

2005
Annual Report



South Asian Clinical Toxicology Research Collaboration
(1st of January 2005 to 31st of December 2005)

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Executive Summary

Last year was a year of transition for SACTRC. It was the first full calendar year of the capacity building international collaborative research grant, and as a result much more effort has been put into training activities running in conjunction with the clinical research program. The most important developments were a large increase in the numbers of postgraduate research students, development and organization of a central office to support the existing clinical units, the opening of an additional clinical unit, continuing productivity of the core research program and the commencement of collaborative research programs with other academic units and NGOs.

SACTRC has been extremely fortunate to be able to build upon the physical and intellectual infrastructure established by the Ox-Col collaboration (between the Universities of Oxford and Colombo, and in particular between Professors David Warrell and Rezvi Sheriff). This collaboration has given us a strong foundation for more recent studies. One of the key people in this collaboration, Dr. Michael Eddleston, has been coordinating much of the Ox-Col clinical research in Sri Lanka for the last four years. His return to the UK in October 2005 perhaps marked the end of this transition period from Ox-Col to SACTRC, although he remains a key senior researcher within SACTRC. One of SACTRC's initial goals was to consolidate this clinical research program and at the same time to rapidly expand its postgraduate research student program. This has required the development of a management structure to service the research goals of an expanding number of investigators while providing accountability to granting bodies and creating an environment that seeks and takes advantages of new opportunities for collaboration.

As one of SACTRC's major goal is to build research capacity we have sought to build a career path for those involved in research support positions and to provide assistance to all research projects as well as to ensure balanced development of research management in the future. New support roles for the research program have been developed in clinical management, logistics and supply, database programming, statistics, and auditing.

Last year saw the commencement of research activities by four postgraduate research students and one coursework Diploma of Clinical Epidemiology student. Three more postgraduate research students are preparing to commence their work in the first half of 2006 and four more students will enrol in the Diploma of Clinical Epidemiology this year.

SACTRC has developed a MoU with the London Poison Centre who are the WHO-SEARO collaborating centre for clinical toxicology. This MoU sees us become a partner with London and therefore part of the WHO collaborating centre. We will be the major local provider of clinical toxicology education within the region and utilize London as one of our training sites for postgraduates. SACTRC has also developed a partnership with the University of Copenhagen and the Dhaka Medical School. Students from these universities will be doing postgraduate research with SACTRC.

SACTRC has applied to the Sri Lankan government to register as a NGO. This will give us more formal recognition and enable us to get small grants to expand some aspects of our work and to work with other NGOs in improving infrastructure in the hospitals. SACTRC investigators have obtained three new grants, which will help us to carry out our field work

SACTRC organized an agrochemical poisoning workshop in Colombo in August 2005. Thirty eight doctors and researchers, predominantly from South and South East Asia, participated in the 3-day workshop. It highlighted the magnitude of the problem, the extreme diversity of

current management practices and the lack of evidence in this area. However, it also indicated the depth of interest in addressing the problem through research and has led to a number of plans for collaborative research in the region.

SACTRC researchers participated in several other local and international collaborative meetings, and presented over 21 educational talks. This gave further opportunities to develop strong collaborative links with other researchers. A number of international experts visited our research units and have committed themselves to support our research program. We have also organized monthly clinical meetings for the clinical research assistants and have initiated some training programs.

Last year, I became the president of the Asia Pacific Association of Medical Toxicology (APAMT) and work commenced on organizing the next scientific meeting, which will be held at the Colombo Plaza Hotel from August 6th to 8th, with some satellite training workshops on conducting clinical trials and the treatment of poisoning. See <http://www.asiattox.org/> to register or obtain further details as they develop. Secretarial support for both the APAMT and the European Association of Poison Centers and Clinical toxicology (EAPCCT) are now organized out of the SACTRC office.

It was a productive year for clinical studies. Data were collected on 3479 patients with poisoning from three centers. The interim analysis of a randomized clinical trial of super activated charcoal was completed after reaching its target of 4500 patients. There are 16 other active clinical studies recruiting patients. There are also three major field studies examining different strategies of primary prevention.

The group has continued to publish its findings. In 2005, 21 articles were published or accepted for publication in peer-reviewed journals and one article is currently under review. There were 8 book chapters on agrochemical poisoning written by SACTRC investigators. There were also 9 scientific presentations at major international clinical toxicology research meetings (see pages 17 to 20 for details).

At the current time we have an active research program as well as a number of planned and approved projects in the pipeline. The continued implementation of this research program within busy clinical units will continue to require mutual recognition of the importance of each other's goals by researchers and clinicians. Researchers must accept that the care of individual patients is always paramount, while clinicians must accept that major improvements in the outcome of these patients will most likely come over time from research.

Prof. Andrew Dawson
Program Director
SACTRC
February 2006

Major Activities of SACTRC

Collaborations with Universities and other Organizations

WHO-SEARO

SACTRC developed a MoU with the London Poison Centre who are the WHO-SEARO collaborating centre for clinical toxicology. This MoU sees us become a partner with London and therefore part of the WHO collaborating centre. We will be the major local provider of clinical toxicology education within the region and utilize London as one of our training sites for postgraduates.

University of Copenhagen, Denmark

SACTRC has formed a research partnership with the Faculty of Health Science, University of Copenhagen and the Institute of Policy Studies of Sri Lanka to determine the economic costs of poisoning.

SACTRC has also formed a research partnership with the University of Copenhagen to examine safe storage and disposal of pesticides. This work has been funded to date by a grant from the DanAid.

University of Dhaka, Bangladesh

SACTRC has formed a partnership with the Dhaka Medical College and the Oxford Tropical Medicine Group (Bangkok) to initiate research into poisoning in Bangladesh.

