross sectional sample categorizing respondents according to level of experience with seeing AChE test results, and comparing the groups. Respondents were divided into three groups (no tests, 1-5 tests, or 5-20 tests) based on the number of AChE test they reported they had seen, which was asked in the first section of the survey. Three doctors completed the survey twice during the study period and we only used the first survey response in this group so that the data we analysed was uniform with regards to not having previously completed a survey (see Figure 5-1).

Statistical tests

The mean scores from the knowledge questions were compared using the oneway ANOVA test. The categorical answers to the survey questions were analysed using the Kruskal Wallis test where the data was ordinal, and the Fisher’s exact test where the data was nominal. The answers for some questions were coded as ordinal data where some authors could have viewed it as nominal data. For example, when respondents were asked if AChE could guide oxime therapy; the possible answers were “no”, “not sure” or “yes”, because in this context “not sure” represented a point mid way between “yes” and “no”. Also in the answers where respondents would select the dose of oxime that would be prescribed, the categorical choices were an increasing dose so we coded their responses as an ordinal variable. The scenario data, which comprised multiple responses from doctors, were analysed using generalized estimating equations (GEE). Associations between patient risk factors and the decision to order
AChE test were expressed using odds ratios. All statistical calculations were performed on STATA version 12, and graphs drawn on Prism version 6.

**Results**

The 22 doctors who were included in the analysis consisted of both senior and junior medical staff from departments of medicine (68%) and intensive care (32%), and they reported treating on average 51-100 cases of OP poisoning per year (see Table 5-1). Their experience of seeing the point-of-care AChE test results ranged from never having seen a test previously (i.e. ‘0 tests’) in 11 participants, to having seen ‘1-5 tests’ in 7 participants, and ‘5-20 tests’ in 4 participants.

### Table 5-1 Survey respondent characteristics.

<table>
<thead>
<tr>
<th></th>
<th>Number of respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Seniority</strong></td>
<td></td>
</tr>
<tr>
<td>Consultant</td>
<td>3 (14%)</td>
</tr>
<tr>
<td>House officer</td>
<td>11 (50%)</td>
</tr>
<tr>
<td>Medical officer</td>
<td>5 (23%)</td>
</tr>
<tr>
<td>Senior House officer</td>
<td>3 (14%)</td>
</tr>
<tr>
<td><strong>Specialty</strong></td>
<td></td>
</tr>
<tr>
<td>Medicine</td>
<td>16 (72%)</td>
</tr>
<tr>
<td>Intensive Care</td>
<td>6 (27%)</td>
</tr>
<tr>
<td><strong>No of OP poisoned patients seen</strong></td>
<td></td>
</tr>
<tr>
<td>less than 5</td>
<td>2 (9%)</td>
</tr>
<tr>
<td>5 to 20</td>
<td>5 (23%)</td>
</tr>
<tr>
<td>21 to 50</td>
<td>5 (23%)</td>
</tr>
<tr>
<td>51 to 100</td>
<td>5 (23%)</td>
</tr>
<tr>
<td>greater than 100</td>
<td>5 (23%)</td>
</tr>
<tr>
<td><strong>Exposure to AChE tests</strong></td>
<td></td>
</tr>
<tr>
<td>zero</td>
<td>11 (50%)</td>
</tr>
<tr>
<td>1 to 5</td>
<td>7 (32%)</td>
</tr>
<tr>
<td>5 to 20</td>
<td>4 (18%)</td>
</tr>
<tr>
<td>21 to 50</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>51 to 100</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>
**Knowledge**

Those with most experience of AChE test results (e.g. 5-20 tests) had the highest knowledge with a significant increase noted in the total score ($p=0.034$, see Figure 5-3). This was most marked in the questions to do with “biomarkers of exposure”, “interpreting AChE in OP”, and “oximes in OP poisoning”, but the increase only reached statistical significance for question 5 on “oximes in OP poisoning” ($p=0.046$).

![Experience with AChE test](image)

**Figure 5-3** Knowledge scores for questions (based on answers to true/false statements).

*This column graph shows the differences in scores by level of experience with the AChE test.*
Attitudes: AChE in OP poisoning management

The perception that AChE test was useful in managing OP poisoning was 100% amongst respondents with no AChE test experience (0 tests) and minimal experience (1-5 tests), but was significantly less (50%) in respondents with the most experience of seeing test results (5-20 tests) ($p=0.035$, Figure 5-4a, Table 5-2).

However, the two respondents who stated the test was “not useful” qualified their answers with the following statements suggesting a mixed impression about the utility of the test:

- "Not necessary to manage OP poisoning but useful to identify (diagnosis)"
- "AChE level is not related to the amount of poison or the clinical symptoms but is useful in unknown poison management"

The AChE test was noted to be helpful in guiding oxime therapy in 73% and 86% of respondents with no experience, or minimal experience, but this proportion was significantly less (25%) amongst respondents with the most experience of seeing AChE test results ($p=0.05$, see Figure 5-4b, Table 5-2).

Respondents who reported that the test was helpful in guiding oximes clarified their choice with comments that valued the role of AChE in assessing severity of poisoning, and the titration of AChE levels with oxime administration:

- "I think acetylcholinesterase is a fairly reliable method of assessing the level of poisoning"
- "need to check whether the AChE level is up or down with oxime"
Q: Do you believe an AChE level is useful in treating OP poisoning?

![Bar chart showing attitudes towards AChE testing in organophosphorus management.](chart1)

Q: Do you believe an AChE level is helpful in "guiding oxime therapy"?

![Bar chart showing attitudes towards AChE testing in organophosphorus management.](chart2)

**Figure 5-4 Attitudes towards AChE testing in organophosphorus management.**

The perceived value of an AChE level (a) in the treatment of organophosphorus poisoning, and (b) in the guidance of oxime therapy is shown according to level of experience with the test.
### Table 5-2 Attitudes towards oxime therapy and AChE testing.

<table>
<thead>
<tr>
<th>Question</th>
<th>Response</th>
<th>Level of AChE Experience †</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>What dose of intravenous pralidoxime would you prescribe to a <strong>severely symptomatic</strong> patient?</td>
<td>None</td>
<td>&quot;0 tests&quot; n (%) 1 (14%) 0 (0%) 0 (0%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1g 6 hourly</td>
<td>&quot;1-5 tests&quot; n (%) 6 (86%) 1 (25%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2g bolus + 500mg continuous IV infusion</td>
<td>&quot;5-20 tests&quot; n (%) 3 (75%)</td>
<td></td>
</tr>
<tr>
<td>For what duration would you give the above dose?</td>
<td>None</td>
<td>n (%) 0 (0%) 1 (14%) 0 (0%)</td>
<td>0.008</td>
</tr>
<tr>
<td></td>
<td>24 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>48 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other time period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>What dose of intravenous pralidoxime would you prescribe to a <strong>mildly symptomatic</strong> patient?</td>
<td>None</td>
<td>n (%) 1 (9%) 4 (57%) 1 (25%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1g 6 hourly</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2g bolus + 500mg continuous IV infusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For what duration would you give the above dose?</td>
<td>None</td>
<td>n (%) 1 (11%) 4 (57%) 1 (33%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>48 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other time period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>What dose of intravenous pralidoxime would you prescribe to a <strong>asymptomatic</strong> patient who is not getting atropine?</td>
<td>None</td>
<td>n (%) 6 (64%) 7 (100%) 4 (100%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>1g 6 hourly</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>2g bolus + 500mg continuous IV infusion</td>
<td></td>
<td></td>
</tr>
<tr>
<td>For what duration would you give the above dose?</td>
<td>None</td>
<td>n (%) 5 (56%) 4 (100%) 4 (100%)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>24 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>48 hours</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other time period</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Do you think an acetylcholinesterase level (AChE) will be helpful in guiding treatment with oximes?</td>
<td>Yes</td>
<td>n (%) 8 (73%) 6 (86%) 1 (25%)</td>
<td>0.435</td>
</tr>
<tr>
<td></td>
<td>Not sure</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Is this test was available and affordable. Would it be useful in treating OP poisoning?</td>
<td>Yes</td>
<td>n (%) 9 (100%) 6 (100%) 2 (50%)</td>
<td>0.051</td>
</tr>
<tr>
<td></td>
<td>No</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† The total number of answers for each question do not always add up to 22 as some respondents omitted answering questions.
Others raised concerns regarding the interpretation of test result despite stating that they thought it was helpful:

“Yes. But I am not sure of a cut off point to decide on giving oxime - Evidence is needed on this”

“I think it is useful in guiding the effectiveness of oximes. I don’t think there is a symptomatic correlation”

Conversely, respondents who did not believe that the test was helpful in guiding oximes, expressed concern about the clinical correlation of AChE in OP poisoning:

“(AChE) level does not correlate with clinical symptoms of the patient”

as well as valuing clinical assessment over biomarker evaluation;

“the most important thing is whether the patient is symptomatic or not”

The oxime dose and duration in relation to severity of poisoning, and the range of oxime prescription patterns amongst survey respondents is shown in Table 5-2.

The majority (75%) of the group with most experience chose a dosing regime of “2g intravenous bolus followed by 500mg/hour intravenous infusion”, compared with 9% and 0% of respondents from the subgroups with no experience and minimal experience (p=0.008, see Figure 5-5a). These latter two subgroups chose to use a 1g boluses every 6 hours, 91% and 86% of the time, instead.

The subgroup with most experience also chose a “flexible” duration of therapy contrasting those with no experience or minimal experience, who chose 48 hours of therapy in 67% and 71% of responses respectively (p=0.089, see Figure 5-5b).
Figure 5-5 Attitudes towards oxime dose (a) and duration (b) in a case of severe OP poisoning, show by level of AChE test experience.
The comments for this section clarified that the popular “flexible” duration of therapy in the group of respondents with most experience was related to clinical recovery, (see examples below):

“Until the patient is asymptomatic or off atropine”

“Until the patient gets rid of the OP effects clinically”

No respondents made specific reference to the concept of an AChE level guiding either the “dose” or “duration” of oxime therapy in the clarifying comments for this section.

**Scenario Analysis: Ordering AChE at different time points in admission**

“Time” (since admission) was a factor affecting whether respondents would order an AChE test, with a lower propensity for ordering an AChE test each subsequent day in the hospital admission (OR 0.85 [0.79-0.91], p<0.001, see Figure 5-6). AChE was ordered most frequently on admission (ranging from 86% to 65%, depending on severity and concurrent oxime therapy), and a progressive decline was noted during the following 3 days of hospital admission. Conversely there was an increased propensity for ordering an AChE test with greater severity of poisoning (OR 1.22 [1.10-1.37], p<0.001). There was a trend for increased propensity of ordering an AChE test in scenarios where oxime therapy was concurrent, however the influence of “oxime therapy” was not statistically significant (OR 1.09 [0.96-1.25], p=0.182). We noted a lower propensity for ordering AChE in those with the most experience compared those with no test experience, a difference which approached statistical significance (OR 0.78 [0.61-1.00], p=0.052), when level of experience with seeing AChE test was considered.
Proportion of respondents ordering AChE over time according to the clinical scenario.

(a) The effect of time, clinical severity, and concurrent oxime therapy on willingness to order an AChE test is demonstrated.

Proportion of respondents ordering AChE over time according to clinical scenarios, plotted by number of AChE tests seen (b) 0 tests (c) 1-5 tests (d) 5-20 tests (next page).
(0 tests)

Proportion

PAM (severe poisoning)
- No PAM (severe poisoning)
- PAM (mild poisoning)
- No PAM (mild poisoning)

(1-5 tests)

Proportion

PAM (severe poisoning)
- No PAM (severe poisoning)
- PAM (mild poisoning)
- No PAM (mild poisoning)

(5-20 tests)

Proportion

PAM (severe poisoning)
- No PAM (severe poisoning)
- PAM (mild poisoning)
- No PAM (mild poisoning)
Scenario analysis: Ordering AChE and guidance of oxime therapy

A minority of clarifying comments in this section of the survey stated that ordering of AChE would help with making a decision about oxime therapy:

“to decide whether to prescribe pralidoxime or not” [Severe poisoning, oximes, Day 2]

“can obtain a relative idea of the proportion of aging” (no specific reference to oximes; but reference to ‘aging’ may be implied to relate to the effectiveness of oxime therapy) [Severe poisoning, no oximes, Day 3]

However, such comments were not offered by the majority of respondents, nor were they offered over the range of time points in the scenario.

We noted a trend for higher proportions ordering an AChE test after oximes were stopped, in the scenario of severe poisoning, when comparing respondents with minimal and most experience (100% and 75% respectively), with those with no experience (37%, see Figure 5-6 b-c). This observation suggests the use of AChE in guiding a decision to re-starting oximes, however, the difference in proportions was non-significant ($p=0.450$). Furthermore, the clarifying comments did not clearly identify this as a reason for AChE being ordered at this time point in any of the respondents, regardless of their level of experience.

One comment indicated that AChE may be used in this way by saying the reason for ordering the test post stopping oximes was;

“to compare with initial enzymes”
but there was a lack of detail about what action would be taken if the AChE enzyme levels had decreased, and it is uncertain whether the respondent would use the comparison to restart oxime therapy.

**Scenario Analysis: Early discharge and ordering AChE**

If AChE was perceived as helpful in facilitating early discharge one would expect a high proportion of respondents ordering an AChE test on day 2 or day 3 in the scenarios of a mildly poisoned OP patient, and comments that showed a link between the use of an AChE level to aid the decision to discharge a patient.

This was not the case as respondents suggested they would order an AChE test on only 38% of occasions (6/16) where they said they would discharge a patient home, and there was no association between the decision to order an AChE test and the decision to discharge (see Figure 5-7). We also noted that in general a low proportion (50%) of respondents would opt to discharge a mildly symptomatic patient home on either day 2 or day 3 post admission.

However, two respondents made the following clarifying comments as reasons for ordering an AChE test;

“can discharge the patient early”

“it would decide in keeping or discharging the patient”

which suggests that the role of AChE levels in guiding disposition decisions was considered by at least a minority of respondents.
Figure 5-7 Association of ordering an AChE test with the early discharge of a mildly poisoned patient who has a) initially received oximes, or b) initially not received oximes.
Figure 5-8 Proportion of survey respondents providing clarifying comments in scenarios of a) severe poisoning, with oxime therapy, b) mild poisoning, without oxime therapy.
Other reasons for ordering AChE based on comments

Respondents qualified their answers with clarifying comments for just under half (48%) of the scenario questions in favor of the decision to order an AChE test, with 48% (Figure 5-8), providing some insight into the thinking behind ordering and not ordering an AChE test.

Many answers supported perceived value of AChE testing having a role in diagnosis of OP poisoning, and gauging severity;

“(useful) in cases of unknown pesticide poisoning for guiding treatment on certain occasions”
“I think acetylcholinesterase is a reliable method of assessing level of poisoning”
“It will be an indicator showing the degree of poisoning”

and in guiding oxime therapy;

“Titrating the pralidoxime dose frequency with the enzyme level in the plasma”
“When to start oximes, When to stop oximes”
“(with measurement of AChE) unnecessary treatment can be avoided”

However, the details of specifically how oxime doses would be titrated were absent as highlighted in the previous section.

Many statements that were against the use of AChE in management of OP poisoning highlighted the sentiment that “clinical assessment” should take precedence over biochemical guidance;

“Level does not correlate with clinical symptoms of the patient”
“Most important thing is if the patient is symptomatic or not”

...and other comments raised concerns about the potential wastefulness of such an investigation;

“this will not change patient management, it will waste money”

**Discussion**

The literature states that the AChE levels can help guide OP poisoning management, oxime therapy and disposition decisions, and our study found that “overall” a high proportion of surveyed doctors valued ordering AChE test in accordance with these recommendations. However, paradoxically we noted that doctors with more experience of seeing test results through the study intervention were less likely to value the AChE test in guiding OP poisoning management and oxime therapy, and there was no suggestion it would be used to facilitate early discharge. Respondents raised a number of general concerns about a lack of correlation between test results and the clinical picture, and a perception that ordering a test would be a waste of money when compared to the standard practice of clinical observation.

The experience of seeing test results was associated with improved knowledge scores across all domains. These scores were highest for knowledge in clinical management of OP poisoning (78% improving to 90% post intervention), contrasting the lower scores for questions related to biomarkers and the use of oximes (12-20% improving to 40-50% post intervention). A relative lack of knowledge about the interpretation of biomarkers in guiding general management and oxime therapy may have been one factor explaining our unexpected findings.
Difficulty in interpretation of results: Pitfalls in AChE monitoring

AChE is being increasingly recognized as a complex test with regard to the interpretation of levels in the context of acute OP poisoning. Difficulty with interpretation of AChE levels arises for several reasons including a variation in cholinesterase inhibition from different types of OP agents (47), the wide normal range for both kinds of AChE (plasma cholinesterase and red cell cholinesterase), irreversible inhibition ("ageing") by a proportion of the enzyme, and the fact that inhibition can be non-specific due to other factors that can reduce AChE levels such as concurrent chloroquine therapy, or conditions like pernicious anaemia (3, 54). Re-inhibition of AChE may occur when an oxime is discontinued and there is a residual poison load. Thus, in such situations it may be dangerous to discharge based on early recovery of AChE. Our study found that doctors generally would not use AChE to support discharge decisions, however, the explanations provided suggested that such nuanced considerations were not relevant. Further, comments suggested clinicians found it challenging to negotiate the pitfalls in AChE measurement highlighted in textbooks.

Lack of specific decision rules for AChE guidance

The lack of knowledge regarding AChE interpretation may in part be explained by a lack of precise values of AChE informing decisions rules in OP poisoning management (37, 52-55). This gap in the literature was apparent on further examination of recommendations regarding the use of AChE in guiding oxime therapy and disposition decisions in particular. In relation to re-starting oximes, for example, one text quoted "further deterioration of cholinesterase activity should be treated by reinstituting a pralidoxime infusion, even though the patient may still be asymptomatic" (54), without providing numeric qualification on the 'degree of inhibition' that should lead to action. The challenge of interpretation of such advice, and a similar style of advice in other textbooks was well described in the comments of one respondent in particular from the scenario section of the survey who wrote;
“I am not sure of a cut off point to decide on giving oxime - Evidence is needed on this”.

There is a complete lack of evidence regarding the practical use of AChE in guiding oxime therapy. While some texts have suggested graphical representations of the titration of oximes with AChE levels (56), these only provide guidance on principles of antidote titration rather than specific levels that can be referenced in an algorithmic fashion. More sophisticated laboratory test methods exist to support decision making and oxime therapy; for example the in vitro measurement of response to oximes and estimation of the reactivatable RBC-AChE enzyme (28, 112). However, the practical employment of these methods in POC tests has not yet been described or validated.

There is also little data to guide interpretation of AChE for its role in of supporting disposition decisions. Here many texts recommend discharge in association with other features like cessation of a need for further antidote therapy, clinical improvement and “stable” or “minimally depressed” cholinesterase activity (54, 55).

Clinical correlation of AChE, and outcome
On the other hand, the evidence on how RBC-AChE can provide guidance about diagnosis and severity of poisoning has been more clearly described, with extent of inhibition correlated with clinical findings (27, 28, 39, 56, 113, 122, 123). However, even the when specific ranges of AChE are known, the application of this information in a clinical setting may be complex, as it requires clinicians to incorporate an understanding of the potential pitfalls that can be encountered. Variations in AChE inhibition from different agents may lead to “some patients presenting highly symptomatic after minimal reduction in cholinesterase, whilst others can be asymptomatic after losing 50% of activity” (54).
Thus AChE appears to be a test where background factors, such as understanding its role in pathophysiology of poisoning, are important in making decisions about treatment, but there is no specific guidance available for doctors.

This point can be illustrated by contrasting the use of AChE in OP poisoning management with the use of peak expiratory flow rate (PEFR) in management of acute asthma. PEFR can also be used for guiding diagnosis, severity and disposition decisions in emergency departments. The difference is that published decision rules for the use of PEFR in asthma management, exists (126, 127), whilst similar decision rule research and evidence based guidelines for the use of AChE in OP poisoning management is lacking.

**Study intervention provided without education or training**

No attempt was made to train doctors on how to use the test, the results were presented in a format that would allow the AChE test to show benefit, such as by graphing pre and post oxime doses (see Figure 5-2) to facilitate guidance of oxime therapy. Given national recommendations(37) were available for AChE interpretation we expected the test to be used widely in clinical treatment. Our results highlight the effects of introducing a complex test without specific training in how to interpret test results.

It is interesting that knowledge increased without didactic teaching. One possible explanation is that by seeing the tests results doctors had an increased awareness about the mechanisms of OP poisoning (inhibition of the AChE enzyme), and the use of oximes to regenerate inhibited AChE.

A qualitative study assessing the introduction of a different POC test reported that some clinicians were more likely to use certain tests if they had recent formal education in the domains surrounding the test(125). The difficulties surrounding the interpretation of AChE in the context of OP poisoning, that have been observed in the current study,
emphasise the importance of training doctors who may use the test on the assay’s capabilities and limitations. Such training should include appreciation of the pitfalls of collection, measurement, interpretation of AChE results in the context of guiding oxime therapy and facilitating discharge.

Educational interventions are likely to affect attitudes and practices, and future studies should therefore incorporate concurrent education into the assessment of new POC tests.

**Limitations**
Our initial planned design was pre-post analysis but because of the high turnover of doctors in the study intervention wards, we ended up with data suited to a cross sectional survey, comparing subgroups by "level of experience with seeing AChE test results". Small numbers in these sub groups, despite a fairly good response (26 out of 40) was a limitation. However, the effect of the study intervention was large enough to result in significant differences between subgroups in some domains.

**Less “AChE test experience” than expected**
Whilst we recorded a range of AChE experience amongst survey respondents we expected the range to be broader, with some doctors potentially seeing up to 100 test results (20 tests was the highest reported experience in our study). A total of 81 patients had AChE levels measured during the study intervention and many of these patients had multiple tests. Some respondents may have interpreted “tests seen” as the number of patients with tests seen. More objective data on exposure to tests, or more detail on reported exposure (e.g. asking both how many patients with results and how many tests) may have provided a more accurate classification of level of experience. However, the lower than expected test exposure may just be due to the high staff turnover.
**Mixed methods approach for future research on use of POC tests**

We used a quantitative study design to assess knowledge, attitudes and practices, however, the collection of comments that respondents sometimes used to qualify their survey choices provided a deeper understanding of the main study results. The quantitative answers considered in isolation may have given a different impression. For example, whilst we found that increased experience with AChE tests led to decreased value being attributed to the test, often the same respondents who said they would not order a test also provided nuanced comments about its potential benefits. This highlights the degree of ambiguity amongst experienced respondents in their attitudes towards the test.

However, only 53% of questions had an associated comment, and thus it is possible that certain comments may preferentially highlight the views of a few individuals. We also observed that respondents who answered in favour of the test more frequently qualified their answer with a comment (67%) than when they chose not to order the test (43%), see Figure 5-8.

Blattner et al. assessed the acceptability and effectiveness of POC testing in rural New Zealand, and carried out both a quantitative study, and a qualitative thematic analysis(125, 128). Their quantitative study demonstrated the cost effectiveness of introducing the test through ability to avoid unnecessary transfers, as well as facilitate discharge. However, the qualitative component of their research uncovered some of the challenges of introducing POC testing, such as increased workload, and the challenge of continued professional education given that “up-skilling” of doctors may be required for the interpretation of some of the available test results. These authors also commented that their depth of understanding about the impact of introducing the test would have been missed if they had relied on the quantitative results alone.
We suggest that future research on POC tests use a mixed methods approach with the development of a robust study design for its qualitative component.

**Conclusions**

An AChE POC test was valued by a majority of rural doctors but it was valued less by those with greater experience of seeing test results. These unexpected findings could be related to the complex nature of the test, no decision rules and poor knowledge of the interpretation. The absence of specific education on how to interpret test results may have been a contributing factor.

We recommend that health services that want to introduce a POC AChE test provide doctors with concurrent training on how to use and interpret AChE results, and research the impact through a mixed methods approach. Such research should ideally be conducted with larger numbers, and include medical staff with a wide range of experience and include multiple primary care settings.
Chapter 6: The effectiveness of a ‘train-the-trainer’ model of resuscitation education for rural peripheral hospital doctors in Sri Lanka

Published in a scientific journal.

Abstract

Background: Sri Lankan rural doctors based in isolated peripheral hospitals routinely resuscitate critically ill patients but have difficulty accessing training. We tested a train-the-trainer model that could be utilised in isolated rural hospitals.

Methods: Eight selected rural hospital non-specialist doctors attended a 2-day instructor course. These “trained trainers” educated their colleagues in advanced cardiac life support at peripheral hospital workshops and we tested their students in resuscitation knowledge and skills pre and post training, and at 6- and 12-weeks.

Knowledge was assessed through 30 multiple choice questions (MCQ), and resuscitation skills were assessed by performance in a video recorded simulated scenario of a cardiac arrest using a Resuci Anne Skill Trainer mannequin.

Results/Discussion/Conclusion: Fifty seven doctors were trained. Pre and post training assessment was possible in 51 participants, and 6-week and 12-week follow up was possible for 43, and 38 participants respectively. Mean MCQ scores significantly improved over time ($p<0.001$), and a significant improvement was noted in “average ventilation volume”, “compression count”, and “compressions with no error”, “adequate depth”, “average depth”, and “compression rate” ($p<0.01$). The proportion of participants with compression depth $\geq 40$mm increased post intervention ($p<0.05$) and at 12-week follow up ($p<0.05$), and proportion of ventilation volumes between 400-1000mls increased post intervention ($p<0.001$). A significant increase in the proportion of participants who “checked for responsiveness”, “opened the airway”, “performed a breathing check”, who used the “correct compression ratio”, and who used an “appropriate facemask technique” was also noted ($p<0.001$).
A train-the-trainer model of resuscitation education was effective in improving resuscitation knowledge and skills in Sri Lankan rural peripheral hospital doctors. Improvement was sustained to 12 weeks for most components of resuscitation knowledge and skills. Further research is needed to identify which components of training are most effective in leading to sustained improvement in resuscitation.
Introduction

Resuscitation education is an emerging field in Sri Lanka, run largely by consultant anaesthetists working at tertiary referral centers and the larger secondary hospitals. The heavy workload of these specialists limits the opportunity to provide training to rural peripheral hospital doctors. Previous research has identified that rural peripheral hospital doctors feel professional isolation due to a lack of training opportunities (15). There is a need for good resuscitation knowledge and skills in these doctors as they are the first point of contact for patients who frequently require resuscitation such as those presenting with pesticide poisoning and snake bite injury (87, 129, 130). A common emergency presentation and cause of death in rural Sri Lanka is organophosphorus pesticide (OP) self-poisoning, which is a condition that results in up to 200,000 deaths annually in Asia (1-3, 32, 51). OP poisoning has a case fatality of 8-15% primarily due to respiratory arrest, which progresses to cardiorespiratory arrest (32, 87). Snakebite envenomations also require frequent resuscitation and high proportions (48%) of patients with neurotoxic symptoms who require mechanical ventilation have been reported (131, 132).

At the time of this study advanced cardiac life support training (either according to the American Heart Association, UK or Australian resuscitation councils) was not nationally available for doctors. There are considerable logistic barriers in the delivery of training to doctors in these rural peripheral hospitals. Many peripheral hospitals are run by only one to two doctors, so they cannot be released from clinical duties to travel for up to 2 hours to the central hospitals where resuscitation education occurs.

The train-the-trainer (TTT) model of resuscitation education has been used successfully in higher resourced settings for various levels of resuscitation skills. For example, it has been successfully used to train university students to teach basic life support (BLS) but not advanced life support (ALS) (133, 134). The use of ‘non
specialist’ trainers to teach resuscitation to doctors in teaching hospitals has also been previously described (135), however, the effectiveness of using peripheral hospital doctors as trainers in their own low resource rural hospital setting has not been examined.

