

UPCOMING MEETINGS

The next Pan-American Section IST Congress will be in Miami Beach, USA, September 18-23, 2016. See later in this newsletter for further details. A website for this congress will be available shortly at www.ist2016.com.

IST Council has agreed to a changed schedule for IST congresses, commencing in 2015 with the World Congress held every second year, rotating between the 3 regions, so the next IST World Congress will be in Hainan, China, in 2017.

Clinical Toxinology Short Course, Adelaide, Australia, March 14-19, 2016.

FROM THE IST EXECUTIVE

The IST World Congress, was held in the University of Oxford, UK, September 25th to 30th, 2015. It was an exciting meeting, rather special, because of the historic setting, quite different from meetings in modern hotel or convention facilities. Oxford is a charming town. A big thank you to Muhammad Sohail, Eddie Rowan and David Warrell for making this meeting possible.

The next Pan-American Section congress, to be held in Miami in September 2016, is already in advanced planning, so watch for updated information and especially for Pan-American Section members, don't miss this meeting.

The next IST World Congress will be in Hainan in 2017, probably late in the year, with details to follow soon. Definitely a meeting for all IST members and others interested in toxinology to put in their calendars.

The next European Section meeting, scheduled for 2018, has yet to be organised, though we already have one tentative bid from an interesting country which has never hosted an IST meeting before, so this could be rather exciting. Watch out for details as they emerge.

I will shortly conduct email-based elections for some IST Council positions. See the AGM minutes (page 6) for details on who was nominated. Exercise your vote when this opportunity arises!

In January I will send out notices for payment of annual Membership dues for 2016.

Lastly, I wish all members a Happy New Year for 2016 and, for those who celebrate christmas, a Merry Christmas.

Julian White, Secretary/Treasurer, IST

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President: J Fox
Secretary/Treasurer: J White
President Elect: vacant
Immediate Past President: A Harvey
Toxicon Editor: A Harvey
President European Section: J Calvete
Secretary European Section: R Harrison
President Pan-American Section: D Tambourgi
Secretary Pan-American Section: Y Cury
President Asia-Pacific Section: Song-ping Liang
Secretary Asia-Pacific Section: Sulan Luo
Outgoing General Councillors
Europe: D Warrell & R Stocklin
Pan-America: JM Gutierrez & L Pos-sani
Asia-Pacific: G King & M Kini

julian.white@adelaide.edu.au

MESSAGE FROM THE PRESIDENT (I.S.T)

As I begin my term as President of the IST I wish to first recognize and give thanks to the leadership of my predecessor Dr. Alan Harvey who has maintained our society's focus over the past four years. Also, I wish to congratulate the organizers of the recent IST Congress in Oxford, which was outstanding and served to highlight our society's excellent contributions to basic, translational and clinical research.

Over the next year I wish to charge the IST Council to review our organizational structure with the goal of reaching out to national societies dealing with toxinology and bring them into our fold by virtue of shared vision and goals. This will require us to review the organization and structure of the regional societies and how the national organizations can intercalate with them and then the regional societies with the international structure. I believe we need to have all of these organizations with shared vision working together to strengthen our collective science and representation in the broader world of science. Dr. Manjanatha Kini, IST Council Member is the chair of this new ad hoc committee. Currently discussions are underway with the Toxinology Society of India (TSI) and Bangladesh Society of Toxinology.

Another area that I have asked the Executive Council to review and revise is how we conduct our IST Congresses. Traditionally we have essentially "contracted" out the meeting and left it totally in the hands of the local organizers. While this model has been reasonably successful I believe the society must have greater leadership in our international congress and help the meetings grow and begin to make financial contributions to the society. This is necessary for our out-reach programs to grow as well as enhancing the participation of young investigators in our society.

As just mentioned I wish to reach out to young investigators to participate in our society. Dr. Brian Fry has accepted the leadership of a committee to work on new social media communications tools as well as developing new avenues for young scientists to present their work at the regional and international meetings. We need to identify the future leaders in our field and in our society and help them develop their careers.

I have asked Council Member Dr. Juan Calvete to review our relationship with Toxicon as the official journal of the society and look for new avenues for collaboration to strengthen the society as well as the journal.