Department of Statistics, University of Colombo

SACTRC has formed a collaborative partnership with Department of Statistics, University of Colombo. This will give statistics support to SACTRC research projects. In return SACTRC will fund a statistician in their department for the duration of their training and support further training in medical statistics.

CSIRO and the University of Massachusetts Medical School

SACTRC has worked with these groups to examine the use of synthetic organophosphate hydrolases in acute organophosphate poisoning. At this stage proof of concept studies in animals have been very encouraging, but clinical trials are unlikely to be commenced within the next few years.

The National Poison Information Centre, Colombo

The Director of the centre, Professor Ravindra Fernando, is arranging for review of medical records from the National Hospital, Colombo over the last 4 to 5 years. These data will be used for projects looking at longitudinal trends in poisoning, differences between rural and urban poisoning, variability in management strategies across Sri Lanka, and the pharmacoconomics of antidotes. We have upgraded the internet and network systems in National Poison Information Centre, which now serves as a resource for post-graduate students doing literature searches.

Web Site

The web site at www.sactrc.org has been developed. As well as information about SACTRC it includes full text of all our publications and regular reports of activities as well as links to regional toxicology sites. Further developments to support researchers in the region are being planned.

Developments at Clinical Units

1. Anuradhapura

We welcome the return to Sri Lanka from the London poison unit of Dr Lakshman Karalliedde. The formation of an Anuradhapura medical clinical toxicology research centre has been a long-standing aim of his and we hope with his impetus to make it a reality over the next few years. A draft MoU to help facilitate additional infrastructure funding for a Clinical Toxicology Research unit is undergoing the required consultation from the hospital, province and central Ministry of Health and SACTRC. We were grateful to the Medical Superintendent at Anuradhapura for providing additional space for our researchers.

2. Polonnaruwa

This unit has continued to function very well. A number of new research projects have been developed by the clinicians, coordinators and the clinical research assistants. New accommodation was arranged to accommodate the Clinical Research Assistants

3. Nuwara Eliya

A new clinical research unit was established in Nuwara Eliya Hospital with significant assistance from medical and non-medical staff. The pattern of poisoning in this area is different to NCP and reflects the different agriculture of the highlands. The demographics also differ with a high proportion of patients being plantation workers

3. Peradeniya

We had extensive discussions with the Director and Deputy Director of the Teaching Hospital at Peradeniya and agreed upon the location of a Clinical Research Unit in the hospital. The health ministry has appointed Dr Keerthi Kularatne as a fulltime toxicology physician to this unit. A MoU has been drafted and agreed to by all concerned and is awaiting ratification. We have purchased additional equipment to assist the toxicology ward with funding from the Swiss embassy. This new research unit should open in early 2006.

Research collaborations

SACTRC is a clinical research collaboration that extends beyond the 40-50 people it directly employs. All the clinical trials are dependent upon active contribution of the visiting physicians and their clinical teams in each hospital. In addition we continue to receive generous support particularly from colleagues in Germany, Australia and the United Kingdom. Already it is clear that the international interest in SACTRC's work is expanding. The following is an alphabetical list of SACTRC collaborators who contributed to research studies, educational programs and/or supervised research students in 2005

Mr. Stuart Allen (Aus)	Prof. Ravindra Fernando (SL)
Ms. Manel Abeyawardane (Aus)	Dr Rohini Fernandopulle (SL)
Prof. Ariyananda (SL)	Prof. Nick Freemantle (UK)
Dr. Steve Bird (USA)	Dr. John Fountain (NZ)
A/Prof. Nick Buckley (Aus)	Dr. Indika Gawarammana (SL)
Dr. James Davies (UK)	Dr. Ariyaranee Gnanathas (SL)
Prof Andrew Dawson (SL)	Prof. David Henry (Aus)
Prof. Krishna Devarakonda (SL)	Ms. Mary Hodge (Aus)
Dr. Geoffrey Eaglesham (Aus)	Dr. Lakshman Karralliedde (UK)
Dr. Michael Eddleston (UK)	Prof. Flemming Konradsen (Den)
Prof. Peter Eyer (Ger)	Prof. Alison Jones (UK)

Dr. Ed Juszcak (UK)
Dr. Gamini Manuweera (SL)
Prof. Ludwig von Meyer (Ger)
Dr Alison Moffat (Aus)
Ms. Renu Patel (Aus)
Prof. Julia Potter (Aus)
Dr Shalini Sri Ranganathan (SL)
Prof. Michael Roberts (Aus)
Prof. Nimal Senanayake (SL)
Prof. Rezvi Sheriff (SL)

Dr. Emma Southcott (Aus)
Dr. Tara Sutherland (Aus)
Prof. Ladislaus Szinicz (Ger)
Dr. Horst Thiermann (Ger)
A/Prof. Bala Venkatesh (Aus)
Prof. David Warrell (UK)
Dr. Vajira Weerasinghe (SL)
Prof. Ian Whyte (Aus)
Dr. Franz Worek (Ger)

We also gratefully acknowledge assistance from collaborators who are visiting physicians at Clinical Research Units

Polonnaruwa General Hospital

Dr. Shaluka Jayamane
Dr. Rajarathne Hettiarachchi
Dr. Shifa Azhar

Anuradhapura General Hospital

Dr. K. Jeganathan
Dr. A. Hittarage
Dr. Dharshana De Silva

Nuwara Eliya District Hospital

Dr. Yamuna Dasanayake
Dr. S.M.S.B. Samarakoon

Peradeniya Teaching Hospital

Dr. Keerthi Kularathne
Dr. S.A.M. Kularathne

Activities of Postgraduate Students

Dr. Pradeepa Jayawardane

Pradeepa's project "Development of a Pharmacokinetic/pharmacodynamic model that predicts intermediate syndrome" commenced in Nuwara Eliya in April 2005. This occurred after she received training in the appropriate EMG techniques in Peradeniya under the guidance of Dr. Vajira Weerasinghe and Prof. Nimal Senanayake and also attended a training workshop in Thailand in January.