Those experienced in the global development of emergency medicine have advocated the TTT model of education to help leverage limited resources (136). However, there have been no studies in the adult resuscitation education literature to date that have evaluated the effectiveness of this model by analysing validated knowledge and skills endpoints (137). Two studies from Africa investigated the use of a TTT model but this was specifically for neonatal resuscitation (138, 139), and another study commented on the success of the TTT approach in training nurses in cardio pulmonary resuscitation (CPR) in the Middle East, but did not objectively assess resuscitation skills in their course participants (140). The only identifiable study that referred to a TTT model in either Sri Lanka or India was in the context of trauma care rather than cardiopulmonary resuscitation (141).

We sought a potentially sustainable solution to overcome the barriers to education and training for rural Sri Lankan peripheral hospitals by assessing the effectiveness of a TTT model that used non-specialist peripheral hospital doctors as trainers, who taught basic and advanced life support (ALS) training to their colleagues. Effectiveness was defined as a statistically significant improvement in components of resuscitation knowledge and skills towards an internationally recognised standard (based upon the International Liaisons Committee on Resuscitation – 2005 resuscitation guidelines).
Materials and Methods

This study was approved by the Ethical Review Committee at the Faculty of Medicine, University of Peradeniya, Sri Lanka. As the study was carried out in conjunction with the regional government health training authority within the framework of usual practice the ethics committee did not require written consent. However as per protocol, trained research assistants described details of the study to participants and verbal consent was obtained prior to the commencement of the peripheral hospital workshop. Participant data was subsequently de-identified.

The study was conducted in the North Central Province of Sri Lanka between November 2008 and July 2009. The province has 45 peripheral hospitals with inpatient facilities supported by 2 central secondary referral hospitals. The TTT resuscitation training program was developed and conducted collaboratively with the North Central Provincial Department of Health. Our study population consisted of non-specialist doctors working at peripheral hospitals who were participants in the resuscitation training workshops and attended both the pre and post training assessments, including follow up at 6 and 12 weeks.

Training the trainers

The first phase of the study involved training of the trainers who consisted of 8 non-specialist doctors from five peripheral hospitals in the North Central Province of Sri Lanka. These 8 were selected from 20 candidates at an initial resuscitation workshop organized in conjunction with the provincial department of health, and were chosen because of their interest in becoming trainers and their observed competence. The prospective trainers each underwent two further sessions of residential training based at the tertiary teaching hospital for the province, which was centrally located (see Appendix C1 for an overview of the workshops).
In the first one day session the candidates’ knowledge of the resuscitation syllabus was reinforced. In the second session, which was a two day ‘instructor workshop’, they were taught “how to teach” and how to run a peripheral hospital workshop (see Appendix C2 for schedule). The instructors who taught the prospective trainers were certified resuscitation instructors from schools of teaching affiliated with the International Liaisons Committee on Resuscitation (ILCOR). All instructors were experienced in teacher training according to either the ACLS (Advanced cardiac life support - American Heart Association standard) or ALS (Advanced life support - UK/European/Australasian resuscitation council standard) courses overseas. The manual for the course that the trainers were trained to teach was largely based upon the content of the UK resuscitation council’s “Intermediate ALS” course, which is also endorsed by the Australian and New Zealand resuscitation councils.

The teacher training included adult education theory, how to run interactive lectures with digital video disc (DVD) support for content, and how to teach using a mannequin in skill stations and scenario stations. This session concluded with a practice workshop using volunteer participants who were junior doctors from the central hospital. The ‘trained trainers’ were directly observed and assessed on their ability to deliver lectures, run skills stations and conduct simulated scenarios according to a standardized checklist at this practice workshop (see Appendix C3 for checklists).

A comprehensive instructor manual describing the workshop schedule and teaching goals was provided to the instructors and the trainers (see Appendix C3 for instructor manual). This also outlined the skills stations and scenarios being taught, and relevant adult education theory that would aid the delivery of course content. This manual also contained teacher assessment checklists that were used by the instructors to facilitate the feedback and assessment of the trainers, and allowed standardisation of the teacher training process. Our clearly defined teacher training methodology meant that
outcomes measured later in the study could be linked to the effectiveness of teaching by the trainers, and thus the TTT model of resuscitation education being tested. The adult education theory and teacher training module in the manual was taken from the “Pocket guide to Teaching for medical instructors” by the BMJ group(142).

Prospective trainers from remote locations were accommodated in the same residential facility provided for by the course. This allowed time for orientation to the course goals, and for group reflection and consolidation of learning at evening meals, a situation that was likely to be different to their previous educational experience (see Appendix C2 includes schedule of workshop). This strategy was used in recognition of the time intensive nature of the instructor workshop, and in hope of supporting a team approach to learning that could increase esteem and self confidence during the process of ‘learning how’ to teaching.

Peripheral Hospital Resuscitation Workshops (Training Intervention)

The second phase involved sending the “trained trainers” to selected larger peripheral hospitals where they delivered eight resuscitation training workshops, teaching BLS and ALS, over a two month period (see Appendix C4 for course outline and contents). In this phase the resuscitation ‘Trainers’ worked in pairs to deliver education to 6-12 participants per session maintaining a minimum ratio of 1 instructor to 6 participants at all sessions. The participants were peripheral hospital doctors who were either from the same hospital where the trainers worked or who had travelled from a nearby smaller hospital. The aim of this workshop was to teach resuscitation to doctors who were assumed to have had no prior post-graduate resuscitation knowledge. The focus of the workshop was on the practical skills of BLS and ALS that would be required by these doctors in their daily practice, including an approach to the unresponsive patient, performance of chest compressions, and performance of ventilations using a bag valve mask apparatus, intubation and ventilation of an intubated patient.
Participants of the peripheral hospital workshops were supplied with a resuscitation training manual, (which was a modification of the ALS manual for ‘intermediate life support’), and a wallet card with the cardiac arrest algorithm printed on it. Trainers carried out resuscitation education with the aid of training mannequins and other supporting equipment including a DVD containing video lectures, and wall charts of the resuscitation algorithm (see Appendix C5 for a list of supporting material for trainers and participants). Baseline data on the characteristics of the participants and their feedback on the training workshop were collected. Real resuscitation experiences that the participants encountered during the 12 week study period were also collected through a log sheet that was supplied to them at the beginning of the workshop.

Each workshop was held from 0800hrs to 1645hrs, which included one and a half hours for multiple choice question (MCQ) testing and scenario testing, immediately before and after the resuscitation training intervention. The training intervention started with a series of lectures about BLS and airway management, which were pre-recorded and played from a DVD lasting approximately an hour. During this time the trainer would periodically pause the DVD and interact with participants about the content of the DVD lecture. A practical session teaching bag mask ventilation and intubation followed where each trainer worked with 6 participants in skills stations that were equipped with either a mannequin or an airway-training device. The practical skills were taught using Peyton’s 4-stage teaching approach as described in the European Resuscitation Council resuscitation course strategy(143).

The afternoon DVD lectures covered treatment algorithms for shockable and non-shockable cardiac arrest, and these skills were practiced in the same groups under the supervision of the trainer who made use of resuscitation mannequins to run two set scenarios. The trainers were required to give positive feedback and constructive criticism to participants during all the practical session including the scenarios. Posters
of the cardiac arrest treatment algorithms were also supplied to each hospital that participants came from as part of the service component of the educational intervention.

The knowledge and skills of participants was assessed before and after they received resuscitation education from the trainers. This assessment was carried out by 3 research assistants, however, the workshop participants were taught exclusively by the “trainers”. The research assistants were all junior doctors and were trained and overseen by the principal investigator (PI). At 6 and 12 weeks participants were followed up with an identical assessment. Feedback on performance in the scenario was not given for the pre-training assessment, but provided for the post-training assessment, 6-week and 12-week follow ups.

Outcomes

The primary outcome was to assess the effectiveness of this model of teacher training in improving resuscitation knowledge and skill endpoints among the peripheral hospital doctors taught by the ‘trained trainers’. Knowledge and skills were judged by scores in an MCQ test and performance in a simulated cardiac arrest scenario with concurrent video analysis. Assessment was carried out immediately pre and post training, and again at 6 and 12 weeks, following the advice of international guidelines that recommended repeat assessments to ensure adequate retention of knowledge and skills following resuscitation training(144). The secondary endpoint of this study was to investigate how long any improvements in knowledge and skills would be sustained.

Knowledge assessment: MCQ test

The MCQ was a modified version of the American Heart Association (AHA) advanced cardiac life support (ACLS) course, which tested aspects of BLS and ALS including ECG arrhythmia recognition (see Appendix C6). One mark was awarded for every correctly answered question for each of the 30 questions, and no penalty was given for
missed or incorrect answers. Five questions were modified to fit the Sri Lankan medical context of health care. For example, terms like “ER”, an acronym for ‘emergency room’ didn’t exist in the Sri Lankan health care terminology, so this was replaced with more appropriate terms such as “OPD” (outpatient department), or “ETU” (emergency treatment unit) for the written scenario statements that formed the basis of some questions. The same MCQ test was used at all assessments, but participants were not told their test scores nor were they given feedback on their answers to previous tests.

Skills assessment: performance in a cardiac arrest scenario

Participant’s knowledge and skills in the initial response to an unconscious patient, and performance of CPR was tested through a video recorded simulated scenario of cardiac arrest involving an instrumented mannequin(145).

A temporary ‘simulation suite’ was established in the room where the peripheral hospital training session was being conducted (see Appendix C7). The simulated patient was a male mannequin lying in a hospital bed wearing local attire, cordoned off from the rest of the room by hospital screens. The participant was read the scenario script from outside the simulation suite and was told that a 50 year old man had collapsed and the participant was asked to “do what you would do in real life” (see Appendix C7 for script). The participant then entered the suite and was expected to check the responsiveness of the patient, call for help, open the airway, perform a breathing check and after this assessment initiate single rescuer CPR. If CPR had not commenced by 60 seconds they were given the following prompt:-

“I want you to start cardiopulmonary resuscitation on this patient please”

The scenario was continued to capture 60 seconds of chest compressions once CPR had commenced and the participant was then told that help had arrived.
Assessment of compression and ventilations

The instrumented mannequin, Resusci Anne Skill Trainer™ (by Laerdal), was connected to a laptop, which recorded the following measurements of resuscitation skill; ventilation count, adequate ventilation volume, average ventilation volume (milliliters), compression count, compression with no error, average depth (millimeters), adequate depth, compression rate, and adequate rate. We analysed the data by describing any changes in the raw scores of these variables in relation to the training intervention. We also described the changes in proportions of participants achieving clinically relevant benchmarks described in the literature reflecting the quantity and quality of compressions and ventilations. The benchmarks we reported were; mean compression depth between 40-50mm, mean compression depth ≥ 40mm, mean compression rate 80-120/min, and mean ventilation volume 400-1000mls.

Assessment of initial approach and steps of CPR

Video assessment of simulated scenarios is an established methodology in measuring effectiveness of resuscitation training (145-149). A video recorded scenario was to measure objective endpoints on quality of compression and ventilations, and steps of cardiopulmonary resuscitation (CPR) employing validated metrics (145, 146).

The video recorded scenarios were marked by 3 trained research assistants who coordinate the assessments at the peripheral hospital workshops. A marking schedule was adapted from a validated assessment tool for CPR performance called the ‘Cardiff Test version 3.1’(145), and these variables were modified to be consistent with the 2005 ILCOR guidelines for CPR where necessary. The marking criteria assessed whether participants correctly carried out the following steps of initial approach and performance of CPR; calls for help, checks for responsiveness (shouting), checks
responsiveness (shaking victim firmly), opens airway (using either head tilt, chin lift or jaw thrust), checks for airway obstruction, performs a breathing check, uses correct compression ratio, and uses appropriate facemask technique (see Appendix C8 for marking checklist). The participants’ practice of checking for a pulse centrally, or utilising a precordial thump was also observed.

The video assessors were trained on how to mark the video scenarios according to the marking schedule by the principal investigator (PI) in an initial 30 minute teaching session. Thereafter they independently marked 5 video recordings of scenario assessments, and a kappa score for inter-observer reliability of 0.69 was calculated for the variables that the study was reporting. This score was within the range of kappas reported by the original article for the Cardiff Test(145). They subsequently received a second group training session where any discrepancies in marking were discussed and consensus was achieved.

The remaining participant videos were then divided and allocated to each video assessor to mark independently. Participant’s sequential assessments were staggered between the three assessors, and they were blinded to their previous results when marking. The score from each assessment was recorded on a checklist, followed by subsequent data entry into an excel spreadsheet. The skills variables were analysed as binary outcomes where the task was either performed correctly or not.

**Statistical analysis**

A power calculation estimated a total of 50 participants were needed to provide more than 90% power to detect a statistically significant difference between the before and after composite scores using a two-sided paired t-test at significance level 0.05. This calculation was performed under the assumption that the performance scores would increase by an average of 15 points (from 50% to 65%) with a standard deviation of 30
points, based on observations from a previously conducted pilot study. The sample size calculation was performed using Stata v12. We aimed to recruit 75 doctors, to allow for attrition.

The mean MCQ scores were compared using a Wilcoxon signed rank test for paired non-parametric data. Continuous variables were compared between assessment sessions using the repeated measures ANOVA test looking for a change in performance over time, and we have presented unadjusted p-values. Differences in proportions were tested using the McNemar exact test. Statistical tests were carried out using STATA v12, and graphs were created using GraphPad Prism (v6).

**Results**

57 participants attended the peripheral hospital workshops but two participants were excluded because they did not have a pre-intervention assessment leaving 55 participants for analysis. One participant did not complete the baseline data survey so demographic data was represented for only 54 participants (Table 6-1). Some participants were unable to sit the post-training and follow up assessments due to work commitments. 52, 44 and 47 participants received the post-training, 6 week and 12 week follow up MCQ assessments respectively (Figure 6-1). 51, 43 and 38 participants received the post training, 6 week and 12 week follow up scenario assessments respectively (Figure 6-2). In addition, data was lost for 7 participants in the 12 week follow up assessment due to a technical error involving the computer backup of data. A complete set of assessment data was available for 32 participants due to a combination of non-attendance for follow up assessments and missing data. The median age of participants was 34 years and there was a male predominance (39/55, 71%). The participants ranged from 2 to 28 years post graduation from their medical degree, and there was a median of 6 years postgraduate experience in the study group. 14/54 (26%) had experienced some form of previous resuscitation
education, but only 3/54 (6%) experienced this education within the last year. Just one participant reported scenario training or interpretation of cardiac rhythms as a component of previous education. 3/14 (21%) from the subgroup reporting prior educational experience felt their resuscitation training was adequate, and overall 20/54 (37%) felt their resuscitation training experience was adequate prior to taking part in the study (Table 6-1).

![Flowchart](Image)

**Figure 6-1** Flowchart showing the number of participants recruited to the study, receiving the training intervention and receiving follow up MCQ assessments.
Figure 6-2 Flowchart showing the number of participants recruited to the study, receiving the training intervention and receiving follow up scenario assessments.

The number of participants that did not attend follow up assessment and where there were technical errors leading to missing data is also shown.
Table 6-1 Demographics and baseline characteristics of the study population.

<table>
<thead>
<tr>
<th></th>
<th>n=54 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Age and Seniority</strong></td>
<td></td>
</tr>
<tr>
<td>Median age (range)</td>
<td>34 (28-53)</td>
</tr>
<tr>
<td>Median years post graduation (range)</td>
<td>6 (2-28)</td>
</tr>
<tr>
<td><strong>Other characteristics</strong></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>39 (71%)</td>
</tr>
<tr>
<td>Any previous resuscitation education experience</td>
<td>14 (26%)</td>
</tr>
<tr>
<td>- Education included Scenarios</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>- Education included Cardiac Rhythms</td>
<td>1 (2%)</td>
</tr>
<tr>
<td>Course attended within last 12 months</td>
<td>3 (6%)</td>
</tr>
<tr>
<td>Level of resuscitation training felt to be adequate</td>
<td>20 (37%)</td>
</tr>
</tbody>
</table>

MCQ Assessment

The mean MCQ score increased from 54.1% pre intervention to 66.6% post intervention, and 69.8% and 72.9 % at 6 week and 12 week follow ups, and this change over time was significant (p<0.001, Wilcoxon signed rank test) (Table 6-2). The repeated measures ANOVA also showed a difference in scores over time (p<0.001).

Table 6-2 Mean scores and 95% confidence intervals for MCQ assessment.

*Data was analysed with the non-parametric Wilcoxon signed rank test, and a significant difference between pre-training score and subsequent post-training assessments. The \( p \) value is also shown for the repeated measures ANOVA test which compared differences in mean scores over time.*

<table>
<thead>
<tr>
<th><strong>MCQ Assessment</strong></th>
<th>Pre-training, ( n=55 )</th>
<th>Post-training, ( n=52 )</th>
<th>6 weeks post, ( n=44 )</th>
<th>12 weeks post, ( n=47 )</th>
<th>( p ) value**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean score</td>
<td>54.1</td>
<td>66.6*</td>
<td>69.8*</td>
<td>72.9*</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>95% CI</td>
<td>49.1-59.1</td>
<td>62.1 - 71.1</td>
<td>65.1-74.5</td>
<td>67.7-78.0</td>
<td></td>
</tr>
<tr>
<td>Median (p50)</td>
<td>52</td>
<td>68</td>
<td>72</td>
<td>76</td>
<td></td>
</tr>
</tbody>
</table>

*\( p <0.001 \) Wilcoxon signed rank test

** Repeated measures ANOVA
Table 6-3  The effect of training on variables of resuscitation skills as recorded by the Laerdal mannequin.

<table>
<thead>
<tr>
<th>Category</th>
<th>Time Variable</th>
<th>Mean</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ventilation count (number of ventilations)</td>
<td>Pre-training</td>
<td>4.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-training</td>
<td>5.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 weeks post</td>
<td>3.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 weeks post</td>
<td>3.3</td>
<td>0.213</td>
</tr>
<tr>
<td>Adequate ventilation volume</td>
<td>Pre-training</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>(number of ventilations)</td>
<td>Post-training</td>
<td>2.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 weeks post</td>
<td>1.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 weeks post</td>
<td>1.7</td>
<td>0.134</td>
</tr>
<tr>
<td>Average ventilation volume</td>
<td>Pre-training</td>
<td>307.2</td>
<td></td>
</tr>
<tr>
<td>(milliliters)</td>
<td>Post-training</td>
<td>458.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 weeks post</td>
<td>398.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 weeks post</td>
<td>342.5</td>
<td>0.004*</td>
</tr>
<tr>
<td>Compression count (number of compressions)</td>
<td>Pre-training</td>
<td>40.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-training</td>
<td>75.6</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 weeks post</td>
<td>73.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 weeks post</td>
<td>70.4</td>
<td>0.001*</td>
</tr>
<tr>
<td>Compressions with no error</td>
<td>Pre-training</td>
<td>2.5</td>
<td></td>
</tr>
<tr>
<td>(number of compressions)</td>
<td>Post-training</td>
<td>19.2</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 weeks post</td>
<td>14.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 weeks post</td>
<td>19.6</td>
<td>0.001*</td>
</tr>
<tr>
<td>Adequate depth (number of compressions)</td>
<td>Pre-training</td>
<td>4.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-training</td>
<td>25.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 weeks post</td>
<td>21.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 weeks post</td>
<td>27.3</td>
<td>0.001*</td>
</tr>
<tr>
<td>Average Depth (millimetres)</td>
<td>Pre-training</td>
<td>28.8</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-training</td>
<td>36.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 weeks post</td>
<td>37.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 weeks post</td>
<td>39.1</td>
<td>0.001*</td>
</tr>
<tr>
<td>Compression rate (compressions/minute)</td>
<td>Pre-training</td>
<td>106.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-training</td>
<td>116.3</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 weeks post</td>
<td>107.1</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 weeks post</td>
<td>105.2</td>
<td>0.016*</td>
</tr>
<tr>
<td>Adequate rate (no of compressions)</td>
<td>Pre-training</td>
<td>46.9</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Post-training</td>
<td>59.4</td>
<td></td>
</tr>
<tr>
<td></td>
<td>6 weeks post</td>
<td>75</td>
<td></td>
</tr>
<tr>
<td></td>
<td>12 weeks post</td>
<td>75</td>
<td>0.054</td>
</tr>
</tbody>
</table>

The p value was calculated using the repeated measures ANOVA test checking for a difference in mean performance over time.
Scenario Assessment

The mannequin data showed a significant difference over time for 6 out of 9 variables related to performance of compressions and ventilations after analysis by the repeated measures ANOVA test. A significant change was noted for average ventilation volume, compression count, compression with no error, adequate compression depth, average compression depth, and compression rate (Table 6-3). The mean number of compressions almost doubled from 40 to 75.6, and compression with no error numbers improved from 2.5 to 19.2 when comparing pre with post (p<0.001), the latter variable reflecting the correct hand position, and depth considered together.

Table 6-4 Percentage of participants appropriately performing aspects of chest compression and bag valve mask ventilation pre-training, immediately post-training and at 6 week and 12 week follow up.

<table>
<thead>
<tr>
<th>Percentage performing (95% CI†), n=32</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td>Mean compression depth 40-50mm</td>
</tr>
<tr>
<td>Mean compression depth ≥40mm</td>
</tr>
<tr>
<td>Compression rate 80-120 per minute</td>
</tr>
<tr>
<td>Ventilation volume 400-1000mls</td>
</tr>
</tbody>
</table>

*p<0.05

** p<0.001

p-values based upon a comparison of pre-training and post training intervention percentages using McNemar’s test (immediately post training, at 6 week follow up, and 12 week follow up)

† 95% exact CI were used
Figure 6-3 Graphs plotting percentage of participants achieving clinically relevant benchmarks (those achieving benchmark/total number in studied);
a) mean compression depth of 40-50mm, b) mean compression depth ≥ 40mm, c) mean compression rate 80-120, and d) mean ventilation volume of between 400-1000mls. (The mean percentage has been plotted with error bar representing the 95% confidence of the mean)
Clinically relevant benchmarks of compression and ventilation after the training intervention also improved. The proportion of participants with a mean compression depth \( \geq 40\text{mm} \) (\( p<0.05 \)) and proportion of participants with ventilation volumes between 400-1000mls (\( p<0.001 \)) increased from the pre-training (baseline) to the post-training assessment (Figure 6-3, Table 6-4). There was a trend for sustained improvement at 6 and 12 weeks, for the “compression depth \( \geq 40\text{mm} \)” variable, however, the improvement in proportions reached statistical significance only at the 12 week follow up. Conversely, the improvement in “ventilation volume between 400-1000mls” was not sustained beyond the post-training assessment. However, the proportion of participants achieving this benchmark at the 6 and 12 week follow up assessments was still greater than the baseline proportion (56% and 50%, versus 34%). Similarly a trend for increasing proportion for participants who achieved a “mean compression depth of 40-50mm”, and “compression rate of 80-120” was observed after the training intervention, but statistical significance was not achieved for these increases.

Results for the video assessment showed significant improvements in checking for responsiveness (shouts), airway opening, breathing check, performance of the correct compression ratio, use of an appropriate facemask technique, \( p<0.001 \) for all mentioned variables, (Figure 6-4a,b, Table 6-5). There was also a reductions proportions performing precordial thump (\( p<0.05 \)), and checking the pulse at a peripheral location (\( p<0.001 \)), which was not recommended.

The greatest proportional increases were observed for initial approach, where the proportion checking responsiveness by shouting “are you okay” increased from 16% pre intervention to 77% post intervention, and in CPR for “airway opening”, and “correct compression ratio”, increasing from 18% to 84%, and from 5% to 84% respectively. The improvement with the pre training scores remained significant at the 6 week and 12 week follow ups in the majority of variables as depicted in Table 6-5.
Table 6-5 Performance in video assessment variables before and after the training intervention.

<table>
<thead>
<tr>
<th>Video assessment variable</th>
<th>Mean percentage achieving variable in relation to training intervention, (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre-training</td>
</tr>
<tr>
<td>Calls for help</td>
<td>55 (38, 71)</td>
</tr>
<tr>
<td>Checks responsiveness - Shouts</td>
<td>16 (6, 31)</td>
</tr>
<tr>
<td>Checks responsiveness - Shakes</td>
<td>3 (0, 14)</td>
</tr>
<tr>
<td>Pulse Check (all)</td>
<td>95 (82, 99)</td>
</tr>
<tr>
<td>- Checks pulse (central location)</td>
<td>50 (33, 67)</td>
</tr>
<tr>
<td>- Checks pulse (only peripherally)</td>
<td>45 (29, 62)</td>
</tr>
<tr>
<td>Airway Opening</td>
<td>18 (8, 34)</td>
</tr>
<tr>
<td>- Head tilt</td>
<td>18 (8, 34)</td>
</tr>
<tr>
<td>- Chin lift</td>
<td>8 (2, 21)</td>
</tr>
<tr>
<td>- Jaw thrust</td>
<td>5 (1, 18)</td>
</tr>
<tr>
<td>Airway obstruction check</td>
<td>47 (31, 64)</td>
</tr>
<tr>
<td>Breathing check</td>
<td>45 (29, 62)</td>
</tr>
<tr>
<td>Correct compression ratio</td>
<td>5 (1, 18)</td>
</tr>
<tr>
<td>Appropriate facemask technique</td>
<td>3 (0, 14)</td>
</tr>
<tr>
<td>Precordial thump</td>
<td>18 (8, 34)</td>
</tr>
</tbody>
</table>

*p<0.05  
**p<0.001

p-values based upon a comparison of pre-training and post training intervention percentages using McNemar’s test (immediately post training, at 6 week follow up, and 12 week follow up).
Figure 6-4a Shows proportion of participants carrying out the following responses from the video assessment component of the scenario (those performing task/total number studied):

i) appropriately checking responsiveness by shouting, ii) using the correct compression ratio when performing cardiopulmonary resuscitation iii) appropriately calling for help, and iv) checking for the pulse only in a peripheral location (incorrect).
Figure 6-4b Shows proportion of participants who correctly performed i) opening of the airway (either head tilt, chin lift or jaw thrust), ii) an obstruction check, iii) a breathing check, and iv) used an appropriate facemask technique (Nb - for Figures 6-4a and 6-4b the mean proportion has been plotted as a horizontal line with error bars showing the 95% confidence interval of the mean).
Resuscitation Logbook

During the 12 week follow up period 31 participants (56%) reported between 1 to 4 real life resuscitation encounters in their hospital jobs (Table 6-6). They also reported that they found the training they received during the study intervention helpful in 91% of these encounters.

Table 6-6 The number of real life resuscitation encounters reported in logbooks of study participants.

<table>
<thead>
<tr>
<th>Experience of real life resuscitation</th>
<th>Number of Participants, n=55 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No reported resuscitation experience</td>
<td>24 (44)</td>
</tr>
<tr>
<td>Reported 1 or more resuscitation events</td>
<td>31 (56)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Number of resuscitation encounters</th>
<th>Number of events, n=57 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>26 (47)</td>
</tr>
<tr>
<td>1</td>
<td>17 (31)</td>
</tr>
<tr>
<td>2</td>
<td>5 (9)</td>
</tr>
<tr>
<td>3</td>
<td>7 (13)</td>
</tr>
<tr>
<td>4</td>
<td>2 (4)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Events where training was helpful</th>
<th>Number of events, n=57 (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>52 (91)</td>
</tr>
<tr>
<td>No</td>
<td>5 (9)</td>
</tr>
</tbody>
</table>

Discussion

The current study tested a novel approach to resuscitation education that has not been previously reported in the literature. Whilst there are other studies that measure the benefit of different educational interventions in improving ALS and BLS outcomes in highly resourced urban settings, the key difference with our study was its focus on the assessment of a train-the-trainer (TTT) model of education using non-specialist doctors in a resource limited peripheral hospital setting. We also reported objective and validated endpoints in resuscitation knowledge and skills, directly after and up to 12
weeks following the training intervention. Our study has direct relevance to rural Asia where there is a high incidence of respiratory failure from pesticide poisoning and snake bite envenomation(1, 130-132), in addition to the standard range of primary cardiorespiratory pathology seen throughout the world.

The main objective of our training intervention and evaluation was to improve outcomes in accordance with the recommendations set out by ILCOR. These guidelines emphasised high quality chest compressions with minimal interruptions, and recommended a cardiac compression to ventilation ratio of 30:2 and a target chest compression rate of 100 per minute(150).

We observed improvement in all the domains of data we collected including knowledge from the MCQ scores, quality of compressions and ventilations from the mannequin data, and knowledge and skills in carrying out the “steps of CPR” through the video assessment. The improvement seen in these metrics was similar to reports of comparable endpoints from training interventions delivered in high resourced clinical environments(146, 151, 152).

**Improvement in Compressions and Ventilations**

The improvements we noted in compression and ventilation skills, as recorded by the instrumented mannequin, were significant, but in general not as large as that observed for the “steps of CPR” as measured by the video analysis. The most prominent improvements were compression counts (number of compressions), and compression depth (including adequate depth), which both significantly improved after the training intervention. The increases in endpoints from the instrumented mannequin data also translated into significant improvement in clinically relevant benchmarks, specifically in the proportion of participants achieving compression depths of ≥40mm, and ventilation volumes of 400-1000mls (Table 6-4). However, the absolute proportions of post intervention compressions depth was suboptimal, reflected by low absolute proportions
(38 - 47%) of participants achieving ≥40mm depth, despite improving significantly from the baseline proportion (13%).

Suboptimal chest compression depth is a recognised challenge in ALS training and other studies have reported similar, or lower, chest compression depths than reported in the current study despite being conducted in high resourced settings (151-153). Perkins et al. studied the quality of CPR achieved by health care professions attending ALS training courses in the UK, and reported mean chest compression depths of between 24.1 – 28.2mm(151), whereas the mean compression depth in our study increased from a baseline 28.8mm to between 36.9 - 39.1mm post training. Two studies identified that poor chest compressions depths in mannequins placed on hospital beds may be due to pressure dissipation through the mattress rather than due to lack of chest compression skill (152, 153). Another study reported higher proportions (70-79%) of participants achieving an adequate compression depth (≥40mm)(146), however, it is likely that the mannequin they used was placed on the floor which may have aided their compression depth recordings(153).

While there was no increase in the “ventilation counts” there was a significant increase in the “volume of ventilation”, and the proportion of participants who delivered a clinically acceptable ventilation volume, i.e. 400-1000mls when comparing baseline with post intervention assessments (Tables 6-3 and 6-4). The proportion of participants who delivered an acceptable ventilation volume following training increased from 34% to 78%, this was higher than that reported by Mpotos et al. who reported between 52-59% of participants achieving the same following training intervention(146).

The skills that improved the most were use of the correct compression: ventilation ratio, correct airway opening, and delivery of adequate ventilation volume. The improvement in correct compression ratio is notable because it was in alignment with the CPR guidelines taught at the peripheral hospital workshops. The observed improvements in
ventilation and airway opening skills were of particular importance in the study setting of rural Sri Lanka because airway compromise is commonly encountered due to the high incidence of organophosphorus poisoning and snakebite injury in the region(3, 32, 52, 87, 130, 132).

The skills that improved the least were calling for help, checking responsiveness through shaking the victim, and checking for an airway obstruction. The latter two variables were difficult to measure through video analysis and are known to have a lower inter-observer reliability than for other measured variables measured(145).

Retention of knowledge and skills over time

The retention of knowledge and skills at 6 weeks and 12 weeks, was a secondary endpoint in our study, and we noted that the mean post-training MCQ scores stayed elevated compared to the baseline assessment scores, and the improvements in most categories of the video assessment evaluating correct steps of CPR were also sustained until 12 weeks. However, when looking at the skills of chest compression and delivery of ventilations, only improvement in chest compressions (mean compression depth ≥40mm) was sustained until 12 weeks. The percentage achieving ventilation volumes of 400-1000mls dropped down from 78% at the post intervention assessment to 56% and 50% at the 6 and 12 week follow up assessments respectively. This suggests that the improvement in ventilation skill was not significantly sustained beyond the post intervention assessment.

We also observed non statistically significant trends for increasing outcomes at the 6 week and 12 week follow up assessments for MCQ score, at the 12 week follow up for “initial airway opening” and “initial breathing check”, and at the 6 week follow up for “mean compression rate of 80-120” (Figure 6-3, and Figure 6-4b). One would expect a decrease in skill outcomes the greater the time from training intervention, so these
trends were unexpected. In search of a plausible explanation we considered the possibility of continued learning following the initial training intervention, and the possibility of the follow up assessments having an educational benefit. Kromann et al. showed testing as a final activity in a resuscitation skills course increases learning outcomes (a so called “testing effect”), however, the effect of multiple testing without preceding formal training was not studied (154, 155). Our study was not designed to evaluate the role of repeat testing, but it would be worthwhile asking this question in future research investigating what factors lead to a sustained improvement of knowledge and skills in the peripheral hospital setting.

This study confirms previous reports of a deficit in resuscitation training in the rural Sri Lankan setting (15). Whilst 14 participants (26% of study group) had received previous resuscitation education (and only 6% had attended one within the previous year), none had received education equivalent to the standard of an ALS course. We know this because ALS training was not available for rural hospital doctors at the time of the study intervention. However, it was also confirmed through the participant data where only one participant reported prior exposure to scenario based education and education about cardiac rhythms as part of their previous resuscitation training experience (Table 6-1), which is an essential characteristic of ALS training. The lack of equivalency between the previous resuscitation education that was reported by participants and the education provided in the current study meant that prior training was unlikely to be a confounding variable in our analysis. In addition, the fact that 57% of the entire group, and 79% of the 14 participants had received previous resuscitation education, felt their level of resuscitation training was inadequate prior to the study intervention, perhaps provides further evidence of the magnitude of the resuscitation training deficit that exists in the peripheral hospital setting.

In contrast to other studies reporting resuscitation training interventions, which are often set in urban teaching hospitals, our study delivered training to quite a diverse
range of doctors who had between 2 and 28 years of post graduate experience. The heterogeneity of clinical experience within the study group, suggests a range of different learning aptitudes, and it is possible that this diversity could have been a challenge for the training model, and may have impaired the effect of the training intervention. It would be useful for further research to investigate the impact diversity of age and clinical experience on learning and teaching future studies in similar settings, as this appears to be a feature of rural doctor populations.

The logbook data showed that 54% of participants were involved in real resuscitations over the 12 week follow up period and that they considered the training intervention helpful in a large majority (91%) of these events (Table 6-6). A subgroup analysis of those participants who reported real life resuscitation exposure is limited by the low numbers of resuscitation events per participant, even though a relatively high proportion of the group experienced real-life resuscitation. Furthermore, a meaningful correlation of real life exposure with the study endpoints would be flawed given that many of the resuscitation events occurred at different times in relation to the follow up assessments. In addition there was no unified experience with exposure as participants reported a number of different cardiac arrest scenarios ranging from myocardial infarction, snakebite, electrocution, trauma to intentional overdose (data not presented in results). Whilst a detailed analysis of the logbook data was beyond the scope of the current study, further research investigating the impact of real life resuscitation exposure on the learning and retention of resuscitation skills would be valuable in further developing course content. This is of particular relevance to the rural developing world setting, where the most common causes of cardiac arrest are likely to differ from the countries from which most of the clinical evidence behind the ALS courses originates.

Study limitations
As our study did not have a control arm there was the potential for participants to self
learn between the intervention and assessment. However, improvement in the assessment immediately post intervention, when compared with the baseline assessment, strongly supports the finding that the study intervention was effective in this setting. It is conceivable that learning independent to the training intervention, could have affected the 6 and 12 week follow up assessments, but this was unlikely given the lack of institutional resuscitation training routinely available to participants in the study setting. Another study that did not have a control arm, reported a study design that involved testing immediately after the training intervention similar to that of our study(156). By contrast, other studies where there was either no baseline(146, 157, 158) or a long interval between the baseline and post training assessment(154, 155, 159), a control arm was necessary because candidates could conceivably practice or learn independent to the training intervention. Nevertheless, we would recommend a randomized controlled trial in particular for research whose primary focus is on retention of resuscitation skills.

The use of the same MCQ test in each assessment was a potential limitation as it is possible that repeated testing may have contributed in part to the increased scores that we attributed to increased theoretical knowledge. However, we attempted to minimise the learning of specific answers by not providing feedback to participants after they sat their MCQ tests. The alternative of using different MCQ tests for repeated assessment has reported limitations related to a lack of equivalency between tests (160). A study by Ringstead et al. attempted to validate the reliability of different tests, and found a small, but significant, difference (4%) between MCQ tests scores that were designed by an expert panel from the European Resuscitation Council, and thus suggested caution should be used in interpretation of learning outcomes from different tests(161).

Missing data resulting from non-attendance by some participants for the follow-up assessments also limited our study. The most common reason for non-attendance was participants working as peripheral hospital doctors in situations of relative professional
isolation with limited back up for clinical duties, precluding them from attending training sessions, a problem that has been identified in previous research (15). Three participants were lost to follow up due to personal health factors; two participants became pregnant, and one participant developed chronic illness. Financial pressures were also a factor as many rural hospital doctors would often work a second clinical job that started in the late afternoon and evening, sometimes close to the time when follow up assessments were being conducted. This same issue affected the trainers themselves who devoted the most personal time toward this training intervention out of all the peripheral hospital doctors involved in the study. It is also possible that follow up assessments themselves were initially viewed as less educationally valuable than the resuscitation training workshop, which could have accounted for the initial drop in numbers between the post training assessment and the 6 week follow up assessment. However, the positive feedback that participants provided and the lack of increasing numbers of non-attendees in the 12 week follow up (Figure 6-2) suggests that participants may have seen benefit in the follow up assessment despite their work challenges, after attending one and understanding what it entailed.

Data from the instrumented mannequin was missing in 8 participants and this also contributed to the study limitations. Stored data was lost from the computer in 7 participants due to a problem with backing up of laptop data, and data was lost from the mannequin itself in 1 participant due to a power failure at the peripheral hospital where testing was being conducted (lasting 30 mins). These technical errors were not easily avoidable given the context of “remote testing” in a rural part of a developing world country, and given our experience we recommend that any research using mobile simulation devices in a similar setting should employ a robust strategy for maintaining mannequin power supply and ensuring adequate computer storage of mannequin data.

Despite these challenges the missing follow up data did not affect the comparison
between the pre and post intervention which lead to the main conclusions of the study, and it also did not preclude us from making statistically significant findings regarding the sustained improvement of resuscitation knowledge, and some aspects of resuscitation skills, up to 12 weeks following the training intervention. Nevertheless, the problems of non-attendance and technical difficulties illustrate the challenges of conducting a study in a resource limited rural setting. In the same vein, other studies looking at resuscitation education in similar contexts have argued the value of research being based in a “typical” setting despite the challenges associated with it(162). Other researchers reporting methodology guidelines for studies introducing complex interventions have also suggested that researchers need to carefully consider the trade off between the “importance of the intervention” and the value of the evidence that can be gathered given the constraints(11). In accordance with this message we considered that the limitations of conducting research in our study setting (such as needing to use a mobile simulation suite rather than testing participants in a simulation centre that was absent in the region) may have been outweighed by the gaining a real life practical analysis of the intervention in question.

The scenario we used was validated for initial approach and cardiopulmonary resuscitation(145, 146). However, it was not sensitive enough to capture the assessment of all the components of ALS such a specialised resuscitation treatment algorithms (such as ventricular fibrillation), some other areas of decision making, and team leadership. Some other studies coming from teaching hospital settings have used more complex metrics, involving more then one scenario where participants also worked in teams, but these metrics relied upon experienced ALS instructors to be assessors (156, 159, 161, 163). Such an approach would not have been possible in the rural setting that our study was conducted, as access to experienced ALS instructors was not possible for the duration of the study follow up. We chose to use a single video recorded scenario on an instrumented mannequin rather than multiple
scenarios that were assessed real time because this approach had been validated\(^{(145)}\), and was more practically suited to our study setting.

**Future research directions**

There have been no studies that compare and contrast the delivery of a standard ALS course through the TTT model of training, with other methods of resuscitation training. Self-learning using multimedia and other educational technology are becoming increasingly employed as strategies in resuscitation training, with the advantage of learner flexibility, and the (unproven) suggestion of cost effectiveness\(^{(146, 156, 158, 164)}\). However, there have been mixed results from this approach in the context of ALS training and it has been suggested that face to face learning is unlikely to be replaced by education technology \(^{(158, 164)}\). One study of ALS training yielded positive resuscitation outcomes from a multimedia learning strategy compared with reading alone\(^{(156)}\), and another RCT evaluating e-learning failed to show improvement in objective outcomes despite positive evaluations by students of the course. These studies were all conducted in urban teaching hospital settings, in contrast to our resource limited study setting, where training hardware (including computers and resuscitation mannequins) were lacking. The effectiveness of these newer educational interventions needs to be assessed against current benchmarks for training in various clinical and resourced settings.

**Train the trainer resuscitation education: complex intervention**

The implementation of a train-the-trainer system of education in a rural resource limited setting represents a complex intervention because the infrastructure necessary to conduct a standard resuscitation education course does not exist in the same way that is present in an urban teaching hospital environment. We recommend that our results should also be interpreted in the context of the complex intervention that occurred
which were probably essential for the results we observed. The in-depth teacher training component described in the methods and appendices, and collaboration with a local training authority (the Provincial Department of Health), which allowed the appropriate leave and provision of residential training for the trainers, as well as provision of a course manual, and wallet card and poster visual aids were either directly or indirectly part of our study intervention and therefore likely to be linked to the results we observed. However, the relative importance of these non-core training activities in achieving these results remains a topic for further process-based research to differentiate. For instance, the same course taught without the same level of emphasis on teacher training, or same support and collaboration offered by the local training authority may not have achieved the same results. Thus whilst we can be confident of our findings in the setting in which they were studied, we suggest that policy makers and researchers pay attention to the detail contained within the methodology of the “teacher training” and “assessment” components. We also suggest that the systems and processes employed in the use of this model of train-the-trainer resuscitation education be taken into account when planning and developing future related research and educational policy.

**Conclusions**

We found that the train-the-trainer model of resuscitation education reported in this study, which used non-specialist trainers, was effective in improving resuscitation knowledge and skills amongst peripheral hospital doctors in Sri Lanka. Furthermore many variables of assessment showed improvement that was sustained for up to 12 weeks post training intervention. Further research investigating the components of a training course that lead to improved knowledge and skills retention would be of benefit in developing effective resuscitation education programs for rural developing world emergency care systems.
Supporting Information

Appendix C1 - Resuscitation training intervention – overview of workshops
Appendix C2 - Instructor workshop ('training the trainers') – course outline
Appendix C3 - Resuscitation Training “Instructor Manual”
Appendix C4 - Peripheral hospital resuscitation workshop – course content and outline
Appendix C5 - Supporting material for trainers & checklists of performance
Appendix C6 - MCQ test used at assessments
Appendix C7 - Script for resuscitation scenario & picture of assessment room
Appendix C8 - Marking schedule for video assessment
Chapter 7: Conclusions

The first section of this concluding chapter outlines the main contributions of the research presented in this thesis in two areas aimed at improving OP poisoning management: acetylcholinesterase measurement and resuscitation training.

The second section discusses some limitations of this research in improving the medical management of OP poisoning. It also provides reflection upon the conceptual frameworks used to structure the thesis, and insights from carrying out health services research and training having used a ‘participatory action research’ methodological approach.

The third section outlines future directions that research to improve the acute management of OP poisoning could take based upon the findings of research contained within the thesis, and concluding comments.
Summary of contributions

This thesis contributed to the literature on OP poisoning management by addressing two deficiencies in acute clinical care that contribute to mortality and morbidity. The studies were conducted in a resource limited rural setting in Sri Lanka. However, the findings also have some relevance to high income settings where acute OP poisoning also has high mortality(23).

AChE POC testing in resource limited secondary referral hospitals

One stream of research addressed the provision of a point-of-care acetylcholinesterase (AChE) activity test. This biomarker is widely recommended in the management of OP poisoning (3, 165, 166). It has been suggested that AChE may have a role in guiding patient discharge decisions and oxime antidote therapy, both of which would aid overall management(3, 63, 72). It was hypothesized that an AChE point-of-care (POC) test originally designed for occupational settings may also be of benefit in acute OP poisoning in rural Sri Lanka. To investigate this hypothesis a series of studies were carried out starting with the validation of a POC test (the Test-mate ChE field kit) against a reference laboratory (Chapter 4).

A concurrent study was set up to observe changes that occurred in the knowledge, attitudes and practice of treating clinicians through the provision of the AChE test at the point-of-care, when managing OP poisoned patients. This study found that a high proportion of doctors valued the test in general, but also surprisingly found that doctors who were more experienced in seeing AChE results valued the test less (Chapter 5). Low proportions valued the test in guidance of acute poisoning management (e.g. to direct oxime therapy and early discharge).
These findings prompted a systematic review to examine in more detail the specific parameters provided in texts to guide the use of AChE in acute poisoning, and to what extent a consensus on the use of AChE had been achieved in the literature (Chapter 2). This review highlighted a lack of primary evidence supporting guidelines for the use of AChE in relation to oxime use and discharge decisions. This finding suggested that the lack of decision support in the interpretation of test results may have been accountable, at least in part, for the observed changes in knowledge, attitudes and practices from exposure to the test results.

The systematic review also showed that whilst AChE was recommended in most OP management texts, evidence was lacking on the use of AChE in oxime therapy and to facilitate early discharge. These are both complex areas of management. In contrast, there was abundant evidence for the use of the test in diagnosis and severity, despite the clinical diagnosis being generally straightforward. The lack of evidence for specific cut-off points for AChE, limited the capacity of even the more detailed texts to provide decision support for clinicians. There was a widespread failure of translation of existing evidence on pitfalls in measurement and interpretation of AChE into texts guiding the management of OP poisoning.

The conclusion from this stream of research was there is a need for more primary evidence to support specific guidance in the use of AChE in relation to oxime use and discharge decisions, and whether this approach improves clinical outcomes. Also training in test interpretation and pitfalls of measurement should be delivered concurrently with the provision of AChE POC devices.

**Resuscitation training in rural peripheral hospitals**

The other stream of research addressed the deficit in resuscitation training for primary care doctors in the peripheral hospitals where OP poisoned patients usually make first
contact with the health system. Here early effective resuscitation using skills such as “airway management” (32) could avoid preventable complications like pulmonary aspiration (44). Despite the recognition of the importance for resuscitation in OP poisoning management (Chapter 1) a lack of specialist trainers and the professional isolation of the peripheral hospital doctors were barriers to the delivery of training.

To overcome this isolation, a train-the-trainer (TTT) model of resuscitation education was evaluated in the rural Sri Lankan setting (Chapter 6). Despite advocacy for this approach (136), its effectiveness through objective learning outcomes had not previously been reported for advanced life support in adults. The conclusion of this study was that the described TTT model of resuscitation education was effective in improving resuscitation knowledge and skills in rural peripheral hospital doctors, and improvements in most components was sustained for 12 weeks (Chapter 6).

This paper made a number of contributions to the resuscitation literature, and in particular the literature coming from lower-to-middle income countries where educational studies reporting objective endpoints are limited (137). It was the first study reporting the effectiveness of using non-specialist doctors to conduct peer-led ALS training in a low resource peripheral hospital setting, using objective knowledge and skills endpoints according to standardized metrics. The study also focused on the analysis of the TTT model of training rather than the specific course.

Previous reports of deficiencies in rural doctor professional education were confirmed. No participants had previous resuscitation education to an ALS standard prior to the study intervention, and only 6% of participants reported having attended any form of resuscitation education (e.g. lecture) within the past year. This was despite over half of participants being involved in real resuscitations (many from OP poisoning) over a 12-week period. The majority (91%) reported their education through TTT resuscitation training intervention was helpful in managing these clinical events. These findings
highlight a gap between the availability of international resuscitation guidelines and its practice in a rural doctor population. The results of the current study suggest that a TTT model of resuscitation education could be a strategy that could help close this evidence-practice gap.

Given the effectiveness of the TTT model in rural resuscitation education the next step in using ALS training as a means to improving OP poisoning management was to find out what literature based course modifications, if any, should be applied to standard ALS guidelines. This was the goal of the systematic review (Chapter 3); the specific aims were to determine the sequence ALS steps, including where specific antidotes fit in that sequence, and describe this in an instructive format that a junior and isolated peripheral hospital doctor could follow. The review found no text that was solely focused on the acute initial management and resuscitation in OP poisoning, and very few texts were written in an instructive ALS format, which made assessment of recommended sequence of ALS steps difficult. From the components and sequence of ALS an ‘OP specific’ ALS guideline incorporating the key review findings was proposed. This instructive guideline highlighted the priority of rapid atropine administration and specified that its delivery should be at the same time as immediate airway, breathing and circulation management. By contrast, the uncertain role of oximes in general meant these had even less of a role in early ALS, and they should not be in the ALS guideline. The guideline identified gaps in literature recommendations for specific treatment of a patient in an OP induced primary cardiac arrest. The was a lack of consensus on issues such as maximum initial bolus dose of atropine that would be beneficial, and the duration of CPR that should be delivered before ending a resuscitation in OP poisoning. Systematic collection of data on cardiac arrest in the rural developing world setting would be useful to collect data on the treatment and subsequent outcomes to address these questions. Such an approach needs further research and validation, which could be carried out through incorporation in ALS training programs.
The future of resuscitation education in addressing OP poisoning management involves further modification and validation of OP specific ALS guidelines. Thereafter future ALS training studies should be performed with this modified content incorporated.
**Conceptual frameworks & research strategy**

OP poisoning is a complex problem that is multifactorial in origin and conceptual frameworks such as the Haddon matrix have been used to argue that a comprehensive public health approach may be of benefit to identify strategies to decrease the high mortality and morbidity in OP poisoning\(^4\). Within this framework I chose to look at improvement of treatment through health services research and training, but it is important to consider my research in the context of the range of other strategies. For example, preventative strategies banning the most lethal poisons have been shown to be highly effective strategies in reducing mortality\(^{48, 167}\). Improved medical management has also been shown to improve outcomes. Within this domain of ‘improved management’ I focused on early primary and secondary hospital management, but other strategies could be employed to try and reduce mortality and morbidity, such as development of pre-hospital care, or first aid delivery by community members, for example.

My research on health professional training was limited to a focus on early initial management and the treatment of primary cardiac arrest. Longitudinal data suggests that only one third of deaths are from primary cardiac arrest, and approximately two thirds of deaths occur between 6 and 100 hours from admission\(^{32, 47, 50, 168}\). This suggests that medical training might also usefully focus on strategies to improve ongoing monitoring and supportive care, perhaps paying particular attention to assessment of the respiratory system as highlighted in ALS guidelines presented in Chapter 3.

**Health services research and training as knowledge translation**

The health services research and training presented in this thesis also could be conscribed within the framework of translational research or “knowledge translation”
(KT) because these studies were aimed at closing the evidence-practice gap (Figure 1).

The studies within both streams of research encompass more than one of the 3 domains for KT, described in the heading of the diagram: knowledge synthesis, exchange, and application. The systematic reviews carried out in Chapters 2 and 3 are forms of knowledge synthesis; the assessment of stakeholders knowledge, attitudes and practice in Chapter 5 are forms of knowledge exchange; and the train-the-trainer study are forms of implementation.

Considering the research within this framework further raises the key question “when is evidence ready for translation into practice?”. The two health systems addressed (provision of a POC AChE test, and resuscitation education) illustrated the challenge of knowledge translation when knowledge may not be optimised for translation. With the TTT study the focus was on effective implementation of relatively established evidence, with the availability of published international guidelines for resuscitation. In hindsight, the AChE translational studies were possibly conducted prematurely when there was no clear consensus about guidelines and major gaps in the clinical science.

There are no black or white answers to the question of when evidence is ready to be translated and many consensus teams struggle with this conundrum.

Some have promoted the use of quantitative assessment to address this problem. They suggest that once research evidence has been established there should be prior integration with the values and perspectives of all the relevant stakeholders. To some extent this approach was used through the use of a systematic review, and engagement with stakeholders through the assessment of knowledge, attitudes and practices of the rural hospital doctors. However, the implementation of an accurate and
reliable AChE POC was still unsuccessful, perhaps because there was not a robust research base providing evidence for its utility in improving outcomes.

‘Participatory action research’ framework for methods

The methods used in the research presented in this thesis had many features of participatory action research (PAR). The focus the research was on addressing locally recognized problems geared towards action and implementation. Both streams of research also involved collaboration with local authorities and an understanding of the local context and stakeholder needs, which in this case was represented by research evaluating the knowledge, attitude and practices of clinicians in terms of the AChE study, and also assessment of effectiveness in terms of the resuscitation study.

The AChE studies were carried out in collaboration with local partners through the research collaboration I was working with (SACTRC). This led to support from the local clinical leaders within the hospital, and access to patients and doctors upon who I carried out survey based research. Later on when carrying out the TTT study, collaboration proved to be essential for the running of workshops that formed the backbone of the study methodology. The major issues of 65 doctors getting leave 3 times over a 3 month period to attend training were minimized as there was strong support from the health department.

The interventions studied interacted with multiple levels of the health system and were thereby inherently “complex interventions”. Medical research council (MRC) guidelines suggest that complex intervention research works best if tailored to local contexts(11). Both the AChE and resuscitation interventions studied in this thesis had to be extensively revised to fit in with local hospital requirements, requests and restrictions. The MRC guidelines also emphasize the need to carefully trade off between the importance of intervention, and the limitations imposed by evaluation taking place
Figure 7-1 Photos showing participation between the research team and the hospital staff whilst conducting health services research on the use of POC AChE tests in a rural secondary referral hospital.

A research team, principal investigator and research assistants (top, left), who were responsible for measurement of AChE in consenting OP poisoned patients. A research assistant transcribes a patient’s AChE result (top, right) obtained from the POC device to worksheets clinicians will have access to at the bedside. Interaction of research team with clinical collaborators (i.e. health service workers) who were responsible for delivery of care for patients recruited in the observational studies (bottom). The presence and contributions of research assistants in the senior medical staff’s ward rounds was essential to the support given to the research and clinical studies (bottom).
Figure 7-2 Photos showing the collaboration and participation between the researchers and local health service and policymakers (i.e. the North Central Province Provincial Department Health Service, NCP-PDHS) in train-the-trainer rural hospital resuscitation study.

Peripheral hospital resuscitation workshop education delivered by a trained trainer (top, left). Data collection setup necessary for the research component (top, right). Award ceremony run by NCP-PDHS in collaboration with researchers (middle and bottom).

Empowerment of the research participants was assisted through presentation of certificates, and feedback and discussion was facilitated between participants, researchers and officials. The main research findings were summarized and disseminated to participants and local policymakers to allow incorporation into future programs.
alongside implementation(11, 18). In the TTT project the local health authorities viewed the education being implemented as part of their annual training program, whilst my focus was on evaluation and demonstrating clinically relevant improvements. This collaborative approach encouraged human resource and financial support that was helpful, but at the same time required extra non-research activities such as certificate presentations for the doctors who attended the course/study evaluation and demonstrating clinically relevant improvements. This was also critical to assess feasibility in both the AChE and resuscitation training streams of research.

Figure 7-1 and Figure 7-2 show scenes from the research fieldwork depicting the participation between the research team and health service community in the respective secondary referral hospital and rural peripheral hospital settings. PAR is becoming increasingly recognized as a useful paradigm in health service research in indigenous populations in Australia(171, 172) and North America(173, 174), and the current research contributes to the literature reporting this approach being used to address problems in the health systems of the Indian sub-continent(10).

**Benefits for local participants and systems**

During the course of conducting research for the AChE study, cholinesterase testing was provided for 13 months to clinicians looking after OP poisoned patients in two secondary referral centres. Also, 65 doctors were trained in resuscitation, 8 of whom were ALS trainers. A key feature of participatory action research used in health services research and training is the empowerment of the research communities resulting in direct benefit(9). Research findings should also be disseminated and fed back to the researched community(16). For example, the participants of the TTT study received group feedback at an awards ceremony organized by the provincial director of health for the region at the end of the 3 month training intervention and follow up period. Here preliminary results were shared with the group so that participants were
aware of some aspects of the data that was collected from them. This, in turn, contributes to trust, empowerment and engagement for the behavior being promoted\(^9\). Other features of PAR or CBPR are the dissemination of research into policy and practice, which is dependent on high levels of community and stakeholder engagement. Interestingly the study protocol for the TTT study was also used for a national resuscitation curriculum module in an ongoing World Bank project called the “health sector development project”\(^{175}\).
**Future Directions**

There are many possible directions for future research to build on this work and experience. Those with the potential to fill a translational gap, engage key participants, and potentially improve patient outcomes are the following:

**AChE in guiding management**

- Development of decision support rules that provide specific values of AChE that can guide clinicians in oxime therapy (e.g. when to start, modify dose and stop therapy), and in patient discharge (e.g. identification of cases of non-significant poisoning).