Dr. Tharaka Dassanayake

Tharaka's project "Neurophysiological assessment of delayed effects of acute organophosphate poisoning on perceptual-motor skills in Sri Lankan patients: a study on reaction time, evoked potentials, event-related brain potentials and motor conduction" commenced in 2005. Training in these techniques was provided by Dr. Vajira Weerasinghe and Prof. Nimal Senanayake. This study while based in Peradeniya Hospital also studied patients from Anuradhapura and Nuwara Eliya.

Dr. Gihan Gunawardena

Gihan's PhD project "Management of Paraquat poisoning with special emphasis on minimizing Pulmonary Fibrosis" involves laboratory studies aimed at developing markers for oxidative stress and pulmonary injury in Queensland, Australia under the guidance of Prof. Mike Roberts and will later involve clinical studies on immunosuppression. He is expected to return to Sri Lanka for the clinical component of his PhD in 2007.

Mrs. Ganga Senarathna

Ganga's project on the "Pharmacoeconomics of antidotes" will initially focus on paracetamol poisoning, an emerging and important poisoning within Sri Lanka. Management is complicated by the inability to assay paracetamol concentrations in many hospitals and the expense of N-acetylcysteine. This work will give her skills in the techniques to evaluate antidotes for pesticide poisoning. She participated in several workshops with Prof. Freemantle in the United Kingdom in December 2005.

Dr. Darren Roberts

Darren's project "Development of outcome measures that facilitate development of new antidotes" involves studies on the pharmacokinetics and pharmacodynamics of oleander and many different agrochemicals. His work started in August 2003 with 18 months of fieldwork in Sri Lankan hospitals. He will now undertake further training on pharmacokinetic and pharmacodynamic methodology to help him analyze these data and is expected to complete his PhD at the end of 2006.

Mr. Lalith Senarathna

Lalith enrolled in the Masters of Clinical Epidemiology program at Newcastle University (Australia). He completed the coursework in 2005 with distinction. He has now returned to Sri Lanka and will do his Masters research project "A cross-sectional study to identify variation between Sri Lankan rural hospitals in their treatment of acute poisoning patients."

Dr. Chandrani Nirmala Wijekoon

Nirmala is currently finishing her MD in clinical pharmacology and general medicine in Newcastle Australia and is returning to Sri Lanka to commence her PhD in February 2006.

Dr. Indika Gawarammana

Indika is currently finishing his MD training in clinical toxicology and general medicine at the Guys and Thomas's Hospital and the London Poison Centre. He is expected to return to Sri Lanka and commence his PhD in mid 2006.

Dr. Bishan Rajapakse

Bishan is an emergency medicine trainee from New Zealand. He has enrolled in an MPhil and will commence his research in March 2006. He will be examining diazepam as an antidote and the use of cholinesterase assays with rapid turn around as an aid to management of OP poisoning.

Dr. Mark Perera

Mark is working as a Clinical Trial Manager for research units in Central Province. He is also in the process of completing the post-graduate Diploma in Toxicology at the University of Colombo. He will enrol in an MPhil in 2006 and intends to do research on clonidine as an antidote for OP poisoning.

Dr. Aroona Abdullah

Aroona will enrol in the Masters of Clinical Epidemiology at the University of Newcastle by distance education. She will also be conducting research projects during the year on paediatric poisoning and behavioural science.

Other Training Activities

- A formal introduction and orientation is undertaken by new research assistants and is followed by a supported period in the ward.
- A monthly meeting takes place in North Central Province (NCP) for the clinical research assistants, postgraduate students and physicians.
- Professor Ravindra Fernando has established a postgraduate diploma course in toxicology. The course is delivered on weekends at the University of Colombo.
- The Program director in collaboration with a number of colleagues has established a diploma or masters distance-learning course in clinical toxicology at the University of Newcastle (Australia). This course utilizes some units of an established internationally recognized course in clinical epidemiology and public health at the Centre for Clinical Epidemiology and Biostatistics.
- Dr. Roshini Sooriyaarachchi from the University of Colombo statistics department visited the UK from 11th September 2005 – 06th October 2005 to attend a number of courses. These included courses at the University of Edinburgh on “the design and analysis of clinical trials” and “Mixed model analysis using SAS”. In addition Dr Sooriyaarachchi attended postgraduate sessions at the Universities of Reading and Oxford.
- Our administrative staffs, Dilani Pinnaduwa and Nilupa Herath, are doing a short course on Website Design at Singapore Informatics (Pvt) Ltd. Kandy.

The SACTRC Agrochemical Workshop

SACTRC organized a workshop in Colombo from the 14th to 16th August 2005. The main sponsors for this workshop were SACTRC, Crop Life International and the WHO SEARO collaborating centre (London). 38 people attended this meeting and about half were from Sri Lanka. International participants came from Germany, Iran, New Zealand, India, Bangladesh, Australia, Thailand, Vietnam and Singapore.

The primary purpose of the meeting was to explore the diversity of clinical approaches and to create collaborative links. This meeting was intended to explore areas that were a high priority for further research. This was done by examining areas of management and determining whether there was a general consensus or strong majority viewpoints or where agreement on preferred management was poor and practices highly variable.

The workshop was based around six cases and supported by some recent clinical literature and short presentations by a number of the registrants. Three cases were related to different aspects of organophosphate poisoning, one case of paraquat poisoning, one case of aluminum phosphide poisoning and one case of unidentified poisoning. A full report of this workshop is available on the website.