- Translation of existing evidence on pitfalls in collection and measurement of AChE into recommendations in the literature; particularly the possibility of ex-vivo reactivation of samples that are not immediately cooled and diluted after collection.

- Research demonstrating improvement of clinical endpoints (e.g. decreased mortality, frequency of complications, and length of stay) or economic benefits (e.g. a positive cost benefit analysis in the use of the test).

- Reliability of the Test-mate ChE and other point-of-care devices in use for acute carbamate poisoning (as this is a differential diagnosis in the management of OP poisoning, and the test may behave differently).

- Assessment of knowledge, practices and attitudes of treating clinicians introduced to AChE POC test results with concurrent training on pitfalls in
collection and measurement, and instruction on how to interpret the test in aiding clinical decisions.

Resuscitation training in OP poisoning

Further development of a TTT model, by targeting ALS components that improved least in study (Chapter 6);

- Targeting elements where least improvement was seen immediately such as "calling for help", "checking responsiveness (shaking)", and "checking airway for obstruction"
- Targeting elements where there was adequate improvement immediately post intervention but not at 6 or 12 week follow-up
- Investigation of strategies to increase sustainability of the TTT model of resuscitation education
- More detailed investigation of the impact of real life resuscitation exposure on the learning and retention of resuscitation skills

Training course strategy

Comparison of ALS training workshops presented in this work with other approaches or training modalities, with the aim to increase objective knowledge and skill endpoints;

- Self directed learning using multi-media
- Exploration of effectiveness of "assessment only" educational interventions (e.g. MCQ and simulation assessment, with feedback). Hypothesis based upon the observation of delayed increases in MCQ scores and certain components of ALS (initial airway opening, initial breathing check, and mean compression rate), which appeared to be related to a "testing effect".

Training course content

Comparison of standard course content with alternative approaches:
• Evaluation of BLS course content instead of ALS course content. It is possible that a lower level of resuscitation education may better suit resource limited settings, as many hospitals did not have basic resuscitation equipment precluding components of ALS (such as defibrillation)

The introduction of an ALS guideline specific for resuscitation of acute OP poisoning, such as the one proposed in Chapter 3. The translation of these guidelines into practice would be aided by further research in the following areas:

• Evaluation of the efficacy of an OP specific ALS guideline through analysis of clinical endpoints
• Evaluation of the effectiveness of implementation within the health system

Closing evidence gaps in resuscitation and critical care

As highlighted in chapter 3 there is a need for more primary evidence in the following areas;

• Efficacy of treatments in cardiac arrest in OP poisoning. Evidence for the recommended initial bolus of atropine, and ceilings of therapy. Questions such as how long should one carry out CPR for in an OP arrest would be helpful for treating clinicians as well as for those who write guidelines.
• Useful data could be collect by setting up of cardiac arrest registries, particularly in rural Sri Lankan settings where cardiac arrest is frequent occurrence.
• Studies evaluating effectiveness increased monitoring of respiratory status in OP poisoned patients to prevent respiratory arrest and delayed intubation

The goal of improving the medical management of OP poisoning was followed within two different streams of intervention. However, these were related through a common emphasis on knowledge translation. Also both used a community based participatory
approach leading to practical interventions that held the promise of improved patient
care. The findings suggest that progress has been made, but many other areas for
future work have been equally highlighted.

Taking a step back, casting the net wider, and analyzing the OP poisoning problem
through a conceptual framework such as the Haddon matrix, it is apparent that other
avenues may also be worthy of intervention and action. Perhaps a much better and
more cost-effective solution lies just around the corner. I have experienced that being
part of a collaborative research network allows for a change in direction, should it be
necessary. It also allows for the sharing of findings with others pursuing different
avenues of research with the common goal of reducing mortality and morbidity and
improving wellbeing in affected populations.

Thus a keen awareness of how little we still know, whilst sharing what we have found,
is at the heart of the conclusion of this thesis. This proposition is in keeping with a
reflection made by one of the founders of modern science, Sir Isaac Newton, who
understood how little he understood when he said,

“I do not know what I may appear to the world, but to myself I seem to have
been only a boy playing on the seashore, and diverting myself in now and then
finding a smoother pebble and prettier shell than ordinary, whilst the great
ocean of truth lay all undiscovered before me”

We may still be only reporting the shells and the pebbles when it when it comes to
making improvements in the management of a complex problem such as OP
poisoning. However, health service research and training, and participatory action
research provides some useful tools, and a worthwhile vessel, to help us navigate the
great ocean that lies ahead.
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Appendices

Appendix A  Publications

Appendix A1  Organophosphorus and Carbamate Agents (Anticholinesterase pesticide poisoning)

Appendix A2  Evaluation of the Test-mate ChE (Cholinesterase) field kit in acute organophosphorus poisoning

Appendix A3  Effect of acetylcholinesterase (AChE) point-of-care testing in OP poisoning on knowledge, attitudes and practices of treating physicians in Sri Lanka.

Appendix A4  The effectiveness of a “Train the trainer” model of resuscitation education for rural peripheral hospital doctors in Sri Lanka

Appendix A5  Knowledge translation in international emergency medical care
Appendix A2  Evaluation of the Test-mate ChE (Cholinesterase) field kit in acute organophosphorus poisoning
Appendix A3  Effect of acetylcholinesterase (AChE) point-of-care testing in OP poisoning on knowledge, attitudes and practices of treating physicians in Sri Lanka.
Appendix A4  The effectiveness of a “Train the trainer” model of resuscitation education for rural peripheral hospital doctors in Sri Lanka
Appendix A5  Knowledge translation in international emergency medical care
Appendix B  Supplementary material for knowledge, attitudes and practice study

Appendix B1  Protocol for study intervention

B1-1 Protocol for blood testing of consenting patients according to the type of poison ingested, and whether the patient is receiving oximes.

B1-2 Time schedule for AChE blood testing

B1-3 Process of documentation of AChE results in clinical record
"Effect of oximes on AChE study - “Testmate pK”

OP Poisoned patient

T0 Blood sample
- Consent for Clonidine/ Mg2+
- Consent for Testmate Pk

Is patient symptomatic? (Requiring Atropine or PAM)

No

Asymptomatic OP poisoned Patient protocol

Repeat daily Blood tests
- Until discharge
  - (Eg T24, D2 samples 24 and 48 hours after T0)

Yes

Is the patient getting PAM? By what route?

No PAM

T0 Blood sample on Admission
- (Consent already granted for all patients
  - Cohort study ERC 05/003)

IV PAM infusion

PAM IV Bolus

T=6 (6 hrs post T0)
- Daily samples thereafter
- Alternate daily samples after 5 days

T=10 (18 hrs post PAM infusion)
- Daily samples thereafter
- Alternate daily samples after 5 days
- (Eg D2, D3, D4, D5, D7, D9 etc)

T=1 (One hour post 1st PAM dose)
- (take T=0 if necessary - see notes below)

T=6 (pre 2nd dose PAM)

T=7 (1 hour post 2nd dose PAM)

T=18: Pre 4th dose of oxime
T=19: Post 4th dose of oxime

T=42: Pre 8th dose of oxime
T=43: Post 8th dose of oxime

Pre and post daily doses of PAM for duration of PAM therapy - eg D3a, D7b etc
- Alternate daily sample if therapy >5days

Study notes:
- If PAM is started >1hr after the T0 blood sample, another pre 1st dose of PAM sample should be taken called T-5
- In addition to above regular samples one further sample will be taken 6 hours post stopping PAM
- Where PAM has been stopped and is later restarted they will go back to the beginning of the algorithm again

Appendix B1-1 Protocol for blood testing of consenting patients according to the type of poison ingested and whether the patient is receiving oximes
Appendix B1-2 Time schedule of blood testing for AChE levels
Appendix B1-3 Study protocol for documentation of AChE results in clinical record (BHT, bed head ticket)
Appendix B2 Survey

B2-1 – True/false statement used to measure knowledge of biomarkers in OP poisoning (answers included)

B2-2 - Questions used to measure attitudes towards AChE testing in relation to OP poisoning management and oxime therapy

B 2-3 - Scenario component used to measure practice of ordering AChE in cases of severe and mild poisoning receiving and not receiving oximes
**True / False Questions (answers)**

Please circle true or false (T / F) – Don’t worry, these questions are meant to be very difficult, and we don’t expect everyone to get them all correct!

- In organophosphorus (OP) poisoning:
  - Acetylcholinesterase in nerve synapses is inhibited
    - T / F
  - Both Muscarinic and Nicotinic related signs and symptoms can occur
    - T / F
  - Atropine is effective at reversing the Nicotinic effects
    - T / F
  - Oximes act by reversing the inhibited acetylcholinesterase enzyme
    - T / F
  - Oximes are equally effective in all types of OP poisoning
    - T / F

- Regarding acetylcholinesterase inhibition, which of the following are true?
  - Acetylcholinesterase that is irreversibly inhibited by OP is know as “aged” acetylcholinesterase
    - T / F
  - Irreversible inhibition of the Muscarinic receptor can occur
    - T / F
  - Acetylcholinesterase undergoes ageing with carbamate poisoning
    - T / F
  - With higher OP concentrations in the blood, oximes will be less effective
    - T / F
  - OP inhibited acetylcholinesterase can undergo spontaneous reactivation
    - T / F

- Regarding biomarkers of exposure in OP poisoning
  - Red blood cell acetylcholinesterase and plasma acetylcholinesterase are the same enzyme
    - T / F
  - Both red blood cell acetylcholinesterase and plasma acetylcholinesterase can be measured in the blood
    - T / F
  - Complete inhibition of red blood cell acetylcholinesterase is incompatible with life
    - T / F
  - Patients with inhibition of plasma acetylcholinesterase are always symptomatic
    - T / F
  - Plasma acetylcholinesterase is more closely correlated with clinical signs of OP poisoning than red blood cell acetylcholinesterase
    - T / F

- On the second day post ingestion of OP poison the AChE level is low and shows no change when measured before and after a bolus of pralidoxime. This could be due to:
  - A high proportion of “aged” acetylcholinesterase
    - T / F
  - Not enough atropine being given
    - T / F
  - Not enough pralidoxime being given
    - T / F
  - The patient has ingested a low dose of OP
    - T / F
  - The patient took carbamates rather than OPs
    - T / F

- Regarding pralidoxime’s effect on inhibited AChE in OP poisoning
  - Oxime therapy is more effective when given earlier than later in OP poisoning
    - T / F
  - Poisoning with chlorpyrifos is more likely to respond than dimethoate poisoning
    - T / F
  - The maximum inhibition of AChE is likely to occur after several days in a patient with fenthion poisoning
    - T / F
  - 4 days following the ingestion of chlorpyrifos pralidoxime will be ineffective
    - T / F
  - AChE inhibition in profenophos poisoning responds well to oximes
    - T / F
Survey on treatment of Organophosphorus insecticide (OP) Poisoning

Please answer the following questions by selecting (underline or circle) the appropriate response.

General

1) Do you believe oximes are effective in the treatment of OP poisoning?
   Yes – in all patients / Yes – in some patients / No – not in any patients / Not sure

Comments ……………………………………………………………………………………………………………………………

2a) In treating an adult male severely symptomatic patient (65kg) having pinpoint pupils, chest secretions, bradycardia and hypotension - What dose of intravenous pralidoxime, if any, would you prescribe? (Select from the following) :-
   None / 1g 6 hourly / 2g bolus + 500mg/hr continuous infusion / Other dose ______

2b) For what duration would you give the above dose? ;-
   None / for 24 hours / for 48 hours / For other time period (comment) ______

3a) In treating an adult male mildly symptomatic patient (65kg) who is getting atropine but has no respiratory or cardiovascular compromise - What dose of intravenous pralidoxime, if any, would you prescribe? (Select from the following) :-
   None / 1g 6 hourly / 2g bolus + 500mg/hr continuous infusion / Other dose ______

3b) For what duration would you give the above dose? ;-
   None / for 24 hours / for 48 hours / For other time period (comment) ______

4a) In treating an adult male asymptomatic patient (e.g. 60kg) who is not getting atropine -What dose of intravenous pralidoxime, if any, would you prescribe? (Select from the following) :-
   None / 1g 6 hourly / 2g bolus + 500mg/hr continuous infusion / Other dose ______

4b) For what duration would you give the above dose? ;-
   None / for 24 hours / for 48 hours / For other time period (comment) ______

5) Do think an acetylcholinesterase level (AChE) will be useful in helping guide treatment with oximes? Yes / No / Not sure

Comments ……………………………………………………………………………………………………………………………

6) If this test was available and affordable. Would it be useful in your practice of treating OP poisoning? Yes / No

How would it help you? …………………………………………………………………………………………………………………

7) Roughly how many OP patients have you treated during your working career? (please choose)

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<th>5-20</th>
<th>21-50</th>
<th>51-100</th>
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8) Approximately how may AChE lab results have you seen? (please choose)

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<th>1-5</th>
<th>5-20</th>
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### Scenario 1 – day 1

A 21 year old male has taken an unknown amount of an **unknown** OP poison 3 hours ago. He is symptomatic with pinpoint pupils, chest secretions, bradycardia and tachypnoea. These toxic effects appear to be responding to atropine therapy:

a) Would you prescribe pralidoxime to this patient? **Yes / No**

Why / Why not? ...........................................................................................................................

b) “The benefits of giving pralidoxime to this patient outweigh the risks” (**circle**):

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<th>disagree</th>
<th>uncertain</th>
<th>agree</th>
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c) If the test were available, would you order an acetylcholinesterase (AChE) level in this patient? **Yes / No**

Why / Why not? ...............................................................................................................................

d) “knowing this patient’s admission AChE level would help his management” (**circle**):

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<th>disagree</th>
<th>uncertain</th>
<th>agree</th>
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**Please answer both Scenarios**

### Day 2 – 24 hours after ingestion “No oximes given”

It is now 24 hours post ingestion of poison. **He was not** given oximes. His clinical condition has improved a little but he is still on an atropine infusion. His pupils are no longer pinpoint, his heart rate is 96, BP 120/80 and chest is clear.

a) Would you **start** pralidoxime at this point? **Yes / No**

Why / Why not? ...............................................................................................................................

b) “The benefits of giving pralidoxime to this patient **now** outweigh the risks” (**circle**):

<table>
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<tr>
<th>disagree</th>
<th>uncertain</th>
<th>agree</th>
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</table>

c) If the test were available, would you order an acetylcholinesterase (AChE) level at this point? **Yes / No**

Why / Why not? ...............................................................................................................................

d) “**knowing this patient’s AChE level now** would help his management” (**circle**):

<table>
<thead>
<tr>
<th>disagree</th>
<th>uncertain</th>
<th>agree</th>
</tr>
</thead>
</table>

---

### Day 2 – 24 hours after ingestion – “Oximes given”

It is now 24 hours post ingestion. **He was** given oximes. His clinical condition has improved a little but he is still on an atropine infusion. His pupils are no longer pinpoint, his heart rate is 96, BP 120/80 and chest is clear.

a) Would you **continue** pralidoxime a further 24hours? **Yes / No**

Why / Why not? ...............................................................................................................................

b) “The benefits of giving pralidoxime to this patient **now** outweigh the risks” (**circle**):

<table>
<thead>
<tr>
<th>disagree</th>
<th>uncertain</th>
<th>agree</th>
</tr>
</thead>
</table>

c) If the test were available, would you order an acetylcholinesterase (AChE) level at this point? **Yes / No**

Why / Why not? ...............................................................................................................................

d) “**knowing this patient’s AChE level now** would help his management” (**circle**):

<table>
<thead>
<tr>
<th>disagree</th>
<th>uncertain</th>
<th>agree</th>
</tr>
</thead>
</table>
### Scenario 1 - day 3 (48 hours after poison ingestion)

This patient has now been on the medical ward for 48 hours. He has not received any pralidoxime. This morning he was weaned from his atropine infusion. He has no muscarinic features or cardiovascular impairment. However, he has grade 3/5 neck muscle weakness, mild facial weakness and diminished tendon reflexes.

a) Would you start pralidoxime at this point (48hrs) in this patient? **Yes / No**

Why / Why not?...................................................................................................................

b) “The benefits giving pralidoxime to this patient now outweigh the risks” (circle):

<table>
<thead>
<tr>
<th>disagree</th>
<th>uncertain</th>
<th>agree</th>
</tr>
</thead>
</table>

c) If the test were available, would you order an acetylcholinesterase (AChE) level at this point? **Yes / No**

Why / Why not?...................................................................................................................

d) “knowing this patient’s AChE level now would help his management” (circle):

<table>
<thead>
<tr>
<th>disagree</th>
<th>uncertain</th>
<th>agree</th>
</tr>
</thead>
</table>

---

### Scenario 1 (day 3 - 6 hours later than above)

In the above scenario oximes were given initially and stopped after 48 hours. 6 hours after stopping oximes all the measured clinical parameters remained the same but the patient said he felt worse and slightly weak:

a) Would you re-start pralidoxime at this point? **Yes / No**

Why / Why not?...................................................................................................................

b) “The benefits giving pralidoxime to this patient now outweigh the risks” (circle):

<table>
<thead>
<tr>
<th>disagree</th>
<th>uncertain</th>
<th>agree</th>
</tr>
</thead>
</table>

c) If the test were available, would you order an acetylcholinesterase (AChE) level at this point in this patient? **Yes / No**

Why / Why not?...................................................................................................................

d) “knowing this patient’s AChE level now would help his management” (circle):

<table>
<thead>
<tr>
<th>disagree</th>
<th>uncertain</th>
<th>agree</th>
</tr>
</thead>
</table>
Scenario 2

An 18 year old female claims to have ingested one to two mouthfuls of an unknown OP poison two hours ago. On examination she is slightly tachycardic (heart rate of 90 beats per minute) but otherwise asymptomatic.

a) Would you prescribe pralidoxime to this patient?  Yes / No

Why / Why not?..........................................................................................................................

b) “The benefits of treatment with pralidoxime outweigh the risks in this patient” (circle):

| disagree | uncertain | agree |


c) If the test were available, would you order an acetylcholinesterase (AChE) level in this patient? Yes / No

Why / Why not?..........................................................................................................................

d) “Knowing this patient’s admission AChE level would help her management” (circle) :

| disagree | uncertain | agree |

please answer both Scenarios

Scenario 2A – “No oximes” (day 2 – 24 hours after ingestion)

It is now 24 hours post ingestion of poison. This patient has not received any pralidoxime. Her pulse became normal soon after admission and she has remained asymptomatic thereafter.

a) Would you start pralidoxime at this point? Yes / No

Why / Why not?..........................................................................................................................

b) “The benefits of giving pralidoxime to this patient now outweigh the risks” (circle):

| disagree | uncertain | agree |

c) Would you discharge this patient home at this point? Yes / No

Why / Why not?..........................................................................................................................

d) If the test were available, would you order an acetylcholinesterase (AChE) level at this point? Yes / No

e) “Knowing this patient’s AChE level now would help her management” (circle):

| disagree | uncertain | agree |

Scenario 2A – “oximes given” (day 2 – 24 hours after ingestion)

It is now 24 hours post ingestion of poison. This patient has received pralidoxime since admission. Her pulse became normal soon after admission and she has remained asymptomatic thereafter.

a) Would you continue pralidoxime in this patient for a further 24 hours? Yes / No

Why / Why not?..........................................................................................................................

b) “The benefits of giving pralidoxime to this patient now outweigh the risks” (circle):

| disagree | uncertain | agree |

c) Would you discharge this patient home at this point? Yes / No

Why / Why not?..........................................................................................................................

d) If the test were available, would you order an acetylcholinesterase (AChE) level at this point? Yes / No

e) “Knowing this patient’s AChE level now would help her management” (circle):

| disagree | uncertain | agree |

Scenario 2 (Day 3 - 48 hours after ingestion)
<table>
<thead>
<tr>
<th>It is now 48 hours following the ingestion of poison. The patient <strong>has not</strong> received pralidoxime. She has remained asymptomatic.</th>
</tr>
</thead>
</table>
| a) Would you discharge this patient home at this point? **Yes / No**  
Why / Why not?............................................................................................................... |
| b) If the test were available, would you order an acetylcholinesterase (AChE) level at this point in this patient? **Yes / No**  
Why / Why not?............................................................................................................... |
| c) “Knowing this patient’s AChE level **now** would help her management” (**circle**) :-  
sort: disagree | uncertain | agree |
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>It is now 48 hours following the ingestion of poison. The patient <strong>received</strong> pralidoxime for 24 hours after admission and then it was stopped. In the second 24 hours she did not receive any medical treatment, and has remained asymptomatic.</td>
</tr>
</tbody>
</table>
| a) Would you discharge this patient home at this point? **Yes / No**  
Why / Why not?............................................................................................................... |
| b) If the test were available, would you order an acetylcholinesterase (AChE) level at this point in this patient? **Yes / No**  
Why / Why not?............................................................................................................... |
| c) “Knowing this patient’s AChE level **now** would help her management” (**circle**) :-  
sort: disagree | uncertain | agree |
<table>
<thead>
<tr>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>General comments about these scenarios / any complaints or things you didn’t understand:</strong></td>
</tr>
</tbody>
</table>
Appendix C  Supplementary material for train-the-trainer study

Appendix C1  Resuscitation training intervention – overview of workshops
Appendix C2  Instructor workshop (‘training the trainers’) – course outline
Appendix C3  Resuscitation Training “Instructor Manual”
Appendix C4  Peripheral hospital resuscitation workshop – course content and outline
Appendix C5  Supporting material for trainers & checklists of performance
Appendix C6  MCQ test used at assessments
Appendix C7  Script for resuscitation scenario & picture of assessment room
Appendix C8  Marking schedule for video assessment
Appendix C1  Resuscitation training intervention – overview of workshops

Overview of assessments

Assessments of peripheral hospital participants (PHP’s)

Training Intervention

Assessment

Peripheral Hospital Workshop

Assessment

“Pre” 8 Workshops

- 6-12 PHP’s
- 2 trainers Per workshop

Assessment

“Post”

Assessment

“6 week”

Assessment

“12 week”

Course Completion Certificate from PGIM*

*Post graduate Institute of Medicine
http://www.cmb.ac.lk/pgim/

Appendix C1
## Phase Ia - Initial Resuscitation Workshop – Provider course & selection of trainers, Nov 28th – 29th 2008

Pre course Inauguration for Consultants and Day 1 participants

### Friday 28th November - Inauguration and Dinner (Nuwaraweva Resthouse)

<table>
<thead>
<tr>
<th>Time</th>
<th>Duration</th>
<th>Activity</th>
<th>Presenter/Coordinator</th>
</tr>
</thead>
<tbody>
<tr>
<td>19:00</td>
<td></td>
<td>Registration</td>
<td></td>
</tr>
<tr>
<td>19:30</td>
<td>10 mins</td>
<td>Welcome of distinguished guests and participants</td>
<td>Dr Athupattu, Provincial Director of Health Services – North Central Province (NCP)</td>
</tr>
<tr>
<td>19:40</td>
<td>20 mins</td>
<td>Partnerships with provincial authorities to improve health care service delivery in the peripheries of NCP</td>
<td>Professor Andrew Dawson – South Asian Clinical Toxicology Research Collaboration (SACTRC) Program Director</td>
</tr>
<tr>
<td>20:00</td>
<td>20 mins</td>
<td>Introduction and objectives of the resuscitation training program</td>
<td>Dr Bishan Rajapakse “Resuscitation Training” project coordinator</td>
</tr>
<tr>
<td>20:20</td>
<td>15 mins</td>
<td>Keynote delivery on the &quot;Importance of the development of the health system in the peripheries&quot;</td>
<td>Hon Peshara Jayaratne - Provincial Minister of Health - NCP</td>
</tr>
<tr>
<td>20:35</td>
<td>10 mins</td>
<td>Academic Agenda for the resuscitation workshop</td>
<td>Dr Bishan Rajapakse “Resuscitation Training” project coordinator</td>
</tr>
<tr>
<td>20:45</td>
<td>5 mins</td>
<td>Words from the Peripheral hospital doctors</td>
<td>Nominated Peripheral hospital doctor</td>
</tr>
<tr>
<td>20:50</td>
<td>10 mins</td>
<td>Vote of Thanks</td>
<td>Dr Dhammika De Silva, Medical Officer Planning, Office of the Provincial Director of Health Services (PDHS)</td>
</tr>
<tr>
<td>20:40</td>
<td></td>
<td>Dinner</td>
<td></td>
</tr>
</tbody>
</table>
Day 1 – resuscitation program (first 10 participants)

**Saturday 29th November - Workshop session 1 (Auditorim RDHS)**

<table>
<thead>
<tr>
<th>Time</th>
<th>Duration</th>
<th>Session</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:30</td>
<td>20 mins</td>
<td>Introduction - Overview and prevention of cardiac arrest</td>
<td>Dr Prasanga Palihawadana (Consultant Anesthetist, CA)</td>
</tr>
<tr>
<td>7:50</td>
<td>40 mins</td>
<td>Lecture 1 - Airway management, ventilation and Intubation</td>
<td>Dr Prasanga Palihawadana (CA)</td>
</tr>
<tr>
<td>8:20</td>
<td></td>
<td><strong>Morning Practical Session 1 (rotate between stations)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Simultaneously run (25 mins each station - 5 mins change time)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Station A1 &amp; A2, Basic Airway (airway opening techniques, adjuncts, BVM ventilation)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Station B1 &amp; B2, Advanced Airway (intubation)</td>
<td></td>
</tr>
<tr>
<td>9:15</td>
<td>45 mins</td>
<td>Lecture 2 - &quot;Advance Life Support Algorithm&quot;</td>
<td>Dr Asoka Gunaratne (CA)</td>
</tr>
<tr>
<td>30 mins</td>
<td></td>
<td>Lecture 3 - &quot;Tachycardia, Bradycardia algorithm&quot;</td>
<td>Dr Colin Page (Emergency Physician, EP)</td>
</tr>
<tr>
<td>20 mins</td>
<td></td>
<td><strong>Demonstration Scenario</strong></td>
<td>Consultant trainers and some participants</td>
</tr>
<tr>
<td>10:50</td>
<td>15 mins</td>
<td><strong>Morning Tea Break</strong></td>
<td></td>
</tr>
<tr>
<td>11:05</td>
<td>20 mins</td>
<td>Lecture 4 – &quot;Post Resuscitation Care&quot;</td>
<td>Dr Lushantha Padmasiri (CA)</td>
</tr>
<tr>
<td>11:25</td>
<td>2 hours</td>
<td><strong>Practical Session 2 - rotate through 4 skills stations</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Simultaneously run (25 mins each station - 5 mins change time)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1- Asystole/PEA scenario</td>
<td>Dr Prasanga Palihawadana (CA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2- VT/ VF scenario</td>
<td>Dr Asoka Gunaratne (CA)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3- Tachycardia/ Bradycardia Scenario</td>
<td>Dr Colin Page (EP)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4- Post resuscitation care scenario</td>
<td>Dr Lushantha Padmasiri (EP)</td>
</tr>
<tr>
<td>13:30</td>
<td>1 hour</td>
<td><strong>Lunch Break</strong></td>
<td></td>
</tr>
<tr>
<td>14:30</td>
<td>45 mins</td>
<td>Post test - MCQ</td>
<td>Classroom</td>
</tr>
<tr>
<td>15:15</td>
<td>1 hour</td>
<td><strong>Post test practical Scenarios</strong></td>
<td>(Conducted in Two places simultaneously)</td>
</tr>
<tr>
<td></td>
<td></td>
<td><strong>Afternoon Tea (refreshments served in between assessments)</strong></td>
<td></td>
</tr>
<tr>
<td>16:30</td>
<td>10 mins</td>
<td>Closing comments</td>
<td>Entire Group</td>
</tr>
<tr>
<td>16:40</td>
<td>30 mins</td>
<td>Instructor de-briefing session</td>
<td></td>
</tr>
<tr>
<td>17:00</td>
<td></td>
<td>Instructors - Free time</td>
<td>Nuwaraweva Resthouse</td>
</tr>
</tbody>
</table>