Progress of Clinical Trials

1. Cohort study of acute self-poisoning in Sri Lankan hospitals.
Anuradhpura, Polonnaruwa, Kurunegala (2 months) & Nuwara Eliya
The study is an observational cohort study of all patients presenting with deliberate self-poisoning. This cohort contains a large number of nested studies with different inclusion criteria (see below). 3,479 patients were enrolled in the cohort during year 2005. This brings the total number of patients recruited in the cohort study since 2002 to 10,578.

Completed Randomised Clinical Trials

2. Randomised clinical trial of activated charcoal in poisoned patients (n ≈ 4650).
Anuradhapura, Kurunegala & Polonnaruwa
PI - Michael Eddleston, March 2002 – September 2004. Phase III Trial: planned sample size of 4200 patients. The final interim analysis was presented at EAPCCT in 2005 – full results expected to be published in 2006.

Current Randomised Clinical Trials

3. RCT of Pralidoxime vs Placebo in OP poisoning
Anuradhapura & Polonnaruwa
PI - Michael Eddleston, started May 2004 - Phase III Trial: planned sample size of 1500 patients. 68 patients recruited during year 2005 - plan to expand to more centres in 2006.

Other Clinical Studies

4. Effects of banning Dimethoate & Fenthion in Polonnaruwa District on mortality from pesticide poisoning
Polonnaruwa
PI – Gamini Manuweera & Michael Eddleston. This study started in June 2002 and should finish in 2006. This is an observational study looking at the effects of targeted pesticide restrictions in the Polonnaruwa district on the rates of poisoning and overall mortality.
5. Pharmacokinetics of Pesticides in overdose.
Anuradhapura, Polonnaruwa & Nuwara Eliya
PI –SACTRC Collaboration. This is an on going observational study examining the kinetics of various agrochemicals following deliberate poisoning. 425 patients were recruited in 2005. A number of resulting papers will be presented at EAPCCT 2006.
6. Clinical, Neurophysiological and biochemical predictors of intermediate syndrome following OP poisoning
Nuwara Eliya
PI: Pradeepa Jayawardena. This study is doing frequently repeated nerve conduction studies and blood tests in patients with acute OP symptomatic poisoning to look for predictors of subsequent respiratory failure. 63 patients were studied in 2005.
7. Thermoregulation in acute OP poisoning
Polonnaruwa

PI: Alison Moffat & Fahim Mohammed. This study started in January 2004 and finished in April 2005. This study aimed to monitor the effects of acute OP poisoning on temperature regulation. A manuscript is in preparation.

8. Level of self-harm intent in poisoning patients

Polonnaruwa

PI: SACTRC. This is an observational study looking at the level of intention for suicide in self-harm patients. 979 patients were enrolled in 2005.

9. Cognitive effects of organophosphate poisoning-using reaction time, evoked potential and event-related potential.

Peradeniya

PI: Tharaka Dassanayake. This study is examining novel methods to detect long-term effects of acute organophosphorus pesticide poisoning on cognitive function. The study enrolled 32 patients in 2005. Interim results will be presented at the EAPCCT 2006.

10. Previous self-harm histories in poisoning patients.

Polonnaruwa & Anuradhapura

PI: SACTRC. This study records the previous self-harm histories in self-poisoning patients. 879 patients were enrolled in 2005.

11. Survey on pesticide used for self-harm in acute pesticide poisoning patients

Polonnaruwa

PI: Gamini Manuweera. The study was started in June 2004. This study is conducted in Polonnaruwa in association with the Pesticide Registrar Office. The objective of this study is to interpret the different socio-economic factors of patients with pesticide poisoning. 467 patients were enrolled in 2005.

12. Pilot study of the potential efficacy of FFP in acute OP poisoning

Polonnaruwa

PI: Shaluka Jayamanna. This study started in July 2005. This study aims to recruit 30 patients to examine the effects of fresh frozen plasma in acute OP poisoning. Only 4 patients have been recruited (due to problems with supplies of FFP).

13. Prospective review of each poisoning death to address the need of improve medical care that can reduce CFR (Mortality review)

Anuradhapura, Polonnaruwa & Nuwara Eliya

PI: Kusal Wijeweera and Fahim Mohamed. This study started in October 2005. The purpose of this study is to prospectively record all poisoning deaths and to determine by clinical analysis of the management whether improved medical care might conceivably have altered the outcome. 58 patients were enrolled in 2005.

14. Dose requirements of atropine to prevent bradycardia in oleander poisoning.

Anuradhapura & Polonnaruwa

PI: SACTRC. This study was started in October 2005. This observational study prospectively records the amount of atropine that is required to increase the heart rate in bradycardic patients with oleander poisoning. 49 patients were enrolled in 2005.