Pre-course introduction for Day 2 participants

**Sat 29th November - Welcome Dinner: Sunday participants (Nuwaraweva Resthouse)**

<table>
<thead>
<tr>
<th>Time</th>
<th>Duration</th>
<th>Session</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>20:00</td>
<td>5 mins</td>
<td>Introduction and aims of “Train the Trainer” project</td>
<td>Dr Bishan Rajapakse - project co-ordinator</td>
</tr>
<tr>
<td>20:05</td>
<td>5 mins</td>
<td>Official Welcome to peripheral hospitals doctors</td>
<td>Dr Dhammika De Silva, MO Planning office of the PDHS, NCP</td>
</tr>
<tr>
<td>20:10</td>
<td>15 mins</td>
<td>Guest Lecture - &quot;The importance of resuscitation in the peripheral hospital setting&quot;</td>
<td>Dr Herath (Anuradhapura – CA) or other Consultant Trainer</td>
</tr>
<tr>
<td>20:35</td>
<td>5 mins</td>
<td>Words from the Peripheral hospital doctors</td>
<td>Nominated Peripheral hospital doctor</td>
</tr>
<tr>
<td>20:40</td>
<td></td>
<td><strong>Dinner</strong></td>
<td></td>
</tr>
</tbody>
</table>
Day 2 – (repeat course for day 2 participants, another 10, total of 20 receiving course over 2 days)

**Sunday 30th November - Workshop session 2 (Auditorium RDHS)**

<table>
<thead>
<tr>
<th>Time</th>
<th>Duration</th>
<th>Activity Description</th>
<th>Speaker</th>
</tr>
</thead>
<tbody>
<tr>
<td>7:30</td>
<td>20 mins</td>
<td>Introduction - Overview and prevention of cardiac arrest</td>
<td>Dr Prasanga Palihawadana</td>
</tr>
<tr>
<td>7:50</td>
<td>40 mins</td>
<td>Lecture 1 - Airway management, ventilation and Intubation</td>
<td>Dr Prasanga Palihawadana</td>
</tr>
<tr>
<td>8:20</td>
<td></td>
<td><strong>Morning Practical Session 1 (rotate between stations)</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Simultaneously run (25 mins each station - 5 mins change time)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Station A1 &amp; A2</td>
<td>Basic Airway (airway opening techniques, adjuncts, BVM ventilation)</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Station B1 &amp; B2</td>
<td>Advanced Airway (intubation)</td>
</tr>
<tr>
<td>9:15</td>
<td>45 mins</td>
<td>Lecture 2 - &quot;Advance Life Support Algorithm&quot;</td>
<td>Dr Asoka Gunaratne</td>
</tr>
<tr>
<td>9:55</td>
<td>30 mins</td>
<td>Lecture 3 - &quot;Tachycardia, Bradycardia algorithm&quot;</td>
<td>Dr Colin Page</td>
</tr>
<tr>
<td>10:15</td>
<td>20 mins</td>
<td>Demonstration Scenario</td>
<td>Consultant trainers and some participants</td>
</tr>
<tr>
<td>10:50</td>
<td>15 mins</td>
<td><strong>Morning Tea Break</strong></td>
<td></td>
</tr>
<tr>
<td>11:05</td>
<td>20 mins</td>
<td>Lecture 4 – &quot;Post Resuscitation Care&quot;</td>
<td>Dr Lushantha Padmasiri</td>
</tr>
<tr>
<td>11:25</td>
<td>2 hours</td>
<td><strong>Practical Session 2 - rotate through 4 skills stations</strong></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Simultaneously run (25 mins each station - 5 mins change time)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>1- Asystole/PEA scenario</td>
<td>Dr Prasanga Palihawadana</td>
</tr>
<tr>
<td></td>
<td></td>
<td>2- VT/ VF scenario</td>
<td>Dr Asoka Gunaratne</td>
</tr>
<tr>
<td></td>
<td></td>
<td>3- Tachycardia/ Bradycardia Scenario</td>
<td>Dr Colin Page</td>
</tr>
<tr>
<td></td>
<td></td>
<td>4 - Post resuscitation care scenario</td>
<td>Dr Lushantha Padmasiri</td>
</tr>
<tr>
<td>13:30</td>
<td>1 hour</td>
<td><strong>Lunch Break</strong></td>
<td>Classroom</td>
</tr>
<tr>
<td>14:30</td>
<td>45 mins</td>
<td>Post test - MCQ</td>
<td>(Conducted in Two places simultaneously)</td>
</tr>
<tr>
<td>15:15</td>
<td>1 hour</td>
<td><strong>Post test practical Scenarios</strong></td>
<td><strong>Afternoon Tea (refreshments served in between assessments)</strong></td>
</tr>
<tr>
<td>16:30</td>
<td>10 mins</td>
<td>Closing comments</td>
<td>Entire Group</td>
</tr>
<tr>
<td>16:40</td>
<td>30 mins</td>
<td>Instructor de-briefing session</td>
<td></td>
</tr>
<tr>
<td>17:00</td>
<td></td>
<td>Return to Colombo</td>
<td>Nuwaraweva Resthouse</td>
</tr>
</tbody>
</table>

Appendix C1
Phase 1b - Reinforcement workshop for “trainers” (n=8), 21st December 2008

Overview of Training for subsequent workshops:

Nov 28-30  Phase Ia Initial Resuscitation workshop
Dec 21    Phase Ib (reinforcement workshop) – current
Jan 16-18 – Phase Ic workshop (How to be a trainer)
February  Phase II resuscitation training at peripheral (‘hub’) hospitals

Agenda for Workshop

7:45 – 8:15     Pre-Test
8:15 – 9:45    Review of resuscitation material & pre-test
9:30 – 10:00   Morning Tea

10-13:00    Skills stations (x3)
             - Airway management (approach to an unresponsive patient & Intubation)
             - Megacode station 1
             - Megacode station 2

13:00- 14:00    Lunch
1:45 – 15:00    Further scenarios based on Lunchtime feedback

Phase Ic – “Instructor workshop”, n=8

Jan 16th – 18th 2009 (see Appendix C2)
Figure C1 - showing advertisement for potential peripheral hospital trainers prior to phase 1. Collaboration between the Provincial Director of Health Services (PDHS), Postgraduate Institute of Medicine (PGIM), and the South Asian Clinical Toxicology Research Collaboration (SACTRC)

Workshop in Advanced Life Support & Resuscitation
For peripheral hospital doctors to become “trainers”

The office of PDHS, NCP in collaboration with SACTRC and the PGIM will train 20 peripheral hospital MO’s to be “Resuscitation Trainers”.

Residential training will be held at the office of RDHS Anuradhapura.

It is necessary to follow the entire training course over two weekends to complete the training.

**Workshop 1 (28th-30th November)**

- Inauguration & Dinner - 7:30pm Fri 28th November (Milanos restaurant)
- Group 1 - Sat 29th Nov
- Group 2 - Sun 30th Nov

**Workshop 2 (19th-21st December)**

- Inauguration & Dinner - 7:30pm Fri 19th December (Milanos restaurant)
- Group 1 & 2 - Sat 20th Dec & Sun 21st Dec

All interested doctors please call the office of PDHS NCP on 0257200511, or Dr Bishan Rajapakse on 0773504475

Practical Session

- Airway management
- Defibrillation Practice
- New CPR guidelines
- Scenarios
Appendix C2 Instructor workshop (‘training the trainers’) – course outline

“Instructor workshop” (Jan 16th – 18th 2009)

Friday 16th Jan 2009 – Introduction/Orientation
19:00 – Introduction of Participants to Faculty
19:15 - Objectives of Instructor course
Agenda for 2 days
20:00 - Feedback from last 2 courses – group discussion
20:30 - Dinner faculty and participants

Saturday 17th Jan 2009 (Day 1)
(SG) Small Groups - 3 to 4 instructor candidates per Consultant trainer
(EG) Entire Group – 16 instructor candidates

8:00 Lecture: Becoming a Trainer - Teaching strategy – Dr Mudiyanse Rasnayaka (EG - 30mins) (Consultant Paediatrician)
Lecture: Important aspects of setting up a scenario – Dr Mabel Vasnaik (Consultant Anaesthetist)

8:30 Demonstration of “Skills station 1-Basic airway management and initial response to an unresponsive patient”. Demonstration of how to teach this skills station to instructor candidates
Group discussion – Questions and Answers about skills station and module from the entire group

8:45 Practice of “Skills station 1”. Instructor candidates practice teaching Pre-interns participants under observation of Consultant Instructors, who provide guidance as necessary.

9:45 Demonstration of Skills station 2 – Advanced Airway Management (intubation)
Questions and Answers

10:00 Practice of “Skills station 2”

11:00 Morning Tea

11:30 Demonstration of Skills station 3 – Ventricular Tachycardia and Ventricular Fibrillation scenarios
Question and Answers

11:45 Practice of Skills station 3

12:45 Lunch
13:45 Demonstration of Skills station 4 – Pulseless Electrical Activity & Asystole Scenarios
Questions and Answers

14:00 Practice of Skills station 4

15:00 Afternoon Tea

16:00 Group Discussion – Feed back of Demonstration Participants to the Instructor Candidates and consultant Trainers
Free Practice in Skills stations most in need for improvement
17:00 Close

Sunday 18th Jan 2009 – Day 2

8:00 Demonstration of Skills station 5 – Tachycardia and Bradycardia Algorithms
How to use the Resuscitation Mannequin – Rhythm Generator
Questions and Answers

8:15 Practice of “Skills station 5”
9:15 Demonstration of Skills station 6 – Post Resuscitation care and Transport
Questions and Answers
9:30 Practice of Skills station 6
10:30 Morning Tea

Practice workshop with volunteer participants (11:00 to 3:30)

Consultant Instructors fill out checklist for Instructor candidates as they teach.
Feedback and encouragement also given

Each Instructor Candidate is assigned a skills station to teach (because there are 4 per
 group some will teach two skills stations)

11:00 Show DVD to Participants
 i. Overview of resuscitation
 ii. Airway management
 iii. Intubation video (NEJM)

Answer any questions from the Demonstration Participants
11:30 “Instructor Candidates” teach skills station 1 and 2 to Demonstration Participants

12:30 Show DVD to Participants
 i. ALS Algorithm
 ii. Tachycardia/ Bradycardia
 iii. Post Resuscitation care & Intubation

13:00 Lunch
14:00 Instructor Candidates teach station 2-6 to Demonstration Participants

15:30 Afternoon Tea
15:45 De-brief and group feedback from Demonstration Participants. Individual
feedback from Consultant instructors

16:30 Session Close – plans for Phase 2
Resuscitation Training
“Instructor Manual”

A collaboration between SACTRC and the Provincial Director of Health Services NCP
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Resuscitation Training Instructor Manual
How to use this booklet

This booklet has been designed to aid the instructor workshops with details of the course agenda (subject to change), as well as a resource for Trainers during and after their instructor workshop.

The sections of the booklet are instructor course agenda, adult learning behavior, skills station descriptions, competence checklists and sample pre-test MCQ’s

Goals of the instructor course

The focus of the course is on "how to teach". The final goal is to create a trainer who is able to deliver and promote the resuscitation module's objectives :-

1. Recognition of a critically ill patient – and calling for help
2. Use of a system for assessing a critically ill patient - ABCDE
3. Importance of Basic life saving maneuvers
4. Update of Advanced life support algorithms for the arrested patient
   a. The Nov 2005 guidelines (ILCOR)
5. “Communication” in Resuscitation
   a. Calling for senior support early
   b. Communication and leadership during an arrest
   c. Post arrest communication with family and other staff
6. Post Resuscitation care & Inter-hospital Transfer
7. Practical “Hands on” training
   a. Simulation in real life scenarios using CPR mannequins
   b. Assessment with constructive feedback

NCP Health – SACTRC Resuscitation (Instructor Manual)
Instructor Course

Residential Training

This will be a two day residential training starting with an inauguration session. At the inauguration session we will deliver the objectives of the Instructor Workshop and explain the focus of this workshop, which is to train the participants “how to teach” and how to “become trainers”. The dinner is also an opportunity for faculty to meet the participants, which will help facilitate discussion and feedback during the ensuing training sessions.

The Training Module

The training module that we are teaching the “trainers” how to teach is called the “Peripheral Hospital Training Module” which is a module covering advanced life support which has been accredited by the PGIM and also similar content of the National Training module for Sri Lanka.

This module makes use of a DVD that contains lecture material, and resuscitation mannequins that will be used to carry out training from at total of 6 skills stations to cover the practical aspects of the necessary training in advanced life support.

It was designed to be used by non-specialist staff who are trained to instruct others in resuscitation, hence the use of pre-recorded lectures in the DVD format.

A pilot study showed a positive shift in practice after the deliver of a similar module to participants of a similar resuscitation course.

Structure of the “Instructor Course”

This course will start with a limited number of presentations on adult learning behaviour, and follow on with a detailed training in how to deliver each of the 6 skills stations which make up the bulk of the “Peripheral Hospital Training Module”. Finally on the second day the trainers will deliver the entire Module to peripheral hospital doctors from the NCP under supervision of the Consultant Instructors. This will be the same module that they are expected to teach on their own at peripheral hospital training rooms starting in February 2009.

Skills Station Training

Each skill station will be individually demonstrated to the entire group by Faculty and discussed to make the specific key learning points clear to the trainers.

The trainers will be divided into groups of 4

For each group there will be:
1. 2 consultant instructors,
2. 1 mannequin with auxiliary equipment
3. 1 Skills station instructor guide
4. 4 Simulated course participants (Pre-intern Doctors)
The role of the consultant instructor will be to facilitate each of the 4 Trainers to train take the Pre interns through the skills station in the manner it was shown to them in the entire group.

The consultant instructors is watching to make sure the “Trainer” is able to:-
- Demonstrate the learning contents of the skills station properly
- Engage the participants in Simulation and Scenario based learning
- Assign roles to participants (e.g. “Team leader”) effectively
- Give constructive criticism and feedback to participants

The consultant instructor is also expected to make sure that each of the 4 trainers has an opportunity to teach the skills station (at least in part) to the pre-intern participants.

We have assigned two consultant instructors per station with a view to having one primary instructor, who has been ideally trained as an “instructor” in a standardised resuscitation course (e.g. ACLS, ALS, APLS or EMST) where they will be familiar with this adult learning theory and practice, to give feedback on teaching strengths and weaknesses, and a secondary instructor to give feedback issues pertaining resuscitation.

**Putting it all together – Running a resuscitation Training session**

For each group there will be:
- 2 consultant instructors,
- 1 mannequin with auxiliary equipment
- 1 Skills station instructor guide
- 4 peripheral hospital participants

It is assumed that by the time we reach this segment of the instructor course all the trainers will be very familiar with each of the individual skills stations, and would have had practice in teaching each of the skills stations to participants.

This segment is about practicing the synthesis of this knowledge on how to teach the individual skills stations into the delivery of the actual training module, which involves the following skills to be developed:

1. Delivery of a DVD lecture and encouragement of questions at the end
2. Making sure that all the participants in each skills station get equal opportunity to practice scenarios
3. How to handle different levels of ability within the participant group
4. Keeping to time and schedule
5. Ensuring adequate Breaks

At this stage of the instructor course each trainer should be equipped to deliver all 6 skills station as will be required when they are conducting the training course at the peripheral hospital. However, because there are 4 trainers per group they will only be able to deliver 1 skills station each, and 2 will be able to deliver 2 skills stations.

The consultant trainer will pick a trainer to run the next skills as required. They will have a predetermined list for the group of 4 so that the trainers can be utilised sequentially. The trainers will not be told in advance which station they will be teaching, as all should be able to teach all stations.
For this segment of the instructor course the Consultant instructor has the important role of filling out an assessment checklist on each Trainer that will be later evaluated to determine if they have made the adequate standard to go on to be trainers in the Phase III of the train-the-trainer project, or whether further remediation is necessary.

Bishan Rajapakse
Resuscitation Training Program Coordinator
NCP Health-SACTRC
Ph 0773504475
Instructor Course Agenda

Instructor Workshop – Schedule and Roles

It is important for all to understand their different roles for this workshop to be effective. Because we are creating “trainers” I have reserved the term “instructor” for “Faculty” (ie consultants who are doing the teaching at this workshop)

I have divided the instructors into two kinds of Instructors for the purpose of running the skills stations and assigned different roles to each. I have also done this because of the varying backgrounds of our faculty.

At this workshop we have instructors who either have completed at least a 2 day “instructor training course” or those who haven’t completed a training course but have significant experience in the field of resuscitation (secondary instructors), either with the American heart association (AHA) advanced cardiac life support (ACLS) course, or UK or Australian resuscitation council’s advanced life support (ALS). And one instructor with extensive experience in advanced paediatric life support, himself having attended the instructor course (APLS), and who will be delivering the lecture program.

I have divided the instructors into Primary instructors who’s role will be on the “teaching” aspects, and secondary instructors who role will be to make sure the content of the “resuscitation” education is fulfilled when we break into groups of 4 students and 2 instructors.

The aim is to have 8 instructors at the course to teach 16 participants. All the lectures will be given to the entire group, and all the practicals will be carried out with the class split into four group. Each group will have a primary and secondary instructor.

List of current faculty
(Those who have not yet confirmed are shown in brackets)

Lecture Program – Mudiyanse Rasnayake / Mabel Vasnaik

Skills station Primary Instructors :-
IP1 – Maybel Vasnaik (ACLS instructor – Bangalore)
IP2 – Donnie Woodyard (ACLS instructor – USA)
IP3 – Shakunthala Murthy (ACLS instructor –Bangalore)
IP4 – Jessica Spedding (ALS instructor – UK)

Skills station Secondary Instructors:-
IS1 – Mudiyanse Rasnayake (APLS instructor – Australia & Sri Lanka)
IS2 – Sushila Ranasinghe (Resuscitation Training – Peradeniya Sri Lanka)
IS3 – Chris Nickson (Resuscitation Training – Perth Australia)
IS4 – (to be confirmed)

Schedule Overview

Pre Workshop session – Friday 16th Jan Evening)
Overview lecture – Dr Bishan Rajapake
Lecture on “Why resuscitation Training is important – Dr Mabel Vasnaik
Day 1 – AM *(Saturday 17th Jan)*
Lecture on Lecturing and DVD lecturing
Theory on adult education
Practice of lecturing (dvd lecturing)

Lecture on Skills stations and Scenarios

Day 1 – PM
Demonstration on Skills stations and Scenarios
Practice of Skills stations and Scenarios

Day 1 – evening
Specific description of skills stations 3-6

Day 2 - *(Sunday 18th Jan)* whole day

*“Practice workshop”*

DVD lecture to participants
Skills station 1-2

Morning Tea

DVD lecture 4-6
Skills station 3-6

Lunch

Participants – post test MCQ
Trainers – get lecture and demonstration on how to run a scenario assessment, mark and give feedback

Post Scenario assessments

Close

Detailed Schedule (Subject to change)

Pre workshop session – (see above)

Day 1 - AM
8:00 Lecture: How to give a lecture (including delivering a DVD lecture)
9:00 Demonstration of giving a “DVD based lecture”. Demonstration of how to make use of set, environment, dialog, closure.

Faculty acting as both Trainers and Participants

10:00 Morning Tea

10:45 Practice of “Giving a DVD lecture”. Trainers’ practice teaching Pre-interns participants under observation of Consultant Instructors, who provide guidance as necessary.

Layout (*group splits into 4)*
Key for table:
PN – Prospective trainer (Participant number)
IP – Primary Instructor
IS – Secondary Instructor
DP – Demonstration Participant (Pre-intern)

Numbers
PN : 1-16
IP : 1-4
IS : 1-4
DP : 1-8

Practical session – Practice of giving a DVD Lecture

Instructor roles:
Primary instructor – guiding the situation
Secondary instructor – filling assessment form on giving a lecture

Station Equipment: DVD player, Instructional DVD

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<th>A</th>
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<tbody>
<tr>
<td>Trainer (performer)</td>
<td>PN1, 2, 3, 4</td>
<td>PN 5, 6, 7, 8</td>
<td>PN 9, 10, 11, 12</td>
<td>PN 13, 14, 15, 16</td>
</tr>
<tr>
<td>1° Instructor (evaluator)</td>
<td>IP 1</td>
<td>IP 2</td>
<td>IP 3</td>
<td>IP 4</td>
</tr>
<tr>
<td>2° Instructor (evaluator)</td>
<td>IS 1</td>
<td>IS 2</td>
<td>IS 3</td>
<td>IS 4</td>
</tr>
<tr>
<td>Demonstration participant</td>
<td>DP 1, 2</td>
<td>DP 3, 4</td>
<td>DP 5, 6</td>
<td>DP 7, 8</td>
</tr>
</tbody>
</table>
For this practical the primary and secondary instructors will observe the Trainers deliver the DVD lectures to the demonstration participants, and facilitate each of the 4 trainers to do this in their station within the allocated time.

Schedule (cont.)

11:30 **Lecture:** How to teach resuscitation using “Skills stations and Scenarios”

12:30 **Lunch**

13:30 **Demonstration:** How to teach resuscitation using “Skills stations and Scenarios”
Demonstration of “Skills station 1 & 2” by Faculty – both acting as Trainers and participants.
Group discussion afterwards

14:30 **Practice of “Skills station 1 & 2”**. (Group splits into 4)
Trainers’ practice teaching Pre-interns participants under observation of Consultant Instructors, who provide guidance as necessary.

Practical session – Teaching using skills stations and scenarios

**Instructor roles**:
Primary instructor – guiding the situation
Secondary instructor – filling assessment form on how to teach a skills station

**Station Equipment**: (equip for skills stations 1 & 2) Mannequin, OPA, Suction, ETU, Intubateable Mannequin, Airway head, Laryngoscope, ET Tube, introducer, Syringe,

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<td>IP 3</td>
</tr>
<tr>
<td>2° Instructor (evaluator)</td>
<td>IS 3</td>
<td>IS 4</td>
<td>IS 1</td>
</tr>
<tr>
<td>Demonstration participant</td>
<td>DP 1, 2</td>
<td>DP 3, 4</td>
<td>DP 5, 6</td>
</tr>
</tbody>
</table>

For this practical the primary and secondary instructors will observe the Trainers teach the content of skills station 1 & 2 (initial approach to an unresponsive patient not breathing, basic and advanced airway management) to the demonstration participants. They will also facilitate each of the 4 trainers to do this in their station within the allocated time.

15:45 **Afternoon Tea**

16:00 **Demonstration**: How to teach resuscitation using “Skills stations and Scenarios”
Demonstration of “Skills station 3 & 4” by Faculty – both acting as Trainers and participants.

Discussion
Free Practice in Skills stations most in need for improvement
17:00  Day 1 - Close

**Saturday 17th Jan 2009 – Evening**

19:00  Presentation - “Revision of Training objectives – and Agenda for the next days practice training session” (10 mins)

Feedback from Trainers to Consultant Instructors on Day 1 proceedings – strengths and weaknesses of sessions (20mins)

Demonstration and Informal Practice – Review of Skills stations 3 & 4 (30mins)
Demonstration of how to teach using the defibrillator and how to use the rhythm generator
Opportunity to Practice

20:30  Dinner for faculty and participants

**Sunday 18th Jan 2009 – Practice workshop**

12 Peripheral hospital Doctors who have not attended previous workshops are the participants to this Training module. They will be divided into groups of 4. The “trainers” will then teach the module according to the following schedule

Consultant Instructors fill out checklist for prospective trainers as they teach. Feedback and encouragement also given after each skills stations

Each Instructor Candidate is assigned a skills station to teach (because there are 4 per group some will teach two skills stations)

**Day 2 – Practice Resuscitation workshop**

Group is split in to 4 from the beginning
There are 12 peripheral hospital doctor participants (PHP 1-12)

<table>
<thead>
<tr>
<th>Time</th>
<th>Activity</th>
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</thead>
<tbody>
<tr>
<td>8:00 – 9:00</td>
<td>DVD lectures (deliver presentations 1-3)</td>
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</table>

**Instructor roles:**
Primary instructor – guiding the situation & filling assessment form on giving a lecture
Secondary instructor – filling assessment form on giving a lecture

**Station Equipment:** DVD player, Instructional DVD

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<td>PN 9, 10, 11, 12</td>
<td>PN 13, 14, 15, 16</td>
</tr>
<tr>
<td>1° Instructor (evaluator)</td>
<td>IP 1</td>
<td>IP 2</td>
<td>IP 3</td>
<td>IP 4</td>
</tr>
<tr>
<td>2° Instructor (evaluator)</td>
<td>IS 1</td>
<td>IS 2</td>
<td>IS 3</td>
<td>IS 4</td>
</tr>
<tr>
<td>Peripheral Hospital doctor</td>
<td>PHP 1, 2, 3</td>
<td>PHP 4, 5, 6</td>
<td>PHP 7, 8, 9</td>
<td>PHP 10, 11, 12</td>
</tr>
</tbody>
</table>
For this session the primary and secondary instructors will observe and assess the Trainers deliver the **DVD lectures 1-3** to the demonstration participants. Only one trainer will be able to be observed in the group and if time permits a second person can be asked to run through the skills with the participant (see bolded PN numbers).

*(Trainer Group rotates anticlockwise by one station, and Secondary instructor rotates clockwise by one station)*

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<tr>
<th>Time</th>
<th>Activity</th>
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<tbody>
<tr>
<td>9:00 - 9:30</td>
<td><strong>Practical 1 (Part 1 - teach skills station 1)</strong></td>
</tr>
</tbody>
</table>

**Instructor roles:**
- Primary instructor – guiding the situation & filling assessment form on running a skills station
- Secondary instructor – filling assessment form on running a skills station

**Station Equipment:** Skills station 1 (initial approach & Basic Airway Management)

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<tr>
<td>Trainer</td>
<td>PN 5, 6, 7, 8</td>
<td>PN 9, 10, 11, 12</td>
<td>PN 13, 14, 15, 16</td>
<td>PN 1, 2, 3, 4</td>
</tr>
<tr>
<td>1º Instructor</td>
<td>IP 1</td>
<td>IP 2</td>
<td>IP 3</td>
<td>IP 4</td>
</tr>
<tr>
<td>2º Instructor</td>
<td>IS 4</td>
<td>IS 1</td>
<td>IS 2</td>
<td>IS 3</td>
</tr>
<tr>
<td>Peripheral Hospital doctor</td>
<td>PHP 1, 2, 3</td>
<td>PHP 4, 5, 6</td>
<td>PHP 7, 8, 9</td>
<td>PHP 10, 11, 12</td>
</tr>
</tbody>
</table>

For this session the primary and secondary instructors will observe and assess the Trainers deliver the **skills station 1** to the demonstration participants. Only one trainer will be able to be observed in the group and if time a second person can be asked to run through the skills with the participant (see bolded PN numbers).

*(Trainer Group rotates anticlockwise by one station, and Secondary instructor rotates clockwise by one station)*

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<tr>
<th>Time</th>
<th>Activity</th>
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<tr>
<td>9:30 - 10:00</td>
<td><strong>Practical 1 (Part 2 - teach skills station 2)</strong></td>
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</table>

**Instructor roles:**
- Primary instructor – guiding the situation & filling assessment form on running a skills station
- Secondary instructor – filling assessment form on running a skills station

**Station Equipment:** Skills station 1 (initial approach & Basic Airway Management)

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<tbody>
<tr>
<td>Trainer</td>
<td>PN 9, 10, 11, 12</td>
<td>PN 13, 14, 15, 16</td>
<td>PN 1, 2, 3, 4</td>
<td>PN 5, 6, 7, 8</td>
</tr>
<tr>
<td>1º Instructor</td>
<td>IP 1</td>
<td>IP 2</td>
<td>IP 3</td>
<td>IP 4</td>
</tr>
<tr>
<td>2º Instructor</td>
<td>IS 3</td>
<td>IS 4</td>
<td>IS 1</td>
<td>IS 2</td>
</tr>
<tr>
<td>Peripheral Hospital doctor</td>
<td>PHP 1, 2, 3</td>
<td>PHP 4, 5, 6</td>
<td>PHP 7, 8, 9</td>
<td>PHP 10, 11, 12</td>
</tr>
</tbody>
</table>
For this session the primary and secondary instructors will observe and **assess** the Trainers deliver the **skills station 2** to the demonstration participants. Only one trainer will be able to be observed in the group and if time a second person can be asked to run through the skills with the participant (see bolded PN numbers).