15. Utilisation of previously distributed pesticide safe storage box in Polonnaruwa
PI – Flemming Konradsen and Andrew Dawson. This study was started in July 2005. This study is examining the utilisation of 450 safe storage boxes distributed in an ad-hoc manner by Croplife to farmer's households.
16. Variability in oleander seed ingestion, effects of age, gender & resultant outcome
Polonnaruwa
PI: Mathisha Dissanayake. This study was started on January 2005 – ongoing. The objective of this study is to examine whether age, gender or other factors influence the pattern of oleander poisoning or the outcome. 172 patients were enrolled in 2005.
17. Toxins in breast milk after self-poisoning.
Polonnaruwa
PI: Waruna Wijayasiriwardane. This study is conducted in Polonnaruwa. The study measures the levels of toxins in milk of breast-feeding mothers who self-poison with pesticides or oleander. 23 patients were enrolled in 2005.
18. Oleander pharmacokinetics/pharmacodynamics (PK/PD) study.
Anuradhapura
PI: Darren Roberts. This study was started in March 2005. The study aims to more precisely examine the pharmacokinetics and some pharmacodynamics (potassium and Holter monitoring) in oleander poisoning. 12 patients were recruited in 2005. This study will be expanded in 2006 to include data on atropine pharmacokinetics.
19. Relationship between paraquat ingestion and the development of sign and symptoms of paraquat toxicity.
Anuradhapura and Polonnaruwa
PI: Kusal Wijayaweera. This study was started in December 2005. This study aims to determine whether patients develop burning sensation as an indicator of severe paraquat poisoning and if this correlates with high blood paraquat concentrations. 10 patients were recruited in 2005.
20. Atropine toxicity with fixed high-dose regimens of atropine in OP poisoning.
Nuwara Eliya
PI: Mark Perera. This study started in December 2005. This study started in Nuwara Eliya where different practices of atropine use are standard. 26 patients were recruited in 2005.

SACTRC database studies

21. Validation of OPP severity score in organophosphorus pesticide poisoning.
Anuradhapura, Polonnaruwa
PI: James Davies. This study is evaluating the WHO OPP severity score as an indicator of a subsequent fatal outcome.
22. Validation of paraquat nomogram and bedside testing for paraquat
Anuradhapura, Polonnaruwa & Nuwara Eliya
PI: Lalith Senarathnaa. This study is validating previous studies that have proposed paraquat concentration data can predict a fatal outcome after paraquat poisoning.

SACTRC supported fieldwork studies

1. Syngenta Paraquat Reformulation Study

Principle investigator: Dr. Martin Wilks.

Follow up doctors: Dr. Lumbini De Silva and Dr. Hasantha Ranganath

Clinical Auditor: Ms Nilupa Herath

SACTRC is supporting the paraquat reformulation study conducted by Syngenta. This multi-centre study aims to determine whether a new formulation of paraquat marketed by Syngenta is effective in reducing deaths and complications after self-poisoning with paraquat. The study involves clinical data collection and collection of single plasma samples and urine samples from the patients. The patients are followed up three months after hospital discharge.

2. Safe Storage Project

Principle investigator: Prof. Flemming Konradsen

Field Officers: Mr. Manjula Weerasinghe and Mr. Ravi Pieris.

The major objective of this study is to identify, pilot test and assess feasibility and impact of interventions at household and community levels to improve safe storage and safe disposal of pesticides with the aim of reducing the number of episodes of acute pesticide poisoning. The study was conducted in selected farming village in Anuradhapura district. 200 houses were selected at random in selected villages and safe storage boxes were distributed. The houses were followed up after two and seven months.

3. Zinc phosphide formulation project

Principle investigators: Dr. Darren Roberts & Dr. Gamini Manuweera

Field Officer: Dr. Hasantha Ranganath.

This project is looking at the formulation and percentage active ingredients in Zinc Phosphide formulations. Zinc phosphide poisonings had a large and unexplained variability in toxicity, but were generally in contrast with reports of severe toxicity in the literature. These formulations are often non-proprietary formulations prepared at point of sale and this study will determine the percentage of active ingredients in a selection of products purchased in small pesticide shops in the North Central province.

Clinical Research support staff

Head office -University of Peradeniya, Faculty of Medicine, Peradeniya

Prof. A.H. Dawson

- Program Director

Mr. A.C.M.Fahim

- Manager-Operations

Ms. Dilani Pinnaduwa

- Secretary to the Director/Personal Assistant

Ms. Nilupa Herath

- Auditor/Personal Assistant

Mr. D.L. Wimalasena

- Office Assistant

Mr. Wilson

- Study Driver

Dr. Prabath Amarasinghe

- Clinical Research Assistant

SACTRC Study Centres

Anuradhapura General Hospital

Dr. Kusal Wijayaweera

- Clinical Trial Manager

Mr. Shukry Zawahir

- Clinical Trial Coordinator

Mr. Ashrafdeen Isnan

- Clinical Trial Coordinator

Mr. Ananda Hettige

- Driver

Ms. Anusha Indumathi

- Domestic Worker

Polonnaruwa General Hospital

Mr. Chathura Palangasinghe - *Clinical Trial Coordinator*
Ms. Chandrani - *Domestic Worker*

Nuwara Eliya General Hospital

Dr. Mark Perera - *Clinical Trial Manager*
Mr. Sheyd Shahamy - *Clinical Trial Coordinator*
Ms. M. Thangamma - *Domestic Worker*

Clinical Research Assistants

We currently require about 22-24 clinical research assistants to run three different clinical units. Their conscientious dedication in the year they work with us prior to starting work as interns is essential to the conduct of our activities. We have been fortunate to have many very good applicants each year. In 2005 we interviewed over 200 applicants for these positions. The following people were selected and we now thank them for their work over the year and wish them the best for their future careers.

Dr. Hasantha Ranganath
Dr. Mahi Wickramagamage
Dr. R.U. Wijesinghe
Dr. S.M.I. Senavirathne
Dr. Chinthaka Semasinghe
Dr. Nilundhima Wijekoon
Dr. Kanchana Liyanage
Dr. Sudesh Rathnayake
Dr. Pandula Illangasinghe
Dr. Prasanna Weerakoon
Dr. Gayan Wickramasinghe
Dr. Himali Sepalika Sudusinghe

Dr. Iranga Jayasundara
Dr. Sellakkuddy Selvaganesh
Dr. Vindya Jayasinghe
Dr. Mahesh Dahanayake
Dr. Vethanathan Bavanthan
Dr. Thangavelaautham Suhitharan
Dr. David Selvanayagan
Dr. D.Y. Mohamed Mahir
Dr. Lakshmi Sriskandarajah
Dr. Chaminda Manamperi
Dr. Chinthaka De Silva
Dr. Paramanathan Sajeewan

IT Support: Databases

We have engaged the company Evolution Software (director: Mohamed Gazzaly) for clinical database design and IT support in the study centres. Mr. Stuart Allan, the Australian database designer, continues to provide expert advice and visited Colombo in January 2005 to assist with training and documentation of the database design for future modifications.