*(Trainer Group rotates anticlockwise by one station, and Secondary instructor rotates clockwise by one station)*

<table>
<thead>
<tr>
<th>10:00 - 10:30</th>
<th>Tea break</th>
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</thead>
<tbody>
<tr>
<td>10:30 – 11:30</td>
<td>DVD Lectures (deliver presentations 4-6)</td>
</tr>
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</table>

**Instructor roles :**
Primary instructor – guiding the situation & filling assessment form on giving a lecture
Secondary instructor – filling assessment form on giving a lecture

**Station Equipment :** DVD player, Instructional DVD

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</tr>
<tr>
<td>1° Instructor (evaluator)</td>
<td>IP 1</td>
<td>IP 2</td>
<td>IP 3</td>
<td>IP 4</td>
</tr>
<tr>
<td>2° Instructor (evaluator)</td>
<td>IS 2</td>
<td>IS 3</td>
<td>IS 4</td>
<td>IS 1</td>
</tr>
<tr>
<td>Peripheral Hospital doctor</td>
<td>PHP 1, 2, 3</td>
<td>PHP 4, 5, 6</td>
<td>PHP 7, 8, 9</td>
<td>PHP 10, 11, 12</td>
</tr>
</tbody>
</table>

For this session the primary and secondary instructors will observe and **assess** the Trainers deliver the **DVD lectures 3-6** to the demonstration participants. Only one trainer will be able to be observed in the group and if time permits a second person can be asked to run through the skills with the participant (see bolded PN numbers).

*(Trainer Group rotates anticlockwise by one station, and Secondary instructor rotates clockwise by one station)*

<table>
<thead>
<tr>
<th>11:30 – 12:00</th>
<th>Practical 2 (Part 1 teach skills station 3)</th>
</tr>
</thead>
</table>

**Instructor roles :**
Primary instructor – guiding the situation & filling assessment form on running a skills station
Secondary instructor – filling assessment form on running a skills station

**Station Equipment :** Skills station 3 (Management of cardiac arrest - shockable algorithm VT/ VF)
For this session the primary and secondary instructors will observe and assess the Trainers deliver the skills station 3 to the demonstration participants. Only one trainer will be able to be observed in the group and if time a second person can be asked to run through the skills with the participant (see bolded PN numbers).

(Trainer Group rotates anticlockwise by one station, and Secondary instructor rotates clockwise by one station)

12:00 – 12:30 Practical 2 (Part 2 teach skills station 4)

Instructor roles:
Primary instructor – guiding the situation & filling assessment form on running a skills station
Secondary instructor – filling assessment form on running a skills station

Station Equipment: Skills station 4 (Management of cardiac arrest – non-shockable algorithm asystole/PEA)

For this session the primary and secondary instructors will observe and assess the Trainers deliver the skills station 4 to the demonstration participants. Only one trainer will be able to be observed in the group and if time a second person can be asked to run through the skills with the participant (see bolded PN numbers).

(Trainer Group rotates anticlockwise by one station, and Secondary instructor rotates clockwise by one station)

12:30 – 13:00 Practical 2 (Part 3 teach skills station 5)

Instructor roles:
Primary instructor – guiding the situation & filling assessment form on running a skills station
Secondary instructor – filling assessment form on running a skills station
Station Equipment: Skills station 5 (Management of Tachyarrhythmia’s and Bradyarrhythmias)

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<td>PN 1, 2, 3, 4</td>
<td>PN 5, 6, 7, 8</td>
</tr>
<tr>
<td>1° Instructor (evaluator)</td>
<td>IP 1</td>
<td>IP 2</td>
<td>IP 3</td>
<td>IP 4</td>
</tr>
<tr>
<td>2° Instructor (evaluator)</td>
<td>IS 3</td>
<td>IS 4</td>
<td>IS 1</td>
<td>IS 2</td>
</tr>
<tr>
<td>Peripheral Hospital doctor</td>
<td>PHP 1, 2, 3</td>
<td>PHP 4, 5, 6</td>
<td>PHP 7, 8, 9</td>
<td>PHP 10, 11, 12</td>
</tr>
</tbody>
</table>

For this session the primary and secondary instructors will observe and assess the Trainers deliver the skills station 5 to the demonstration participants. Only one trainer will be able to be observed in the group and if time a second person can be asked to run through the skills with the participant (see bolded PN numbers).

*(Trainer Group rotates anticlockwise by one station, and Secondary instructor rotates clockwise by one station)*

13:00 – 13:30 Practical 2 (Part 4 teach skills station 6)

Instructor roles:

Primary instructor – guiding the situation & filling assessment form on running a skills station
Secondary instructor – filling assessment form on running a skills station

Station Equipment: Skills station 6 (Post resuscitation care & Transport)

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</table>

For this session the primary and secondary instructors will observe and assess the Trainers deliver the skills station 6 to the demonstration participants. Only one trainer will be able to be observed in the group and if time a second person can be asked to run through the skills with the participant (see bolded PN numbers).

*(Trainer Group rotates anticlockwise by one station, and Secondary instructor rotates clockwise by one station)*

13:30 - 14:30 Lunch
14:30 - 15:30 Lecture by Faculty on how do run an assessment
(whilst participants are carrying out a MCQ Post test assessment in another room)

**Lecture**: How to perform assessments

**15:30 - 16:30 Scenario Post test**

**Instructor roles**: Guiding the situation & filling assessment form
Secondary instructor – filling assessment form on carrying out an assessment

**Station Equipment**: Skills station 6 (Post resuscitation care & Transport)

<table>
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<td>PN 1, 2, 3, 4</td>
<td>PN 5, 6, 7, 8</td>
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<td>1° Instructor (evaluator)</td>
<td>IP 1</td>
<td>IP 2</td>
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<td>2° Instructor (evaluator)</td>
<td>IS 2</td>
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<td>IS 4</td>
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<tr>
<td>Peripheral Hospital doctor</td>
<td>PHP 1, 2, 3</td>
<td>PHP 4, 5, 6</td>
<td>PHP 7, 8, 9</td>
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For this session the primary and secondary instructors will observe and **assess** the Trainers get the participants to work take part in a “mega-code” and mark and give appropriate feedback. Each trainer will be given a chance to be primary examiner for one participant, and the others will watch and provide feedback.

**16:30 Session Close**
Adult Learning Behaviour
Becoming a Trainer

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This chapter is prepared by summarizing and extracting essential information from the ‘Pocket Guide to Teaching for Medical Instructors’ of the BMJ group.

Teaching and learning
Understanding the Learners
Qualities of a Good Trainer
Basic Principals of Teaching

Teaching and Learning

Teaching is defined as planned experience, which brings about a desired change in behavior. Learning is defined as ‘a relative permanent change in an individual's behavior resulting from experience’. In real life we gather experience and continue to learn. However in teaching, experience is provided in an organized manner with a greater efficiency. Learning experience can be pleasant or unpleasant. Even though we learn from both experiences, tendency with unpleasant experience is to avoid or defense response. Neither of these responses is helpful for achieving teaching goals and therefore should be avoided. Negative remarks, shaming, condemning and even finding and highlighting errors can be consider as unpleasant experience. In practice teachers tend to point out what is wrong even though it may constitute only a small part of the performance. Therefore appreciation of correct performance would be essential for effective teaching. This will be discussed further at the section on giving feedback. The domains of learning includes

- Knowledge
- Skills
- Attitudes (being considerate, responsible, arrogant, patronizing)
- Relationships (being able to communicate, delegate, lead)

All four component of learning would be essential for effective performance.
**Knowledge**

Knowledge is acquired in six stages
- **Knowledge** – collection of facts
- **Comprehension** – Use the knowledge in different situations
- **Application** – Learner relies upon his/her knowledge to do it in real life of simulated situation
- **Analysis** – Learner attempt to observe in the light of his/her prior knowledge
- **Synthesis** - Analysis leads to a new level of understanding
- **Evaluation** – whole process and the outcome is reflected and judge leading to next course of action

**Skills**

There are four stages involved
- **Perception** – learner become aware of the skill and its steps. (skill training stage 1 & 2)
- **Guided response** – Learner is actively involved (skill training stage 3 & 4)
- **Mastery** – able to perform the skill competently. This is achieved by practice
- **Autonomy** – Further practice will achieve a stage when the skill is performed with little conscious thoughts

**Attitudes**

The learning of attitudes involves four stages
- **Perceiving** – attitudes like safety, teamwork, sensitivity should be introduced at the beginning of the course.
- **Complying** – usually learners will comply whether they agree or not
- **Accepting** - Achieved by consistent teaching, role modeling and subsequent testing.
- **Internalization** – Reservations are dropped and attitudes become part of the learner

**Relationships**

In many situations actual interventions are carried out by team effort. Therefore relationships need special attention in training workshops.
- **Decisions** – Friendly or unfriendly
- **Tension** – Agreeing/disagreeing
- **Reintegration** – Providing support
- **Communication** – Asking for and giving information
- **Control** – Asking for and giving opinion
- **Evaluation** – Asking for and giving guidance

All these features are present in a creative group. However the key to success is depend on the ability to resolve tensions and disagreements. This requires a variety of roles in a training course; timekeeper, organizer and a team leader.
Understand the learner

In an adult education course like NLS or APLS student that we have to entertain different students with diverse knowledge, experience, skills, attitudes, expectation, motivation and ability. Therefore becoming a teacher in a NLS or APLS course would be a new challenge even for an experience teacher. Students in NLS or APLS course are expecting respect for their experience and knowledge.

Teachers should adopt a supportive attitude towards students, especially when they have to play a role of mentor. The needs of the student should be addressed. Maslow’s hierarchy of needs describe the needs of a students:

- **Physiological needs** – sleep, rest, food
- **Security needs** – does he feel confident in expressing his opinion.
- **Belonging needs** – Does the candidate feel accepted by the group and teachers.
- **Esteem needs** – Confidence about own abilities and competence
- **Cognitive needs** – Understand the content and mastering the concepts
- **Self actualization** – Is the students potentials maximized. Does the candidate feel that he is progressing?

Adult learns best when

- The content is relevant and has meaning and purpose – at introduction
- Learner is actively involved – interactive lectures
- Objectives are defined and goals are set – by negotiation with learner
- Positive feedback is given – recognize good thing and things need improvements and how to improve also
- Reflection on learning experience is encouraged – though summaries

Even though most of the adult learners are motivated and enthusiastic, you may come across some difficult learners. They can be classified as talker’s, non talkers and destroyers.

**Enthusiastic talkers** can be made use of by giving them a turn to summarize the points discussed. If the discussion is deviated, micro summaries are useful to recapitulate and redirect the discussion. Some time talkers can get in to satellite discussions within the group. Teacher may have to stop the main discussion and listen to the satellite discussion and link it with main discussion. Alternatively teacher may call the particular talker by name to get them back in to the discussion.

**Non talkers** are not equal to non learners. Nervous student need support and encouragement. Teacher should avoid negative, derogatory or destructive responses. If the student fails to answer a question, redirection or rephrasing the initial question may help to avoid embarrassment in front of peers. Teacher may control the situation for example “Sorry I did not phrase the question well”. Repeating and summarizing the candidates ideas may make them feel more comfortable. Questions related his field of work should be given to a nervous candidate as he/she will be more comfortable to answer them.

Third category; **destroyers** can be extremely destructive to learning. They are rare. They consider themselves as having adequate knowledge but fail to share with others, and resist changing or accepting the opinion of the group. Occasionally candidates may be argumentative or rude. This type of learners should be dealt with individually by a senior teacher in private.
Qualities of a Good Trainer

Teacher should be a role model. During a training course their behavior is observed and followed by students. Appreciation is more effective way of enhancing learning and changing attitudes.

Asking questions
Asking questions can facilitate teaching by inducing interactions, allowing student to reflect on their own experiences and providing a feedback to the teacher. However ambiguous and confusing questions, not allowing students to answer or ignoring their response can have negative impact on teaching. Questions should be planned in advance. Intension should not be highlighting lack of knowledge or failures. Lower level of questions can lead to single word answers whereas higher level of questions can lead to a discussion or debate. Too low level questions can be patronizing and too higher level questions can be threatening. Lower level questions are useful in lectures when quick repetition of data is required. Questions can be phrased to address the different stages of knowledge.

Knowledge – Knowing is tested by asking to name, list, describe, write, what, when, how, how many.
Comprehension – Compare, distinguish, show, try to prove, interpret, and explain
Application/analysis – What conclusions, what are the consequences, how could you
Synthesis – Design, create, solve this, what do you suggest
Evaluate – Evaluate this set of data, according your opinion..., What do you think..

Positive feedback
Objective of teaching is to create confident and capable student. Therefore, giving feedback should be carefully planned to achieve the objective. Natural tendency of a teacher is to observe failures/ inadequacies and to give a feedback considering only the wrong part, ignoring the correct part which may be a major portion of the performance.
This cultural inclination of highlighting inadequacies is not helping for effective teaching and could be overcome by following scheme outlined below.

Ask the learner to tell what went well and what part he is pleased with his performance. This helps to develop self reliance and confidence. Teacher should insist to identify good things. Everybody has something good about them and they should realize it.
Encourage the group to tell what went well and good things about the performance. Drifting to point out failures should be discouraged at this stage. The teacher/trainer should tell good things about the performance
Ask the learner what points and how he wish to improve if he/she has repeat the performance
Ask the group to suggest points to improve and how to improve them. At this stage also listing what is wrong is not acceptable and trainer should insist on suggestions for improvements.
Teacher also suggests points to improve and how to improve
At the end of the session summarize good points and suggestions for improvements

This whole process is called positive feedback. This process has helped the learner to identify his/her strengths and capabilities and where improvements are needed and
how to achieve them. Highlighting where went wrong without teaching how to improve becomes a negative feedback and will not help in learning process. Supporting attitude is very important

Basic Principals of Teaching

Basic principles of teaching are applicable in lectures, skill teaching, scenario teaching or in conducting discussion groups. They includes

- **Environment**
- **Set**
- **Dialogue**
- **Closure**

**Environment** – This includes space, seating arrangement, lighting, noise, ventilation, temperature, humidity and any other movements that may disturb or facilitate teaching/learning. Quality of equipments (manikins or audiovisual s) is also very important. Giving attention to environment, organizing them in advance is a responsibility of the instructor and it is essential for an effective teaching session.

**Set** – Mood of the learners will be set by the environment as well as by explaining the objectives, value and usefulness of the session at the introduction. Explaining the expected role of the student (Eg - Whether they should interact or carefully listen) during the teaching session is useful. It is important to explain the peculiarities of using manikins in teaching skills and case scenarios. Manikins will not show any changes or responses to indicate progress or improvement of a disease condition. Therefore during skill training or case scenarios the student will have to depend on the information given by the instructor regarding changes of the condition of parameters. However teacher may give false information in order to facilitate next step of planned training. For example when the student has achieved good chest expansion teacher may say the there was no chest expansion. This situation should be explained to the student in advance to avoid confusion.

**Dialogue** – Actual teaching take place during dialogue. The content should be clear and precise to cover the essentials for the course and delivered within the allocated time. Interactions with the audience to keep the interest and engagement of student also important. For good quality dialogue practice by the teacher is essential.

**Closure** – Closure includes the time for questioning followed by summery and directing the group for next session. Objective of the summery should be to emphasis the key messages.
Lectures

Environment – special attention for audiovisual equipments, noise disturbances and quality of slides.
Set – Good environment can set the mood. Interest and enthusiasm can be created by giving an introduction highlighting the importance of the topic and presenting the lay out the lecture. Asking a question to reflect the experience of students can create enthusiasm.
Dialogue – This is the body of the lecture. The content should be complete, precise, clear and relevant to the course. Audiovisual aids such as computer projectors, overhead projectors, and flipcharts can be used. Content of a text slides should be limited to 3-5 points. Maximum is 7 line and 7 words in each line. Heading should be limited to 5 words. Picture slides can be incorporated to highlight important points relevant to the topic. However it should not distract the audience from the topic. During the lecture questions can be directed to facilitate interaction. Questions should be clear and precise and should allow any body to answer. Taking answers positively will encourage others to participate in the discussion. Audience activities such as brain storming and buzz groups are useful to create enthusiasm and participation. Brainstorming is when a group is encouraged to express their opinion on a specific question/issue and the opinion is written down without any form of feedback. At the end the lecturer should be able to demonstrate a pattern. Buzz group; small groups within a group is asked to discuss a specific subject in middle of lecture for few minutes. At the end they are asked to present what they have discussed. This method is useful to create energy and enthusiasm. A demonstration at the end or in the middle of a lecture is a useful component in practical courses.
Closure – Closure include question time followed by a summery. It is best to keep the summery to the end so that you will be able to give conclusions and the take home message.

Skill Stations

Environment – All the equipments should be available, functioning and familiar to the teacher. Instructor should check all the equipments before starting the teaching session.
Set – By explaining the usefulness and the expected role of the student. Goals of the session should be explained. Four stages of skill training should be explained.
Dialogue – This includes four stage skill training.
Stage one; Silent demonstration by the teacher – This is done at the speed of a real situation. It is important to avoid talking as students tend to look at the teachers moth when the teacher is talking rather than steps of actual skill.
Stage two; Demonstration with a commentary. At this stage teacher will explain the skill while performing it. Skill is broken in to several steps and explained. Students are encouraged to ask questions and clarify doubts.
Stage three; Teacher performs the skill while the student is giving the commentary. At this stage teacher can confirm that the student has understood the procedure. Further questioning is encouraged.

Stage four; student will perform the skill under supervision and positive critique by the teacher

Stage five; Practice- This may take place after the formal teaching session. Usually the group is divided into two at stage three and four to ensure adequate time for all the students.

Closure – Entire group is brought together and allow time for questions and summarizes the important points in the skill and stress the importance of practice. Practice help to master the skill and achieve autonomy when skills are performed almost subconsciously.

Case Scenarios

Case scenario is a form of improvised role-play in which the management of case is practiced using a manikin and suitable equipments. Student is expected to make decisions according to the guided responses from the instructor. In role-play and case scenario participants are expected to act out roles that represent in real life. It helps to teach situations more closely to real clinical situations in life and helps to put knowledge, skills, attitudes and relationships together.

Teaching scenarios help to simulate situations closer to real life. Teamwork can be practiced and experienced teacher could reproduce an almost realistic challenges.

Environment – Environment, equipments and layout should be as realistic as possible. Improvisations should be minimized. Manikins allow procedures to practice. However as they can't give a physiological feedback student have to depend on the instructor for assessment of the condition of the patient or response to treatment. This situation helps teacher to guide the students and create learning points. When real patients or actors are used as models they should be made up and trained to simulate the condition. However procedures can't be practiced.

Set – the group should be briefed together and the performing students should be given separate briefing. It is important to ensure that the student who is going to perform clinical intervention has understood the scenario by asking him to repeat the description before he starts the scenario. Peculiarities of using manikins and responses of the instructor should be explained at the beginning.

Dialogue- teacher retain the control by passive responses ( giving response on learners request) or by active responses (Teacher initiated responses). By these responses teacher retain the control of the direction and outcome of the case.

Closure – Closure should include debriefing when the participant is allowed to express how he felt during and after role play in scenario. Evaluation about the performance with the positive feedback recognizing good things and strengths and pointing out areas to improve and how to improve as explained under the topic 'giving feedback' will help to enhance the learning experience. Question
time and summery are also essential components for closure in a case scenario.

Assessment

Instructors assess students formally when the student knows that he/she is been assessed or informally when the student is unaware that he/she is assessed. Formal assessment can be done by using a checklist of score sheet (see appendix).

Assessment can be of two types; formative and summative. When the assessment is done during the course and inform the student the areas to improve it is called formative assessment. This is done in a formal way at the initial pre-course assessment or informally during the course. Summative assessment is done by a final test. Usually knowledge is tested by MCQ and knowledge psychomotor skills and behavior is tested by case scenario.
Appendix A : Skills station Guides
Airway Management Skill Station (1 instructor, up to 6 students - approximately 30 minutes)

Key teaching objectives
By the end of this session, the participant will:
Show competency and confidence in the principles of establishing and maintaining a patent airway and providing adequate ventilation in an airway training manikin

Equipment at station
ResusciAnne Skillreporter mannequin
Oropharyngeal Airway, Suction, Oxygen
Ambu mask and bag

Instructor Information
The instructor should:
Assess the ability of all participants to maintain an airway and achieve effective ventilation of a manikin measured against predetermined competencies
Allow participants the opportunity to discuss and/or practice airway management and ventilation techniques using an endotracheal tube
"Discuss" the equipment and techniques used for endotracheal intubation including the use of cricoid pressure

This skill station is divided into 2 sections; the first section is the most important.

1. All participants must receive practical instruction and undergo assessment of their competency in the following:
   • Basic airway opening manoeuvres
     - Head tilt / chin lift
     - Jaw thrust
   • Insertion of airway adjuncts
     - Oropharyngeal airway
     - Nasopharyngeal airway
   • Use of suction
     - With expired air +/- supplementary oxygen
   • Ventilation using a self-inflating bag-mask with supplementary oxygen and reservoir
     - One person technique
     - Two person technique
     - Review of ratio of compression to ventilation ratio pre intubation followed by a rate of approximately 10 ventilations/minute (with no pause between compressions for ventilations) post intubation

2. All participants should be offered practical instruction in, and have the opportunity to practice the skills of advanced airway management and ventilation including:
   • Endotracheal intubation
   • Ventilation via the endotracheal tube using a self-inflating bag with supplementary oxygen should be demonstrated.
Instructor Information

Set the mood, establish usefulness and state learning objectives for the session. One method of teaching that you may choose to use is the four-stage approach of:

**Stage 1:** Instructor demonstrates the skill, at normal speed, without explanation
**Stage 2:** Instructor demonstrates the skill more slowly, with explanation
**Stage 3:** Instructor demonstrates the skill while a participant provides explanation
**Stage 4:** Participant demonstrates the skill, with explanation

The practical skills of airway management and ventilation should be taught around a simple scenario. In order not to confuse the participants, this is best achieved by simulating a patient with a respiratory arrest, thereby eliminating the need for chest compressions. The scenario can be broken down into 4 elements:

**Initial approach**
- Airway assessment
- Basic airway opening manoeuvres
- Ventilation with ambu bag
- Confirmation of ventilation

**Arrival of basic adjuncts**
- Use of suction
- Sizing and insertion of oro- and nasopharyngeal airway
- Confirmation of ventilation

**Arrival of additional equipment**
- Assembly of self-inflating bag-mask, reservoir and supplementary oxygen
- Ventilation using one and two person techniques
- Confirmation of ventilation

If time permits, allow participants to practice their skills. Also allow participants to ask questions and reflect on the session content before terminating the session with a succinct review of all the major points covered.
Skills station 2 – Advanced airway management – intubation (1 instructor, up to 6 students - 30 minutes)

Key teaching objectives
By the end of this session, the participant will:
Show competency and confidence in intubating an airway training manikin and coordinating colleagues to support this procedure before during and after the intubation including the application of appropriate cricoid pressure

Equipment at station
ResusciAnne Skillreporter mannequin, Airway Trainer (intubating mannequin)
Oropharyngeal Airway, Suction, Oxygen
Ambu mask and bag, Laryngoscope, ET Tube, Introducer, Stethoscope

Instructor Information
The instructor should:
Assess the ability of all participants to intubate a ventilation of a manikin measured against predetermined competencies
Allow participants the opportunity to discuss and/or practice airway management and ventilation techniques using an endotracheal tube
"Discuss" the equipment and techniques used for endotracheal intubation including the use of cricoid pressure
This skill station is divided into 2 sections – Preparation, and Intubation

1. All participants must receive practical instruction and undergo assessment of their competency in the following:

1. Preparation for intubation (10 min discourse + interactive discussion)

a) Decision to intubate
   • failure to ventilate spontaneously
   • Unprotected or threatened airway
     o Secretions
     o Low level of consciousness for whatever cause (usually GCS < 8 as a guide)
b) Preparation for intubation – explanation of necessary conditions:

1) Checking that all essential equipment necessary for intubation in an ideal situation is there and present in working order. (Can use acronym – PC MALES)

1. **P**ulse Oximetry
2. **C**apnography
3. **M**ask (ie. ambu mask & bag – valve checked in skills station 1) **ESSENTIAL**
4. **A**irway (Oropharyngeal—correct size explained in skills station 1) **ESSENTIAL**
5. **L**aryngoscope (check working light bulb) **ESSENTIAL**
6. **E**ndotracheal Tube (check size and that cuff has no leak) **ESSENTIAL**
7. **S**uction (Yankers suction – check suction working) **ESSENTIAL**
2) Checking there is adequate staff to carry out intubation. Intubator has to assign these roles to others in the group so all understand what they are doing
- 1 - Intubator
- 2 - Assistant to hand ET tube
- 3 - Person to apply cricoid pressure

2. **Endotracheal Intubation (5 min demonstration – 15 mins practice)**

   a) Variations on holding Laryngoscope  
   b) Assigning roles to team members before starting (see above)  
   c) Correct positioning – Head extension & slight neck flexion ("sniffing the morning air")  
   d) Instructing to "start cricoid pressure now"  
   e) Suction of oropharynx  
   f) Insertion of laryngoscope and pushing the tongue to the left side and lifting up – not using Laryngoscope as a “lever” against the upper lip or teeth.  
   g) Communication to the team of either “good view of cords” or “cannot see the cords” and explanation of whether they are either “going to intubate” or “go back to Ambu ventilation”  
   h) Insertion of tube to correct depth – approx 22cm at the lip in an adult male (Vocal cords sit between two black lines)  
   i) Inflation of cuff and ventilation via the ET tube using an Ambu bag  
   j) Confirmation of correct tube placement and instruction to “release cricoid pressure”

_nb_ – if difficulty with intubating within 30 seconds the participant must go back to the ambu ventilation to decrease unnecessary hypoxia (and communicate this to other team members), followed by a further attempt

3. Confirmation of correct positioning of tube and post intubation care  
   a) ET intubation  
      1 – direct visualization for Tracheal intubation (ET tube going through cords)  
      2 – Chest rising with ventilation & Auscultation – equals BS in 4 places (both axillae

**Instructor Information**

The first section on preparation for intubation should be a basic overview and interactive discussion. The practical skills surrounding the actual skill of intubation should be practiced around a simple scenario of a patient with a respiratory arrest to get participants in the mind set of working under emergency conditions.

Eg “Mr De Silva is a 58 year old man who has arrived with a low level of consciousness and is not breathing spontaneously. He still has a pulse. We are now going to place a definitive airway”
The four stage learning model can be used:

**Stage 1:** Instructor demonstrates the skill, at normal speed, without explanation

**Stage 2:** Instructor demonstrates the skill more slowly, with explanation

**Stage 3:** Instructor demonstrates the skill while a participant provides explanation

**Stage 4:** Participant demonstrates the skill, with explanation

Allow participants to practice their skills rotating through the different roles of intubation e.g. Intubator, assistant, cricoid pressure, so that participants in the group who are not actively intubating can also be doing something productive such as being a part of the intubating Team. Also allow participants to ask questions and reflect on the session content before terminating the session with a succinct review of all the major points covered.
Initial Resuscitation/ PEA / Asystole Skills Station (1 instructor, up to 6 students, approximately 30 minutes)

Key teaching objectives
By the end of this session, the participant will be able to:
• Assess the collapsed patient, using an A B C D E approach
• Perform effective cardiac compressions & ventilations
• Practice the algorithm for PEA/Asystole including Atropine administration
• Recognise the need for addressing the reversible causes of cardiac arrest

Equipment at station
ResusciAnne Skillreporter mannequin
Drug trolley, IV Fluids, Oxygen (intubation equipment optional)
Rhythm generating device or Power point presentation/computer program

Instructor Information:
Within this skill station there are three key teaching sections:
  a) Initial assessment using an A B C D E approach
  b) Correct performance of CPR
  c) Recognition of Asystole and PEA and no need for defibrillation

The practical skills of using an A B C D E approach, CPR and defibrillation will be taught around the scenario described below.