Funding

The two major grants funding SACTRC research to date are

Wellcome Trust Career Development Fellowship. GR063560MA. Eddleston M, Warrell D, Sheriff R, Buckley N, Juszczak E. UK£699,801. Organophosphate pesticide poisoning in Sri Lanka- Management, complications and pharmacogenetics. 2002-2007.

The Wellcome Trust/NHMRC International Collaborative Research Grants (ICRG) scheme. GR071669MA. Reducing deaths from pesticide poisoning - Establishing a regional toxicology research centre. UK£1,250,000 (Aus\$3,078,038). Buckley N, Senanayake N, Dawson AH, Sheriff R, Fernando R, Henry DA. 2004-2009.

New Grants

There are a number of other grants that relate to SACTRC activities awarded this year that will support future SACTRC activities.

NHMRC Enabling Grant/Genetic Repositories Australia

A grant of Aus\$2,000,000 was awarded to Schofield P, Cavanaugh J, Forrest S, Hopper J. (N Buckley on behalf of SACTRC was an Associate investigator) for the period of 2006-2010. This grant will be used for the establishment of a genetic 'bank' in Sydney for immortalized cell lines. SACTRC investigators aiming to do toxicogenetic studies will be able to utilize this repository, which will be a major resource for encouraging long-term collaborative research in toxicogenetic on pesticides.

SDC grant for equipping the Clinical Unit in Peradeniya Hospital

The Swiss Agency for Development and Cooperation (SDC), through the embassy of Switzerland in Colombo has donated 40,000 Swiss francs to buy equipment for the establishment of a centre for the treatment of poisoned patients in ward 17 of Peradeniya teaching hospital. The fund will be used to purchase new ventilators and other equipment to the ward.

DanAid grant for the Safe Storage Project

DanAid has granted approximately US\$128,000 to cover the cost of a project entitled "Safe Storage and disposal of pesticide containers at community level in Sri Lanka – Feasibility and Impact". The project will run over 2 years and commence in early 2006. This grant will also be used for supporting research studies of some postgraduate students from Denmark.

International visits and Collaborative meetings

- The Program Director visited Professor Thomas Chan and Dr Charles Gomersall at the Prince of Wales Hospital, Hong Kong and discussed collaborative research and some opportunities for training in their ICU. The Program Director also met with Dr Albert Chan and his analytical toxicology service group at Princess Margaret Hospital and Teresa Ngan from the Hong Kong health ministry who is establishing the Hong Kong poison centre.
- The Program Director met with Ian Simpson in Kerala and visited Little Flower hospital and discussed the collaborative work, in particular involvement in clinical trials of OP antidotes.
- Dr. Kusal Wijayaweera visited Warangal, Andhra Pradesh, India. The main purpose of this visit was to review the protocols for collecting blood samples of patients recruited to a study on the effects of pralidoxime on AChE inhibited by Monochrotophos (a highly lethal pesticide now banned in Sri Lanka).
- Dr. Michael Eddleston visited India and Bangladesh and met with physicians and delivered several educational talks.
- Dr. Darren Roberts visited Chandrigarrh and Vellore, India and San Francisco New York & St Louis, USA to meet with clinical toxicologists and delivered several educational and research presentations.
- The Program Director participated in the WHO IPCS conference in Malaysia. The objective of this meeting was to finalize a multilevel training manual for agrochemicals.
- The Program Director met with Prof. David Warrell, Prof. John Harris, Dr. Ariarane Gnanathas & Dr. Geoff Isbister on two occasions in Anuradhapura and Kandy in 2004 in regard to a further grant application regarding envenomation. A draft proposal was prepared.

Educational Talks

1. Eddleston M. Management of organophosphorus pesticide poisoning. Internal Medicine Grand Round, University of Manipal, Karnataka, India. February 2005.
2. Eddleston M. Differences between organophosphorus pesticides in human poisoning. Istituto Superiore di Sanita, Roma, April 2005.
3. Eddleston M. Preventing deaths from pesticide self-poisoning in rural Asia. Harvard School of Public Health, University of Harvard, Boston, USA. May 2005.
4. Eddleston M. Management of organophosphorus pesticide poisoning. Emergency Medicine Grand Round, University of Massachusetts at Worcester, USA. May 2005.
5. Eddleston M. Management of organophosphorus pesticide poisoning. Toxicology Grand Round, New York Poisons Control Centre, NYU, USA. May 2005.
6. Dawson A. Controversies in Gastrointestinal decontamination. Jaffna, Sri Lanka. September 2005.
7. Dawson A. Clinical trials made simple, Faculty of Medicine, University of Colombo, Sri Lanka
8. Dawson A. Rational prescribing. Medical grand rounds. Nuwara Eliya, Sri Lanka
9. Roberts D, Senarathna L. Prognosis in Paraquat Poisoning. NSW PIC educational meeting, November 2005.
10. Roberts D. Yellow Oleander Poisoning. San Francisco Poisons Control Centre, San Francisco General Hospital, USA.
11. Roberts D. Chlorphenoxy herbicide poisoning. Post Graduate Institute of Medical Research and Education. Chandrigarrh, India. September 2005.
12. Roberts D. Clinical trials on poisoning in Sri Lanka. Christian Medical College. Vellore, India. September 2005.
13. Buckley N. Keynote lecture: Evidence and pesticide poisoning. Australian Conference of Ambulance professionals. Canberra, October 2005.
14. Buckley N. Reducing pesticide poisoning in Sri Lanka. Department of Clinical Pharmacology & Therapeutics. University of NSW. November 2005.
15. Buckley N. Translational research on pesticide poisoning in Sri Lanka. Therapeutics Research Centre, University of Queensland. October 2005.
16. Eddleston M. Preventing deaths from pesticide self- poisoning in rural Asia. University of Bristol, UK
17. Eddleston M. Management of organophosphorus pesticide poisoning. Internal Medicine Grand Round, Dhaka Medical College, Bangladesh. September 2005.

18. Eddleston M. Use of antidotes in the management of organophosphorus pesticide poisoning. Department of Pharmacy, Kakatiya University, Warangal, India. October 2005
19. Eddleston M. Pesticide self-poisoning in Polonnaruwa District. Presentation to the Pesticide Technical Advisory Committee, Ministry of Agriculture, Colombo. August 2005.
20. Dawson A. Organophosphate Poisoning Practical Management Issues and Controversy, The Hong Kong Clinical Toxicology Society at United Christian Hospital in Kowloon, Hong Kong November 2005
21. Dawson A. SACTRC The challenge and Opportunity. Hong Kong Poison Centre United Christian Hospital. November 2005
22. Perera M. Use and Misuse of Agrochemical-the Sri-Lankan experience. PGRC auditorium, Department of Agriculture, at Gannoruwa, Peradeniya.
23. Dawson A. Controversies in gastrointestinal decontamination. Sri Lankan Medical Association, Colombo, October 2005.
24. Dawson A. MCPA poisoning. Sri Lankan Medical Association, Colombo, October 2005.

Publications

Books/Book Chapters/Electronic publications

1. Roberts DM, Buckley NA. Alkalinisation for Organophosphate poisoning. In: **The Cochrane Library**, Issue 1 2005: CD004897. Oxford: Update Software.
2. Buckley NA, Eddleston M, Szinicz L. Oximes and Organophosphate poisoning. In: **The Cochrane Library**, Issue 1 2005: CD005085. Oxford: Update Software.
3. Eddleston M, Singh S, Buckley NA. Acute organophosphorus poisoning. **Clinical Evidence** 2005;13:1744-55. Continually updated compendium of evidence published by the American Society of Internal Medicine and the BMJ Publishing Group, London
4. Roberts DM, Eddleston M. Yellow Oleander poisoning: Nayyar V (Ed). **Critical Care Update** 2005: 189-200. New Delhi. Jaypee Brothers Medical Publishers (P) Ltd.
5. Hexdall A, Eddleston M. International perspectives on medical toxicology. In: **Goldfrank's Toxicologic Emergencies**, 8th edition. Ed: Flomenbaum NE et al, McGraw-Hill: New York, 2005, in press.
6. Dawson A. Barium Poisoning In: **Goldfrank's Toxicologic Emergencies**, 8th edition. Ed: Flomenbaum NE et al, McGraw-Hill: New York, 2005, in press.
7. Roberts DM, Buckley NA. Urinary alkalinisation for acute Chlorphenoxy herbicide poisoning (protocol). In: **The Cochrane Library**, Issue 1 2005. Oxford: Update Software.

8. Roberts DM, Buckley NA. Antidotes for acute cardenolide (cardiac glycoside) poisoning (protocol): **The Cochrane Library**, Issue 1 2005. Oxford: Update Software.
9. Eddleston M. Organophosphorus and carbamate pesticides. For BASICs intensive care course. <http://www.aic.cuhk.edu.hk/web8/pesticides.htm>

Articles in Refereed Journals

1. Eddleston M, Eyer P, Worek F, Mohamed F, Senarathna L, von Meyer L, Juszcak E, Hittarage A, Azher S, Dissanayake W, Sheriff MHR, Szinicz L, Dawson AH, Buckley NA. Differences between Organophosphorus Insecticides in Human Self-Poisoning – A Prospective Cohort study. **Lancet** 2005;366:1452-59.
2. Eddleston M, Wijeratne T, Karalliedde L, Hurrell M, Dawson AH. Case report does not give enough data to support a diagnosis of fatal organophosphorus poisoning. **Clinical Toxicology** 2005, 43:887-8.
3. Konradsen F, van der Hoek W, Gunnell D, *Eddleston M*. Missing deaths from pesticide self-poisoning at the IFCS Forum IV. **Bulletin of the World Health Organization** 2005, 83:157-158
4. Eddleston M, Gunnell D, Karunaratne A, De Silva D, Sheriff MHR, Buckley NA. Epidemiology of Intentional Self-Poisoning in Sri Lanka. **British Journal of Psychiatry** 2005;187:583-584.
5. Buckley NA, Eddleston M, Dawson AH. The need for translational research on antidotes for pesticide poisoning. **Clinical and Experimental Pharmacology and Physiology** 2005;32:999-1005.
6. Roberts DM, Fraser JF, Buckley NA, Venkatesh B. Experiences of anticholinesterase pesticide poisonings in an Australian tertiary hospital. **Anaesthesia and Intensive Care** 2005; 33(4):469-76.
7. Roberts DM, Seneviratne R, Mohamed F, Senarathna L, Abeyasinghe M, Hittarage A, Dawson A, Buckley NA, Sheriff MHR, Eddleston M. Deliberate Self-Poisoning with the chlorophenoxyherbicide 4-chloro-2-methylphenoxyacetic acid (MCPA). **Annals of Emergency Medicine** 2005; 46(3):275-84.
8. Srinivas Rao CHR, Venkateswarlu V, Surender T, Eddleston M, Buckley NA. Pesticide poisoning in Warangal District – Opportunities for better Medical Management. **Tropical Medicine International Health** 2005; 10(6):581-588.
9. Buckley NA, Eddleston M. The Revised Position Papers on Gastric Decontamination (editorial) **Clinical Toxicology** 2005;2:127–128.
10. Dawson A, Buckley NA. Comment on “Survival Pattern in Patients with Acute Organophosphate Poisoning Receiving Intensive Care”. **Clinical Toxicology** 2005; 43(4):317.
11. Roberts D, Wijayaweera K, Eddleston M. Yellow oleander poisoning. **Anuradhapura Medical Journal** 2005; 4; 12-17