Clinical case
"Mr Silva is a 58 year old man who had been complaining of central chest pain 2 hours previously. He has a history of hypertension and is on a “blood pressure pill”. In trying to identify the pill you notice the bottle is empty. His wife tells you that there have been a lot of problems at home lately. On arrival he had a weak pulse of 60bpm, and BP was 90/60. His respiratory rate was 30. When you see him, his is distressed and disorientated".

For ease of teaching, the scenario should be broken down to reflect each section and the four stage teaching approach must be used.
Stage 1 Instructor demonstrates the skill, at normal speed, without explanation
Stage 2 Instructor demonstrates the skill more slowly, with explanation
Stage 3 Instructor demonstrates the skill while a participant provides explanation
Stage 4 participant demonstrates the skill with explanation

A team approach should be used where the instructor is the team leader calling others for help and co-ordinates others to perform a resuscitation. The participants who are not actively involved could critique, and in turn be critiqued when they are being active

Section A: Initial assessment using an A B C D E approach
The patient is still conscious but critically ill with rapid breathing and bradycardia and hypotension.
The ECG shows bradycardia

Instructor information
The defibrillator is not available during the initial assessment. Here the instructor just speaks aloud how they would approach this patient in terms of their airway, breathing and circulation.

During participant practice (stage 4), the participants are nominated to take the role of team leader. Here instructors may like to alter the scenario between participants to encourage them to think about their clinical decision-making.

- Assess responsiveness
- Airway (e.g. patency, debris) and administer high flow oxygen
- Breathing adequacy (e.g. respiratory rate, expansion, percussion, breath sounds, SpO₂ e.g.)
- Circulatory status (e.g. pulse, blood pressure, capillary refill, urine output, look for evidence of haemorrhage (drains, PR bleeding) – IV fluids, management of bradycardia
- Disability (conscious level) (e.g. AVPU, pupils)
- Exposure

Section B: Correct performance of CPR
Clinical case progression
- The patient becomes unresponsive, and there is NO carotid pulse palpable, but the cardiac monitor still shows a Bradycardia

- Call for help
- Open airway
- Check breathing and circulation
- Call resuscitation team and send for defibrillator
- Deliver effective chest compressions
  - Instructs assistant to commence bag-mask ventilation
  - Correct ratio 30:2
  - Follow algorithm – ie Atropine, and Adrenaline

Section C: Recognition of Asytole and the Non-shockable limb of the algorithm
Clinical case progression
- CPR 30:2 is in progress. The defibrillator arrives – nurse alerts doctor that it is here. (Instructor can use different members of the group to role play). They rhythm has now changed to:-
Instructor information

Emphasise “team leadership” in running the arrest.
Also emphasise going through the list of “reversible cause of cardiac arrest” and that this applies to both Shockable and Non-shockable rhythms

1 participant can take on team leader while 2 participants should perform the chest compression / ventilation. The other participants can help the team leader focus on running the cardiac arrest, but take on other roles such as being the scribe etc. The scenario can be stopped at any point to get comments from the participants who are not running the arrest for “critique”. The different participants should be rotated through all roles during the course of the station.

Instructor Information – points for discussion / further demonstration

1. Early assessment addressing ABC’s with treatment potential role of poisoning in this case (one of the reversible causes)
2. Calling the resuscitation team
3. The role of the precordial thump (in this case –“No role”)
4. Combined assessment of the breathing and circulation
5. Minimise interruption to chest compressions
6. The role of prevention of arrest by early resuscitation
7. Understanding what PEA is and how there can be electrical activity without a pulse
8. Understanding Asystole (and how fine, low amplitude VF is treated as asystole)

Allow participants to ask questions and reflect on the session content before terminating the session with a succinct summary of all the major points covered.

Summary
- Rapid and effective patient assessment
- Provision of effective ventilation and compressions
- Recognition of PEA and Asystole
- Non-Shockable limb of the ALS treatment algorithm
- Theory and practice of safe defibrillation.
Initial Resuscitation/Defibrilation/V-fb/VT Skills Station
(1 instructor, 6 students, approximately 30 minutes)

Key teaching objectives
By the end of this session, the participant will be able to:
• Assess the collapsed patient, using an A B C D E approach
• Perform effective cardiac compressions and ventilations
• Recognise the need for defibrillation
• Perform safe defibrillation

Equipment at station
ResusciAnne Skillreporter mannequin
Drug trolley, IV Fluids, Oxygen (intubation equipment optional)
Rhythm generating device or Power point presentation/computer program
Defibrillator

Instructor Information:
Within this skill station there are three key teaching sections:
a) Initial assessment using an A B C D E approach
b) Correct performance of CPR
c) Recognition of VF and safe defibrillation

The practical skills of using an A B C D E approach, CPR and defibrillation will be taught around the scenario described below.

Clinical case
"Mr Sunil is a 56 year old man with a history of hypertension and Diabetes admitted to the ward with acute severe chest pain. He has been given aspirin, nitroglycerin sublingually and morphine. You are the house officer doing the night shift when you are called to see the patient as he has developed worsening chest pain."

For ease of teaching, the scenario should be broken down to reflect each section and the four stage teaching approach must be used.

Stage 1 Instructor demonstrates the skill, at normal speed, without explanation
Stage 2 Instructor demonstrates the skill more slowly, with explanation
Stage 3 Instructor demonstrates the skill while a participant provides explanation
Stage 4 Participant demonstrates the skill with explanation

A team approach should be used where the instructor is the team leader calling others for help and co-ordinates others to perform a resuscitation. The participants who are not actively involved could critique, and in turn be critiqued when they are being active

Section A: Initial assessment using an A B C D E approach
The patient is still conscious but critically ill with chest pain

Instructor information
The defibrillator is not available during the initial assessment. Here the instructor just speaks aloud how they would approach this patient assign their airway, breathing and circulation.

During participant practice (stage 4), the participants are nominated to take the role of team leader. Here instructors may like to alter the scenario between participants to

NCP Health – SACTRC Resuscitation (Instructor Manual)
encourage them to think about their clinical decision-making.

- Assess responsiveness
- Airway (e.g. patency, debris) and administer high flow oxygen
- Breathing adequacy (e.g. respiratory rate, expansion, percussion, breath sounds, \( \text{SpO}_2 \))
- Circulatory status (e.g. pulse, blood pressure, capillary refill, urine output, look for evidence of haemorrhage (drains, PR bleeding))
- Disability (conscious level) (e.g. AVPU, pupils)
- Exposure

Section B: Correct performance of CPR

*Clinical case progression*
- The patient becomes unresponsive

• Call for help
• Open airway
• Check breathing and circulation
• Call resuscitation team and send for defibrillator
• Deliver effective chest compressions
• Instructs assistant to commence bag-mask ventilation
• Correct ratio 30:2
• Continue until monitor/defibrillator attached

Section C: Recognition of VF and safe defibrillation

*Clinical case progression*
- CPR 30:2 is in progress. The defibrillator arrives. The following rhythm is seen

![ECG Graph]

**Instructor information**

Emphasise “safety” to all participants and be prepared to intervene to stop the scenario if necessary.

2 participants should perform the chest compression / ventilation during stages 1 - 3 so that the other 4 participants can focus on defibrillation. Participants can take over ventilation and chest compression roles during stage 4.

During defibrillation – emphasise the need to minimise delays in chest compression.

• Correctly apply paddles / gel pads (if available), monitoring leads whilst CPR continues
• Select correct energy level (biphasic / monophasic)
• Stop CPR and identity VF on monitor
• Remove free flowing oxygen
• Warn team to stand clear,
• Charge defibrillator, rapid visual check, confirm VF, deliver shock
• Immediately resume CPR without rechecking rhythm
• Indicate that CPR should be continued for 2 minutes prior to checking rhythm

**Instructor Information – points for discussion / further demonstration**
• Calling the resuscitation team
• The role of the precordial thump
• **Combined assessment** of the breathing and circulation
• **Minimise interruption** to chest compressions
• Transthoracic impedance (effect of gel pads, paddle pressure etc)
• Environmental hazards / risks
• **Biphasic / monophasic** waveforms
• ‘Dumping’ the energy from charged paddles
• **Safety** (Participants call “stand back”. Charge paddles on patient or in the defibrillator
Don’t wave paddles in the air, caution with oxygen. No need to remove cardiac monitor leads)

Allow participants to ask questions and reflect on the session content before terminating the session with a succinct summary of all the major points covered.

**Summary**
• Rapid and effective patient assessment
• Provision of effective ventilation and compressions
• Recognition of VF
• Shockable limb of the ALS treatment algorithm
• Theory and practice of safe defibrillation.
Tachycardia/Cardioversion/Bradycardia Skills station

Instructor will review how to read a rhythm strip:
1. Is there any electrical activity?
2. What is the ventricular (QRS) rate?
3. Is the QRS width normal or prolonged?
4. Is atrial activity present? (If so what is it? Normal P waves? Other atrial activity?)
5. How is atrial activity related to ventricular activity?

Tachycardia

Key teaching objectives
• Recognition of broad complex tachycardia and narrow complex tachycardia
• Principles of treatment, indications for chemical/electrical cardioversion
• Mechanics of safe synchronized cardioversion

Show examples of Supraventricular tachycardia, rapid atrial fibrillation, ventricular fibrillation, ventricular tachycardia asking students to describe whether it is narrow/wide complex, regular or irregular
Review indications for synchronized cardioversion
Explain how to set up for synchronized cardioversion, paddle placement.

Stress importance of not shocking during vulnerable ventricular repolarization phase- "T" wave as this could result in the deadly vfib rhythm

Present 2-3 scenarios and choose a participant to go through each scenario:

25 year old woman with no prior medical history presents with palpitations, and lightheadedness. Patient appears anxious.

Vital Signs; BP 115/85 HR 180 RR 20 O2 saturation 98%

ABC approach
Oxygen, IV access, monitor
Monitor shows SVT.
Student should go through algorithm, first recognizing that this patient is stable with a narrow complex regular tachycardia
Then discuss treatment options: vagal maneuvers (ask participants to give examples: carotid sinus massage, valsalva etc)
Vagal maneuvers fail.
Next option: adenosine 6mg IV push (discuss how this medicine has a short half-life on the order of seconds and should be given with a stopcock with a saline flush- so as to facilitate delivery to the heart quickly), may repeat 12mg x2. Another option is verapamil 5mg IV push.
need 12 lead ekg

2nd case:
63 year old man with h/o DM, HTN, 2 days post op from surgery- noted to have tachycardia. pt, c/o some Chest pain and palpitations.
HR 145, BP 80/40 RR22, o2 sat 98%

ABC approach
Oxygen, IV access, monitor
Monitor shows irregularly irregular
Participant should recognize that patient is unstable- needs immediate synchronized
cardioversion
If synchronized cardioversion performed. symptoms resolve, hr 110, bp 110/75
now participant can reassess algorithm: now stable with narrow complex irregular
tachycardia---> atrial fibrillation
treatment options: rate control: digoxin, b-blocker
<48 hours: consider amiodarone.

3rd case:
65 y.o man with h/o multiple myocardial infarction p/w presyncopal symptoms,
palpitations
Hr 170 bp 160/100 rr 20
ABC approach, iv access, o2 monitor
monitor shows ventricular tachycardia
participant recognizes, stable, broad complex, regular tachycardia---> V Tach
Management: amiodarone 300mg IV

Bradycardia
Objectives
Recognise bradycardia and differentiate between the different degrees of heart block
• Understand the principles of treating bradycardia
• Understand the indications for cardiac pacing
• Be aware of the different methods available for cardiac pacing

Choose 3 participants (one as a team leader, the other 2 as assistants) guide them
through the following scenario. prior to starting review algorithm and discuss what is
meant by adverse signs: bp <90, Hr< 40, heart failure, vent arrhythmias, also review risk
factors for asystole)

Clinical Scenario for Bradycardia simulation
You are called to see a 60 year old patient who has developed complete heart block
(CHB) after an acute inferior myocardial infarction.

Clinical Course
• Initially – reduced conscious level.
Airway: clear;
Breathing: RR 14 min-1, fine basal crackles, C: P 40-50 min BP 70/40, CRT 4 sec; D:
verbal response; E: nil
• Unresponsive to atropine.
• Patient collapses – Initial rhythm PEA (CHB 40-50 min-1); continue until relevant
reversible causes excluded
• VF followed by return of spontaneous circulation after 2nd shock; P 80 min-1; BP
90/40; starts to breathe

Interventions – Key treatment points in bold to emphasize
**Initial approach**

Complete heart block  
ABCDE approach  
Oxygen, IV access  
Recognise compromised bradycardia  
Atropine 0.5 mg (further increments up to 3 mg)  
Request transcutaneous pacing  
Cardiac arrest management  
PEA Check patient (breathing / circulation)  
Call resuscitation team / help  
2 min CPR (30:2)  
Airway / ventilation / oxygen  
Attach ECG monitoring (if not already)  
Give first adrenaline 1 mg IV  
Recognise and treat relevant reversible causes  
(drugs / electrolyte disturbances)  
# (further cycle as required)

VF Check monitor / confirm rhythm  
1st shock (150-200 J biphasic or 360 J monophasic)  
2 min CPR (continuous chest compression / ventilation)  
VF Check monitor / confirm rhythm  
Give further adrenaline after 3-5 min*  
Minimise interruptions in CPR  
2nd shock (150-360 J biphasic or 360 J monophasic)  
2 min CPR (continuous chest compression / ventilation)  
NSR Check monitor / confirm rhythm  
Check patient (signs of life / pulse)  
Post resuscitation care Comments
Post Resuscitation Care Skills station

Instructor will review important elements of post resuscitation care:
Indications for Intubation
Post Intubation Management
Ongoing reassessment and monitoring of patient

**Indications for Intubation:**
1) Airway Protection Ask yourself can they talk? Can they swallow and manage secretions?
   What is the level of consciousness?
   GCS <9 indicate “potential” airway compromise due to lack of pharyngeal muscle tone & reflexes

2) Failure to maintain Ventilation/Oxygenation:
   Is the SaO2 <90% on High Flow O2 or PaO2<60 on FiO2>40%?
   Is the PaCO2 >55 if baseline is normal, or >10 increase from baseline
   What is the Respiratory Rate and can this rate be maintained?

3) Expected decline in Clinical Status (Instructor should spend time discussing need for early intubation if you expect that a patient’s status is likely to decline during transport)
   Deterioration/Impending Compromise
   Transport
   Airway protection during procedures (ie. endoscopy)

**Post intubation Management**

1) Confirm intubation (end tidal CO2, calorimeter, Chest x-ray)
2) Secure tube
3) Post Intubation Medications (sedation, paralysis)
   Diazepam 0.2 mg/kg
   Lorazepam 4-6 mg
   Midazolam 0.1 mg/kg bolus, then 0.1 mg/kg/hr 2-5 mg/hr (Drip 50 mg in 250 cc NS, Start at 10-25 cc/hr)
   Propofol .5-1 mg/kg then 25-100 mcg/kg/min, start at 10 cc (100 mg)/hr which correlates with 1 mg/kg/hour
   Vecuronium .1 mg/kg then .03 mg/kg q25-45 min or 1-2 mcg/kg/min
4) Patient position: if possible place head of bed at 30 degrees
5) Nasogastric tube
6) ABG
7) Cuff pressure
8) foley catheter

**Ongoing assessment and Monitoring**

- all patients after resuscitation should have close monitoring of vital signs, and be placed on a continuous cardiac monitor
- foley catheter should be placed and urine output should be monitored
3) approach all changes in vital signs in a systematic fashion as described below:

**Bradycardia**
Assume hypoxia and therefore tube displacement until proven otherwise

**Desaturation (mnemonic DOPE)**

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Appendix C3
Displaced tube

Obstruction-pass suction catheter through tube

Pneumothorax

Equipment failure-take off vent and bag patient

if all of the above have been evaluated, consider shunt physiology

Hypotension
  · Pneumothorax
  · Decreased Venous Return from positive pressure ventilation, disconnect from vent for 30-60 seconds and observe for increased Blood Pressure and decreased heart rate. Consider reducing PEEP and decreasing Tidal Volume. Auto-PEEP in obstructive airway disease.
  · Excessive hyperventilation-
  · Induction Agents-diagnosis of exclusion, give fluid bolus
  · Cardiogenic-fluid bolus

Present scenarios and choose a participant to go through each scenario:

Mr. Chandradasa, a 62 old man, with a history of Hypertension, Diabetes presented with CHF exacerbation subsequently developed PEA underwent resuscitation had return of spontaneous circulation- and now has been intubated. What steps are you going to take to manage this patient post intubation? Student should discuss post intubation care as outlined above (securing tube, sedation, nasogastric tube) as well as ongoing assessment and monitoring of the patient.

Now present another student with a change in the hemodynamics of the patient-

“A nurse comes to you and says, Doctor, Mr. Chandradasa BP is 70/40 and his Heart rate is 130” Have the student go through the differential of Hypotension (as discussed above) and discuss what they may do to correct the problem.

In this case the patient could be off the vent and receiving bag-mask ventilation but the ventilation is excessive. Instructor can simulate a Nurse who is bagging the patient excessively and see if the student notices and instructs the nurse to decrease rate of ventilation in which case the hemodynamics improve.

Now present another student with a desaturation in Mr. Chandradasa. Help them go through the differential of desaturation (DOPE mnemonic) and describe what they would do to rule out items in the differential. (i.e recheck tube placement, in line suction to rule out obstruction, repeat physical exam and/or CXR to look for pneumothorax, and taking the patient off the vent and performing bag mask ventilation to evaluate for equipment failure) Instructor should emphasize to students the importance of taking patient off ventilator in this situation as well as during any need for repeat resuscitation.
Scenario 2 – Patient Transfer

This scenario is to make sure that doctors do the basics before transferring patients to another Hospital

1) Organise the transfer with receiving hospital – e.g. Consultant or ICU SHO/MO in General or Teaching hospital. Important to communicate
   a. Name, Age, Sex
   b. Condition of the patient – Especially Airway Status – (e.g. intubated or not, Bag mask ventilated or not, level of oxygen delivery-prongs mask etc, and GCS)
   c. Reason for Transfer (e.g. Intubated or no facilities, critical illness)
   d. Plan for transfer (e.g. With or without medical staff, bag mask ventilated or mechanical ventilation, Fluids running, Catheter or other tubes insitu)
   e. Expected duration of trip and time of arrival in their institution

2) Reasses and monitoring of patient prior to transfer

3) IV Access and start fluids if necessary
   a. Enough fluids if necessary & Long Journey and

4) Oxygen Delivery Plan
   a. Is Nasal prongs adequate?
   b. If via mask – is oxygen supply adequate?
   c. Do they need to be intubated?

5) Medical staffing Plan
   a. Is Solo transfer adequate
   b. If no resources for accompanying patient what precautions have been taken
      i. Position patient on side? Airway adjunct?

6) Position of Patient
   a. Supine in intubated or well patient
   b. On side if airway threatened and not intubated

7) DOES THE PATIENT NEED TO BE INTUBATED PRIOR TO TRANSFER
   a. See indication for intubation above
   b. If in doubt Call the person at the receiving hospital and Ask for their advice stating:
      i. Patients age & sex, co-morbidites
      ii. Airway status (secretions or not), respiratory rate, Saturations, Chest movements, and GCS
8) Have you written a detailed transfer note with all the vital signs at the time of transfer?
   
a. Transfer notes are a good way of remembering vital information

Instill in the student that the most important reversible causes of cardio respiratory arrest are HYPOXIA and HYPOVOLAEMIA - this frequently occurs after interhospital transfer which are both preventable by good care and forward planning, and taking precaution

A good strategy is “PLAN for the WORST situation, and then HOPE for the BEST”

Mr Tikirbanda is a 58 year old farmer who presented with sudden onset left sided paralysis. He also has slurred speech and he is only responsive to verbal stimulation. His pulse is 60, BP 120/80 and RR 24, and saturations are unavailable.

You suspect a stroke and want to organize a transfer to the General hospital which is 1 hour away.

Whilst doing this the nurse tells you that Mr Tikirbanda’s breathing pattern has changed, now more rapid and there is some drooling. He does not respond to your voice, but is easily stimulated by a sternal rub, and localized the pain, and also give you a groan. His eyes are now closed but open with the pain also

Get participant to act out the scenario:

Instructor pretends to be the Doctor on the Receiving station and has a conversation with the MO in the language of their choice.

Participant is led through the phone call, and has to demonstrate management of ABCD, and a plan for transfer.

Also go through to the stage of transfer onto a trolley an position of the Mannequin (Patient)
Patient transfer should occur with at least 3 people with one for the head
Patient should be managed on the side
### Trainer Competence Assessment - overall

This checklist is to be carried out by Consultant Instructors to ensure that the Trainers demonstrate adequate skills in teaching resuscitation. Theses are based on “General observations” of Trainer particularly in the first part of the workshop - Skills Station Training, and “Objective assessment” in the Teaching of a scenario based skills station in the Peripheral Hospital Training Module.

<table>
<thead>
<tr>
<th>Consultant Instructor Name:</th>
<th>Date:</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trainer being Assessed:</td>
<td>Setting of</td>
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<tr>
<td>observation: General Observations / Objective Assessment</td>
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</table>

<table>
<thead>
<tr>
<th>Competency</th>
<th>Successful (comments)</th>
<th>Needs Remediation</th>
<th>Plan / advice given</th>
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</thead>
<tbody>
<tr>
<td><strong>Communication</strong> - Communicates ideas and concepts clearly, maintains positive rapport with learners. uses appropriate nonverbal communication skills, uses appropriate terminology for audience</td>
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<tr>
<td><strong>Manage Technology</strong> – Uses technology associated with teaching (such as manikins, rhythm)</td>
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</table>

NCP Health – SACTRC Resuscitation (Instructor Manual)
<table>
<thead>
<tr>
<th>generators and other teaching aids) and uses audio/video technology effectively</th>
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<tbody>
<tr>
<td><strong>Stimulation and Motivation</strong> – Provides a stimulating learning environment that maintains the interest of students. Encourages interaction from participants.</td>
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<tr>
<td><strong>DVD presentation</strong> – able to make sure that participants understand the main points of the DVD presentations</td>
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<tr>
<td><strong>Questioning and Feedback</strong> - Interacts with participants with appropriate questions to evaluate their understanding and thinking process. Gives feedback appropriately, particularly when skill is not being learned</td>
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</table>
**Lecture – Feedback Form**

**Name of the lecturer - ………………………………Name of the Evaluator-……………..**

**Topic - ……………………………………Time starting -----------, End …**

**Set and environment**

<table>
<thead>
<tr>
<th>Did not achieved</th>
<th>Achieved</th>
<th>Good</th>
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<tbody>
<tr>
<td>1. Check and adjust lay out</td>
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<tr>
<td>2. Check equipments</td>
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<tr>
<td>3. Welcome and introduce self</td>
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<tr>
<td>4. Sets the mood</td>
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<tr>
<td>5. Establishes the usefulness</td>
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<tr>
<td>6. States learning objectives</td>
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<tr>
<td>7. Overall performance of SET</td>
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**Dialogue**

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<tr>
<th>Did not achieved</th>
<th>Achieved</th>
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<tbody>
<tr>
<td>1. Presents material in a clear, logical sequence</td>
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<td>2. Uses visual aids appropriately</td>
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<td>3. Ensure voice projection</td>
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<td>4. Address/involves the audience</td>
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<td>5. Uses the eye contact appropriately</td>
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<td>6. Demonstrates enthusiasm</td>
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<td>7. Uses humour appropriately</td>
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<td>8. Uses personal/ audience experience</td>
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<td>9. Asks appropriate questions</td>
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<td>10. Responds positively to answers</td>
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<tr>
<td>11. Keeps to time</td>
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<tr>
<td>12. Attitude/behavior encourages learning and interactions</td>
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**Closure**

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<tr>
<th>Did not achieved</th>
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<tbody>
<tr>
<td>1. Invites and answer questions</td>
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<tr>
<td>2. Returns to learning objectives and summarizes</td>
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<td>3. Terminate the session</td>
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<td>4. Overall performance of closure</td>
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**General Comments (what do you feel if you are a trainee )**

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Appendix C3
Skill Teaching – Feedback Form

Name of the Teacher - ……………………….. Name of the Evaluator - ………………

Topic - ……………………………………………….. Time starting - ……………….., End …

Set and environment

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<th>Did not achieved</th>
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<td>2. Check equipments</td>
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<td>3. Ensure all the candidates can see</td>
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<td>7. Clarifies the role of learners and teacher</td>
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<td>8. States learning objectives</td>
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Dialogue

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<tr>
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<tbody>
<tr>
<td>1. Describe 4 stage method of teaching skills</td>
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<td>2. Demonstrate the skill without commentary</td>
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<td>3. Demonstrate the skill with commentary</td>
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<td>4. Demonstrate the skill with candidate commentary</td>
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<td>5. Candidate demonstrate with appropriate commentary</td>
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<td>6. Keep check on safety</td>
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<td>7. Relate skill to the other aspects of the course</td>
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<td>8. Enables practice if time allows</td>
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General Comments


### Scenario Assessment – Feedback Form

**Name of the Teacher** - …………………………….. **Name of the Evaluator**

**Topic** - …………………………………………. **Time starting** ---------, **End** …

#### Set and environment

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<tr>
<td>3. Check whether assistant is familiar with scenario and his/her role</td>
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<tbody>
<tr>
<td>1. Brief candidate</td>
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<td>2. Allows questions</td>
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<td>3. Checks understanding</td>
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<td>4. interact constructively</td>
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<td>5. Keeps check on safety</td>
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<tr>
<td>7. Attitudes and behavior encourage learning and interaction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Overall performance of dialogue</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### Closure

<table>
<thead>
<tr>
<th>Did not achieved</th>
<th>Achieved</th>
<th>Good</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Asks the candidates to Waite out side confirm results with the colleague</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. Reaches a correct decision</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. Inform the candidate of the satisfactory result</td>
<td></td>
<td></td>
</tr>
<tr>
<td>OR</td>
<td></td>
<td></td>
</tr>
<tr>
<td>4. Counsel the candidate of the need for reset</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Terminate the session</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. Overall performance of closure</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

#### General Comments

---

NCP Health – SACTRC Resuscitation (Instructor Manual)  
Appendix C3
### Peripheral Hospital training session: course components

<table>
<thead>
<tr>
<th>Component</th>
<th>Topic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>DVD lectures</strong></td>
<td>Introduction: Resuscitation Training Module overview</td>
</tr>
<tr>
<td></td>
<td>NEJM (online video) – “How to intubate”</td>
</tr>
<tr>
<td></td>
<td>ALS Treatment algorithm</td>
</tr>
<tr>
<td></td>
<td>Tachycardia algorithm &amp; cardioversion</td>
</tr>
<tr>
<td></td>
<td>Bradycardia algorithm &amp; cardiac pacing</td>
</tr>
<tr>
<td><strong>Skills stations</strong></td>
<td>Basic Airway management</td>
</tr>
<tr>
<td></td>
<td>Advanced Airway management</td>
</tr>
<tr>
<td><strong>Scenario Stations</strong></td>
<td>Initial Resuscitation – PEA/Asystole</td>
</tr>
<tr>
<td></td>
<td>Resuscitation/Defibrillation – VF/VT</td>
</tr>
<tr>
<td></td>
<td>Tachycardia/ Bradycardia algorithms - cardioversion &amp; pacing</td>
</tr>
<tr>
<td></td>
<td>Post resuscitation care</td>
</tr>
</tbody>
</table>
## Peripheral Hospital Training Session: course agenda

<table>
<thead>
<tr>
<th>Time</th>
<th>Program for Training Session</th>
</tr>
</thead>
<tbody>
<tr>
<td>8:00 - 9:30am</td>
<td><strong>Pre-assessment (MCQ and Scenarios)</strong></td>
</tr>
<tr>
<td>9:30 - 10:15am</td>
<td><strong>Lectures on Airway management</strong></td>
</tr>
<tr>
<td>10:15 - 10:45am</td>
<td><strong>Morning Tea</strong></td>
</tr>
<tr>
<td>10:45 - 10:45am</td>
<td><strong>Practical sessions on Airway management</strong></td>
</tr>
<tr>
<td></td>
<td>(Skills station 1 and 2)</td>
</tr>
<tr>
<td>11:45 - 12:20pm</td>
<td><strong>Lectures on management of cardiac arrest &amp; using the</strong></td>
</tr>
<tr>
<td></td>
<td>current algorithms for arrhythmias</td>
</tr>
<tr>
<td>12:20 - 13:00pm</td>
<td><strong>Lunch</strong></td>
</tr>
<tr>
<td>13:00 - 15:00pm</td>
<td><strong>Practical sessions:</strong></td>
</tr>
<tr>
<td></td>
<td>Managing PEA/Asystole (skills station 3)</td>
</tr>
<tr>
<td></td>
<td>VT/VF/cardiac arrest (skills station 4)</td>
</tr>
<tr>
<td></td>
<td>Tachycardia and Bradycardia (skills station 5)</td>
</tr>
<tr>
<td></td>
<td>Post resuscitation care and Transport (Skills station 6)</td>
</tr>
<tr>
<td>15:00 –15:15pm</td>
<td><strong>Afternoon Tea</strong></td>
</tr>
<tr>
<td>15:15-16:30pm</td>
<td><strong>Post-Assessment (MCQ and Scenarios)</strong></td>
</tr>
<tr>
<td>16:30-16:45pm</td>
<td><strong>Closing comments</strong></td>
</tr>
<tr>
<td></td>
<td>(Fill in feedback forms)</td>
</tr>
</tbody>
</table>

### Appendix C5  Supporting material for trainers & checklists of performance

The resource manual, the DVDs and the “Instructor Manual” have been given to you to be used as help before during and after the training sessions. Please use the **Instructor Manual** and **Skills Checklist** to guide you during the training sessions.