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12. Eddleston M, Sudarshan K, Senthilkumaran M, Reginald K, Karalliedde L, Senarathna L, de Silva D, Sheriff MHR, Buckley NA, Gunnell D. Patterns of hospital transfer for self-poisoned patients in rural Sri Lanka - Implications for estimating the incidence of self-poisoning acts in the developing world. **Bulletin of the World Health Organisation** 2006; (in press)
13. Davies JOJ, Roberts DM, Hittarage A, Buckley NA. Oral C-4 plastic explosive in humans – a case series. **Clinical Toxicology** 2006;(in press)
14. Roberts DM, Dawson AH, Hittarage A, Jegenthathen K, Sheriff, MHR, Buckley NA. Plasma alkalinisation for acute organophosphorus poisoning - is it a reality in the developing world? **Clinical Toxicology** 2006; (in press)
15. Eddleston M, Karunaratne A, Weerakoon M, Kumarasinghe S, Rajapakshe M, Sheriff MHR, Buckley NA, Gunnell D. Choice of poison for intentional self-poisoning in rural Sri Lanka. **Clinical Toxicology** 2006 ;(in press).
16. Roberts DM, Dawson AH. Antidotes or Anecdotes. **Sri Lankan Prescriber** 2006;(in press)
17. Eddleston M, Haggalla S, Reginald K, Sudarshan K, Senthilkumaran M, Karalliedde L, Ariaratnam A, Sheriff MHR, Warrell DA, Buckley N. A survey of gastric lavage for intentional self-poisoning in the developing world. **Clinical Toxicology** 2006;(in press)
18. Mohamed F, Senarathna L, Azher S, Sheriff MHR, Buckley N, Eddleston M. Compliance for single and multiple dose regimens of superactivated charcoal: a prospective study of patients in a clinical trial. **Clinical Toxicology** 2006; in press
19. Isbister GK, Hodge M, Mills K, Friberg LE, O'Connor E, Eddleston M. Human methyl parathion poisoning. **Clinical Toxicology** 2006; in press
20. Eddleston M, Mohamed F, Davies JOJ, Eyer P, Worek F, Sheriff MHR, Buckley NA. Respiratory Failure in Acute Organophosphorus Pesticide Self-Poisoning. **Quart J Med** 2006; in press
21. Eddleston M, Dissanayake M, Sheriff MHR, Warrell DA, Gunnell D. Increased physical vulnerability as a cause of fatal self-harm in the elderly. **Brit J Psych** 2006; in press

Submitted Papers-Under review

1. Roberts D, Wijayaweera K, Eddleston M. Management of yellow oleander poisoning. **Sri Lankan Prescriber**

Scientific Presentations and Abstracts

1. Eddleston M, Juszczak E, Buckley NA, Senarathna L, Mohamed F, Sheriff MHR, Warrell DA. Randomised controlled trial of routine single or multiple dose superactivated charcoal for self-poisoning in a region with high mortality. **European Association of Poisons Centres & Clinical Toxicology Scientific Meeting**, Berlin, May 2005. *Clinical Toxicology* 2005; 43(5):442-443 (Abstract 69)
2. Mohamed F, Senarathna L, Azher S, Sheriff MHR, Buckley N, Eddleston M. Prospectively measured compliance for single and multiple dose regimens of superactivated charcoal in self-poisoning patients. **European Association of Poisons Centres & Clinical Toxicology Scientific Meeting**, Berlin, May 2005. *Clinical Toxicology* 2005;43(5):444-446 (Abstract 71)
3. Dawson A, Clinical Trials in Sri Lanka: The Challenge and Opportunity. **European Association of Poisons Centres & Clinical Toxicology Scientific Meeting**, Berlin, May 2005. *Clinical Toxicology* 2005;43(5):436-437 (Abstract 63)
4. Roberts DM, Southcott E, Potter J, Eddleston M. Pharmacokinetics of Digoxin-like substances in the plasma of patients with yellow oleander self poisoning. **European Association of Poisons Centres & Clinical Toxicology Scientific Meeting**, Berlin, May 2005. *Clinical Toxicology* 2005;43(5):422-423 (Abstract 43)
5. Eddleston M. New trends in organophosphorus pesticide poisoning. **South Asian Confederation of Anaesthesiologists** 6th Congress, Kandy, Sri Lanka. February 2005.
6. Eddleston M. Pesticide self-poisoning in the developing world - an overlooked tragedy. 2nd **New York Symposium on International Emergency Medicine**, New York, USA. May 2005.
7. Dawson A. Organophosphates: New antidotes from old drugs, **ToxCon (The Indian Toxicology Society)**, Kochi, India. October 2005.
8. Dawson A. Recent understanding in the treatment of pesticide poisoning. Annual scientific meeting, **Bangladesh Society of Medicine**, Dhaka, Bangladesh. October 2005.
9. Whyte I, Dawson A. Environmental and Occupational Toxicology in Sri Lanka: The serendipitous opportunity of acute poisoning, **North American Congress of Clinical Toxicology (NACCT)**. Orlando, USA. September 2005.