### Objectives of the Training module

Use the DVD lectures and Skills stations to teach principles outlined in manual:-

- **Recognition** of a critically ill patient – and calling for help
- **Use of a system** for assessing a critically ill patient - **ABCDE**
- **Importance of Basic** life saving maneuvers
• **Update of Advanced life support algorithms** for the arrested patient
  o The Nov 2005 guidelines (ILCOR)

• **“Communication” in Resuscitation**
  o Calling for senior support early
  o Communication and leadership during an arrest
  o Post arrest communication with family and other staff

• **Post Resuscitation care & Inter-hospital Transfer**

• **Practical “Hands on” training**
  o Simulation in real life scenarios using CPR mannequins
  o Assessment with constructive feedback

**4 stage teaching approach for skills stations**

Stage 1 – Instructor demonstrates the skill, at normal speed, without explanation
Stage 2 – Instructor demonstrates the skill more slowly, with explanation
Stage 3 – Instructor demonstrates the skill while a participant provides explanation
Stage 4 – Participant demonstrates the skill with explanation

Example of above approach is included in the Trainer’s DVD
Resuscitation Pack for participants and participant hospitals

1) A4 Colour laminated Algorithm card and Bradycardia/Tachycardia algorithm card (for resuscitation trolley or bag)
2) Wall poster of Advanced life support Algorithm
3) Training DVD

Additional Resource material

• For Hospitals & Trainers
  – Resuscitation Posters
  – Resuscitation Training DVD
  – Resuscitation Trolley Card

• For all Participants
  – Resource manual
  – Wallet card
  – Resuscitation Folder
  – Printed Materials
Checklist for Trainers

DVD lectures
Lecture topics:
  - Introduction
  - Airway management
  - Intubation
  - ALS algorithm
  - Tachycardia/ bradycardia
  - Post-resuscitation care

Skills station 1 – Airway management
Airway Opening maneuvers and Adjuncts:
  - Head Tilt
  - Chin Lift
  - Jaw Thrust
  - Yankers suction
  - Inserts correctly sized Oropharyngeal airway
  - Inserts correctly sized Nasopharyngeal airway

Bag mask Ventilation:-
  - Assembly of self inflating Ambu bag and mask
  - Correct positioning and seal of facemask
  - Effective ventilations (causing chest to rise)
  - Rate of ventilation 8-10/mins (not >12)
  - Ventilating intubated patient (again rate 8-10/mins)
  - Single vs. two person technique
  - Confirmation of ventilation
Skills station 2 – Advanced airway management

Preparation and Equipment Check
Assigns roles
Ideal equipment and monitoring (PCMALES)
Check laryngoscope light is working
Check ET tube – inflates cuff with syringe
Pre oxygenates (states they would only bag patient if no spontaneous breathing – understands that if patient was breathing themselves bagging may worsen situation)
Correct positioning (“sniffing the morning air”)

Intubation:
Suctions first
Holds laryngoscope in properly (in Left hand)
If takes longer than 30 seconds – should abort and go back to bagging before second attempt
Intubates (states whether they saw the cords or not for the team to hear)
Checks ETT position (breath sounds/ gastric bubbling/ capnography/ etc)
Instructs person doing Cricoid pressures to “Start cricoid now” (prior to intubating) “remove cricoid” at appropriate times
Applies Cricoid pressure appropriately (when assisting intubation)

Skills station 3 - PEA/ Asystole

Initial approach:
Called for help/ resus team
Assesses responsiveness
Uses ABCDE approach
High flow oxygen
Initiates CPR when recognizes patient unresponsive

CPR:
Correct hand position (centre of chest)
Straight arms
Compression depth 4-5cm, approx 1/3 of chest
Allows complete relaxation
Allows same time for compression as for relaxation
Starts with chest compressions rather than giving breaths
Rate 100 per minute
Ratio 30:2
Gives 2 breaths after chest compression (each taking 1 second for breath)
Checks for pulse and rhythm after 2mins of CPR (5 cycles)
Minimises interruptions to compressions
If patient comes back to life – states they would put in recovery position

PEA/ asystole:
Recognition of PEA
Recognition of asystole
Recognises that defibrillation is not indicated
Skills station 4 – VF/VT/Defibrillation

Initial approach:

- Called for help/ resus team
- Assesses responsiveness
- Uses ABCDE approach
- High flow oxygen
- Initiates CPR when recognizes patient unresponsive

CPR:

- Correct hand position (centre of chest)
- Straight arms
- Compression depth 4-5cm, approx 1/3 of chest
- Allows complete relaxation
- Allows same time for compression as for relaxation
- Starts with chest compressions rather than giving breaths
- Rate 100 per minute
- Ratio 30:2
- Gives 2 breaths after chest compression (each taking 1 second for breath)
- Checks for pulse and rhythm after 2mins of CPR (5 cycles)
- Minimises interruptions to compressions
- If patient comes back to life – states they would put in recovery position

Defibrillation

- Recognises pulseless VT/ VF (when CPR stopped)
- Recognises indication for defibrillation and minimizes delay
- Correctly applies paddles/ gel pads/ monitoring
- Selects correct energy level (biphasic/ monophasic)
- Checks and removes hazards (e.g. free-flowing oxygen)
- Warns team to stand clear
- Charges defibrillator, rapid visual check, confirms VT/VF, delivers shock
- Immediately resumes CPR for 2 minutes before rechecking rhythm
Skills station 5 – Bradycardia / Tachycardia/ Cardioversion

Initial approach:
- Called for help/ resus team
- Assesses responsiveness
- Uses ABCDE approach
- High flow oxygen
- Initiates CPR when recognizes patient unresponsive

Bradycardia:
- Recognition of adverse signs of bradycardia
- Recognition of rhythms that have risks for asystole
- Indication for transcutaneous pacing
- Indication for drugs (e.g. atropine, adrenaline)

Tachycardias
- Recognition of an “unstable” tachycardia
- Indications for, and how to perform synchronized cardioversion
- Distinguishes between broad and narrow complex tachycardias
- Distinguishes between regular and irregular tachycardias
- Understands role of vagal maneuvers and drugs
Skills station 6 – Post-resuscitation care and transport

Post-resuscitation care:
  - Indications for intubation
  - Confirms ETT position and secures ETT
  - Post-intubation medications
  - Supportive care and monitoring (NGT, IDC, cuff pressure, ABG)
  - Management of bradycardia, desaturation (DOPE), hypovolemia

Patient transfer:
  - Organises transfer with receiving hospital – name, age, sex, condition of patient, reason for transfer, ETA
  - Consider need for procedures (e.g. intubation) prior to transfer
  - Ongoing assessment and monitoring
  - IV fluids
  - Oxygen delivery
  - Medical staffing plan
  - Patient positioning
  - Documentation

Assessments

Pre-course MCQs
Post-course MCQs
Post-course scenario

Appendix C6  MCQ test used at assessments

For all answers choose the single best choice

1. Ten minutes after an 85-year-old woman collapses, paramedics arrive and start CPR for the first time. The monitor shows fine (low-amplitude) VF. Which of the following actions should they take next?

a. Perform at least 5 minutes of vigorous CPR before attempting defibrillation
b. Insert an endotracheal tube, administer 2 to 2.5 mg adrenalin in 10 mL NS through the tube and then defibrillate
c. Deliver up to 3 precordial thumps while observing the patient’s response on the monitor
d. Deliver about 2 minutes or 5 cycles of CPR, and deliver a 360-J monophasic or equivalent biphasic shock

2. Which of the following facts about identification of Ventricular fibrillation is true?

a. A peripheral pulse that is both weak and irregular indicates VF  
b. A sudden drop in blood pressure indicates VF  
c. Artifact signals displayed on the monitor can look like VF  
d. Turning the signal amplitude (“gain”) to zero can enhance the VF signal

3. A 60-year-old man (weight = 50 kg) with recurrent VF has converted from VF again to a wide-complex non-perfusing rhythm after administration of Adrenalin 1 mg IV and a 3rd shock. Which of the following drug regimens is most appropriate to give next?

a. Amiodarone 300 mg IV push  
b. Lidocaine 150 mg IV push  
c. Magnesium 3 g IV push, diluted in 10 mL of D5W  
d. Procainamide 20 mg/min, up to a maximum dose of 17 mg/kg

4. A cardiac arrest patient arrives in the ED with PEA at 30 bpm. CPR continues, proper tube placement is confirmed, and IV access is established. Which of the following medications is most appropriate to give next?

a. Calcium chloride 5 mL of 10% solution IV  
b. Adrenalin 1 mg IV  
c. Synchronized cardioversion at 200 J  
d. Sodium bicarbonate 1 mEq/kg IV

5. Which of the following causes of PEA is most likely to respond to immediate treatment?

a. Massive pulmonary embolism  
b. Hypovolemia  
c. Massive acute myocardial infarction  
d. Myocardial rupture
6. Which of the following drug-dose combinations is recommended as the initial medication to give a patient in asystole?

a. Adrenalin 3 mg IV  
b. Atropine 3 mg IV  
c. Adrenalin 1 mg IV  
d. Atropine 0.5 mg IV

7. Which of the following causes of out-of-hospital asystole is most likely to respond to treatment?

a. Prolonged cardiac arrest  
b. Prolonged submersion in warm water  
c. Drug overdose  
d. Blunt multisystem trauma

8. Effective bag-mask ventilations are present in a patient in cardiac arrest. Now, 2 minutes after adrenalin 1 mg IV is given, PEA continues at 30 bpm. Which of the following actions should be done next?

a. Administer atropine 3 mg IV  
b. Initiate transcutaneous pacing at a rate of 60 bpm  
c. Start a dopamine IV infusion at 15 to 20 µg/kg per minute  
d. Give adrenalin (1 mL of 1:10 000 solution) IV bolus

9. Which of the following actions helps deliver maximum current during defibrillation?

a. Place alcohol pads between the paddles and skin  
b. Reduce the pressure used to push down on the defibrillator paddles  
c. Apply conductive paste to the paddles  
d. Decrease shock energy after the 2nd shock

10. Which of the following actions is NOT performed when you “clear” a patient just before defibrillator discharge?

a. Check the person managing the airway: body not touching bag mask or tracheal tube, oxygen not flowing directly onto chest  
b. Check yourself: hands correctly placed on paddles, body not touching patient or bed  
c. Check monitor leads: leads disconnected to prevent shock damage to monitor  
d. Check others: no one touching patient, bed, or equipment connected to patient
11. You prepare to cardiovert an unstable 48-year-old woman with tachycardia. The monitor/defibrillator is in “synchronization” mode. The patient suddenly becomes unresponsive and pulseless as the rhythm changes to an irregular, chaotic, VF-like pattern. You charge to 200 J and press the SHOCK button, but the defibrillator fails to deliver a shock. Why?

a. The defibrillator/monitor battery failed  
b. The “sync” switch failed  
c. You cannot shock VF in “sync” mode  
d. A monitor lead has lost contact, producing the “pseudo-VF” rhythm

12. A woman with a history of narrow-complex PSVT arrives in the ED. She is alert and oriented but pale. HR is 165 bpm, and the ECG documents SVT. BP is 105/70 mm Hg. Supplemental oxygen is provided, and IV access has been established. Which of the following drug-dose combinations is the most appropriate initial treatment?

a. Adenosine 6 mg rapid IV push  
b. Adrenalin 1 mg IV push  
c. Synchronized cardioversion with 25 to 50 J  
d. Atropine 1 mg IV push

13. A 34-year-old woman with a history of mitral valve prolapse presents to the ED complaining of palpitations. Her vital signs are as follows: HR = 165 bpm, resp = 14 per minute, BP = 118/92 mm Hg, and O2 sat = 98%. Her lungs sound clear, and she reports no shortness of breath or dyspnea on exertion. The ECG and monitor display a narrow-complex, regular tachycardia. Which of the following terms best describes her condition?

a. Stable tachycardia  
b. Unstable tachycardia  
c. Heart rate appropriate for clinical condition  
d. Tachycardia secondary to poor cardiovascular function

14. A 75-year-old man presents to the ED with a 1-week history of lightheadedness, palpitations, and mild exercise intolerance. The initial 12-lead ECG displays atrial fibrillation, which continues to show on the monitor at an irregular HR of 120 to 150 bpm and a BP of 70/40 mm Hg. Which of the following therapies is the most appropriate next intervention?

a. Call a cardiologist for assistance  
b. Lidocaine 1 to 1.5 mg/kg IV bolus  
c. Amiodarone 300 mg IV bolus  
d. Immediate cardioversion
15. A 25-year-old woman presents to the ED and says she is having another episode of PSVT. Her medical history includes an electrophysiologic stimulation study (EPS) that confirmed a reentry tachycardia, no Wolff-Parkinson-White syndrome, and no preexcitation. HR is 180 bpm. The patient reports palpitations and mild shortness of breath. Vagal maneuvers with carotid sinus massage have no effect on HR or rhythm. Which of the following is the most appropriate next intervention?

a. DC cardioversion  
b. IV diltiazem  
c. IV propranolol  
d. IV adenosine

16. Endotracheal intubation has just been attempted for a patient in respiratory arrest. During bag-mask ventilation you hear stomach gurgling over the epigastrium but no breath sounds, and oxygen saturation (per pulse oximetry) stays very low. Which of the following is the most likely explanation for these findings?

a. Intubation of the esophagus  
b. Intubation of the left main bronchus  
c. Intubation of the right main bronchus  
d. Bilateral tension pneumothorax

17. Which of the following statements correctly describes the ventilations that should be provided after endotracheal tube insertion, cuff inflation, and verification of tube position?

a. Deliver 8 to 10 ventilations per minute with no pauses for chest compressions  
b. Deliver ventilations as rapidly as possible as long as visible chest rise occurs with each breath  
c. Deliver ventilations with a tidal volume of 3 to 5 mL/kg  
d. Deliver ventilations using room air until COPD is ruled out

18. When intubating during an arrest which of the following is INCORRECT?

a. Only intubate if you have been properly trained and have adequate experience  
b. Stop chest compressions while intubation is being carried out  
c. Pre-oxygenation with high concentration oxygen should always be performed when possible  
d. After the patient is intubated the ratio of chest compression to ventilations is 30:2

19. Regarding bag-mask ventilation which of the following is correct?

a. Ambu bags are universal in size so that the same one can be used effectively for all patients  
b. The rate of ventilation should be approximately 10 ventilations per min in an arrest situation, but this rate should be increased if the patient is hypoxic  
c. Effective ventilation cannot be achieved unless there is a good seal between the face mask and the patient’s face  
d. When oxygenating a patient prior to intubation one should actively ventilate the patient, even if the patient is breathing himself  
e. If you are performing bag mask ventilation, you do not need to have an airway adjunct such as an oropharangeal airway in place
20. Which of these statements about IV administration of medications during attempted resuscitation is true?

a. Give adrenalin via the intracardiac route if IV access is not obtained within 3 minutes
b. Follow IV medications through peripheral veins with a fluid bolus
c. Do not follow IV medications through central veins with a fluid bolus
d. Run normal saline mixed with sodium bicarbonate (100 mEq/L) during continuing CPR

21. A patient with a heart rate of 40 bpm is complaining of chest pain and is confused. After oxygen, what is the first drug you should administer to this patient while a transcutaneous pacer is brought to the room?

a. Atropine 0.5 mg
b. Adrenalin 1 mg IV push
c. Isoproterenol infusion 2 to 10 µg/min
d. Adenosine 6 mg rapid IV push

22. Which of the following rhythms is a proper indication for transcutaneous cardiac pacing?

a. Sinus bradycardia with no symptoms
b. First degree AV block
c. Complete heart block with pulmonary edema
d. Asystole that follows 6 or more defibrillation shocks

23. A patient with an HR of 30 to 40 bpm complains of dizziness, cool and clammy extremities, and dyspnea. He is in third-degree AV block. All treatment modalities are present. What would you do first?

a. give atropine 1 mg IV
b. give adrenalin 1 mg IV push
c. start dopamine infusion 2 to 10 µg/min
d. begin immediate transcutaneous pacing, sedate if possible

24. In a conscious patient all of the following are signs of a patient being critically ill EXCEPT for:

a. A sudden fall in GCS < 2
b. HR <40 or >140
c. RR <5 RR>36
d. Fever of > T 38.5
e. Systolic BP <90

25. Regarding “Circulation” in an arrest situation which is correct?

a. Patients are unlikely to need IV fluids in an arrest
b. CPR and fluid resuscitation are unlikely to save the life of someone with Ventricular Fibrillation until a DC shock is given
c. The best place to put an IV cannula in arrest is over the radial side of the wrist
d. Even if no central pulses are felt, it is still useful to check blood pressure during resuscitation of a cardiac arrest
e. After ROSC (return of spontaneous circulation) with a pulse felt peripherally, there is never any reason to check the blood pressure

Appendix C6
Rhythm Recognition
Identify the Following Rhythms (write the single best choice)

26.

![Image of ECG tracing]

a. Normal Sinus Rhythm
b. Sinus Tachycardia
c. Sinus Bradycardia
d. Atrial Fibrillation
e. Atrial Flutter
f. Reentry Supraventricular Tachycardia
g. Monomorphic Ventricular Tachycardia
h. Polymorphic Ventricular Tachycardia
i. Ventricular Fibrillation
j. Second-Degree Atrioventricular Block
h. Third-Degree Atrioventricular Block

27.

![Image of ECG tracing]

a. Normal Sinus Rhythm
b. Sinus Tachycardia
c. Sinus Bradycardia
d. Atrial Fibrillation
e. Atrial Flutter
f. Reentry Supraventricular Tachycardia
g. Monomorphic Ventricular Tachycardia
h. Polymorphic Ventricular Tachycardia
i. Ventricular Fibrillation
j. Second-Degree Atrioventricular Block
h. Third-Degree Atrioventricular Block
28. a. Normal Sinus Rhythm
b. Sinus Tachycardia
c. Sinus Bradycardia
d. Atrial Fibrillation
e. Atrial Flutter
f. Reentry Supraventricular Tachycardia
g. Monomorphic Ventricular Tachycardia
h. Polymorphic Ventricular Tachycardia
i. Ventricular Fibrillation
j. Second-Degree Atrioventricular Block
h. Third-Degree Atrioventricular Block

29. a. Normal Sinus Rhythm
b. Sinus Tachycardia
c. Sinus Bradycardia
d. Atrial Fibrillation
e. Atrial Flutter
f. Reentry Supraventricular Tachycardia
g. Monomorphic Ventricular Tachycardia
h. Polymorphic Ventricular Tachycardia
i. Ventricular Fibrillation
j. Second-Degree Atrioventricular Block
h. Third-Degree Atrioventricular Block
30.

a. Normal Sinus Rhythm
b. Sinus Tachycardia
c. Sinus Bradycardia
d. Atrial Fibrillation
e. Atrial Flutter
f. Reentry Supraventricular Tachycardia
g. Monomorphic Ventricular Tachycardia
h. Polymorphic Ventricular Tachycardia
i. Ventricular Fibrillation
j. Second-Degree Atrioventricular Block
h. Third-Degree Atrioventricular Block
Appendix C6

Answers

1. d
2. c
3. a
4. b
5. b
6. c
7. c
8. a
9. c
10. c
11. c
12. a
13. a
14. d
15. d
16. a
17. a
18. d
19. c
20. b
21. a
22. c
23. d
24. d
25. b
26. g
27. h
28. e
29. i
30. j

Appendix C7  Script for resuscitation scenario & picture of assessment room

Scenario

“When you go behind the screen you will see a mannequin in a hospital bed– we want you to imagine this is a 50 year old man who has collapsed and is unresponsive. You see this patient when you are walking to your clinic.

When I say start I want you to do as you would in real life. During the scenario I will answer any questions you have about the patient’s condition, which you cannot work out for yourself and that you “look for”. But I do not want you to talk to me - You are alone. The only equipment you have is what you see around you.”

[read scenario twice. Press record on the video camera]

“Just one moment as I announce your ID for the video”
[say PHP No…. Scenario 1]

“Do what you would do in real life – continue doing so until I tell you to stop. Start NOW”
Appendix C7

[start stopwatch, play on computer also]

End of Scenario

Assessor steps in and says “And help arrives!!”

Evaluator instructions (scripted responses):

<table>
<thead>
<tr>
<th>Action</th>
<th>Response</th>
</tr>
</thead>
<tbody>
<tr>
<td>Checks for pulse</td>
<td>Say “there is no pulse”</td>
</tr>
<tr>
<td>Checks for breathing</td>
<td>There is no chest movement</td>
</tr>
<tr>
<td>If participant starts to give expired air ventilation or attempts to give expired air ventilation</td>
<td>“if you want to give ventilations, please use the Ambu bag provided”</td>
</tr>
<tr>
<td>If patient asks for details of the patient, e.g. “what is the patient's name” or “how old is he”</td>
<td>“You do not know his name, he is a 50 year old male who has collapsed”</td>
</tr>
<tr>
<td>I would like a “……….“ e.g. Monitor</td>
<td>The only equipment you have immediately available is what you see around you. You are alone. Do as you would in real life</td>
</tr>
<tr>
<td>I would like some help</td>
<td>Help is on its way</td>
</tr>
</tbody>
</table>

After 1 min of the participant performing single rescuer CPR the evaluator stops them and thanks them – immediately go on to scenario 2.
**Time prompts**

<table>
<thead>
<tr>
<th>Time</th>
<th>Prompt</th>
</tr>
</thead>
<tbody>
<tr>
<td>IF no CPR started by 1 min</td>
<td>“I want you to start cardiopulmonary resuscitation on this patient please”</td>
</tr>
<tr>
<td>After 1 min of initiation of compressions</td>
<td>Say “And help arrives”. Please come out of the room” [ie. step behind the screen]</td>
</tr>
</tbody>
</table>

**Setting:**

RA Skill trainer Mannequin in standard hospital bed.
No pulse, No breathing.
Ambu bag and mask is on the bedside table next to patient (not on bed)

Screen covering mannequin from starting point of participant – all scenario briefing to be given out of the line of vision of mannequin, behind the screen.

Assessor stands on the *other side* of the screen to the participant (out of sight but within earshot) – Assessor makes limited scripted responses as appropriate.

*Figure.* Example of a peripheral hospital Assessment station setup

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**Assessments**

- 25 Question MCQ (45mins)
- Scenarios Assessments (10mins)
Equipment

Essential

1) CPR recording Mannequin (see below)
2) Hospital Bed & Mattress x1
3) Ambu bags x2
4) Laryngoscope and x2 blades (Mac 3 and Mac4
5) ET tube with introducer
6) Oxygen mask and tubing
7) Poster with ALS algorithm x2

Non essential (but valuable for simulation)

8) Drip stand
9) Hospital bedside table
10) Old saturation monitor
11) Old defibrillation unit (Better to have a functional defibrillator but this might be economically challenging)

Mannequin requirements

- Full body (for realism)
- Continuous real time feed back for ventilation and compression (LED lights)
- Skill reporting (ability to generate a print-out of the performance, or store this data on a computer.)
- A head piece that allows airway opening manœuvres and INTUBATION
- A body that can simulate arrhythmias and defibrillation. A computer scenario program that comes with the mannequin so that data can be recorded and stored on a computer
## Appendix C8 Marking schedule for video assessment

### Scenario 1 - Guide to entering data in spreadsheet

**PHP:**

- Pre / Post (Circle appropriate)
- Assessor: -
- Date of assessment: -
- Time of assessment: -

<table>
<thead>
<tr>
<th>No</th>
<th>Item</th>
<th>Grade or Time (mins / Seconds):- (enter or circle appropriate)</th>
<th>Comments:--</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Video file Name</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Start time - (at waist)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Time calls for help (mm:ss)</td>
<td>/ didn't call =0</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Time compressions started (mm:ss)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Time ventilation started (mm:ss)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Time informed &quot;Start CPR&quot; - if participant doesn't initiate</td>
<td>/ not informed =0</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Time of last ventilation (mm:ss)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Check Responsiveness: Shouts</td>
<td>Y=1 / N=0</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Check Responsiveness: Shakes</td>
<td>1-Safe Shake / 2-No Shake / 3-Dangerous shake</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Initial airway opening - (circle all that apply)</td>
<td>1-Head tilt / 2-Chinlift / 3-Jaw thrust / 4-Nil</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Check for obstruction</td>
<td>Y=1 / N=0</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Initial breathing check performed? (Circle which apply)</td>
<td>1=Yes (with airway opened) / 2=Yes (airway not opened) / 0=Not performed</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>If Yes, which components of breathing check carried out? (circle all that apply)</td>
<td>1-Look / 2-Listen / 3-Feel / 0-Nil</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>Initial Pulse Check (part a)</td>
<td>1=Yes (&lt; 10s) / 2=Yes (&gt; 10s) / 0-not performed</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>Initial Pulse Check (part b) circle all that apply</td>
<td>1-Central Pulse / 2-Peripheral pulse / 3-No pulse check</td>
<td></td>
</tr>
<tr>
<td>16</td>
<td>Ratio of Compression:Rescue breath (choose closest ratio)</td>
<td>1-30:2 / 2-15:2 / 3-5:1 / 4-Other ( )</td>
<td></td>
</tr>
<tr>
<td>17</td>
<td>Number of &quot;attempted&quot; ventilations (after 1st set of compressions)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>18</td>
<td>Airway opening prior to ventilation (after 1st set of compressions)</td>
<td>1-Head tilt / 2-Chinlift / 3-Jaw thrust / 4-Nil</td>
<td></td>
</tr>
<tr>
<td>19</td>
<td>Facemask Technique</td>
<td>1-&quot;E-C&quot; used / 2-Other Technique / 3-Upside down</td>
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</tr>
<tr>
<td>20</td>
<td>Rescue Breaths &quot;prior&quot; to CPR?</td>
<td>Y=1 / N=0</td>
<td></td>
</tr>
<tr>
<td>21</td>
<td>Number of rescue breaths?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>22</td>
<td>Attempted mouth to mouth?</td>
<td>Y=1 / N=0</td>
<td></td>
</tr>
<tr>
<td>23</td>
<td>Precordial Thump given?</td>
<td>Y=1 / N=0</td>
<td></td>
</tr>
<tr>
<td>24</td>
<td>General Comments</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>