So, this will be a busy year for the IST Council. I will press the council to act and I hope you report significant progress to the membership in one year. Meanwhile, if you have comments or ideas for the IST please contact me or your regional council member. If you wish to participate on one of these ad hoc committees please let me know.

Professor Jay Fox
President, IST

From the out-going President

My term of office ended at the IST's international congress in Oxford in September when I handed over to the in-coming President, Jay Fox. I wish Jay well and I am sure that the Society will be in very good hands in the coming years.

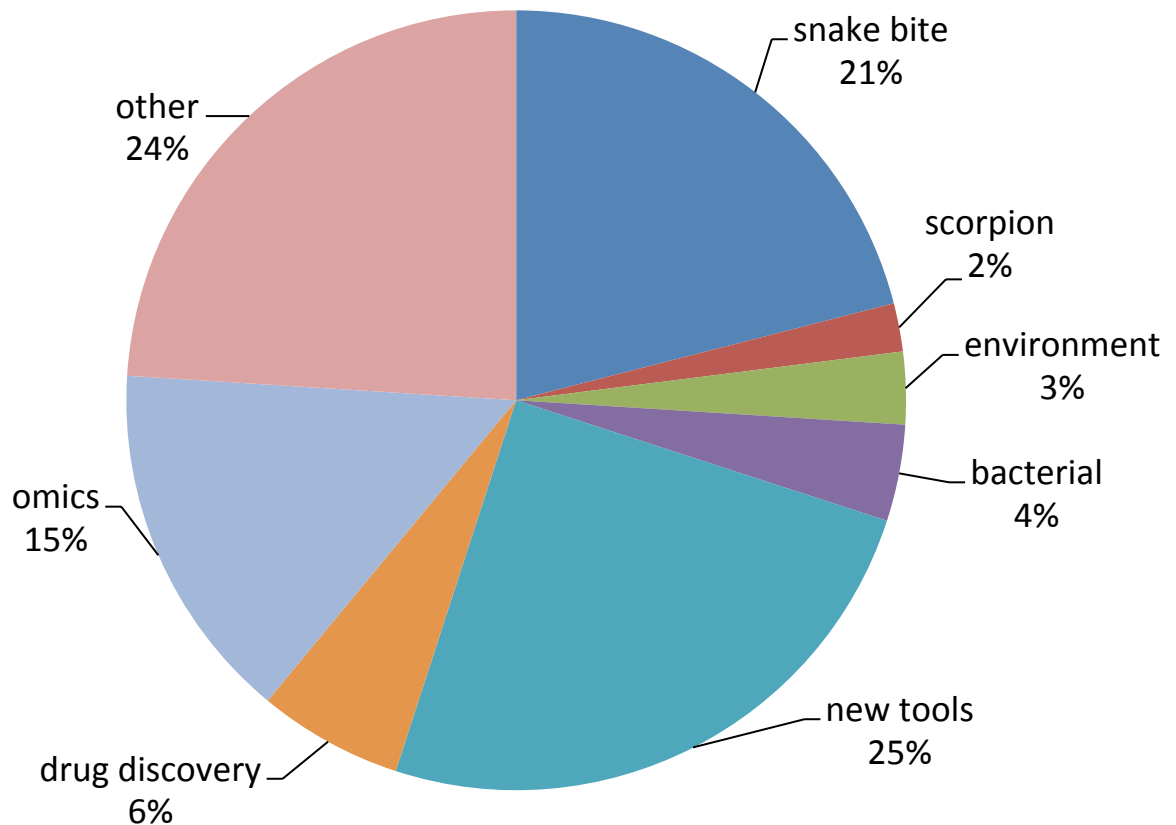
The Congress, as reported in more detail elsewhere, was a great success. The Society owes a great debt of gratitude to the two co-presidents of the congress, David Warrell and Eddie Rowan, plus their organiser Muhammad Sohail. There were around 400 participants and over 300 presentations. The facilities were superb – and the sun shone throughout the congress! We successfully experimented with several innovations, including pre-congress didactic workshops, 'Oxford-style' debates and a public engagement day. The bar has been raised even higher for future congresses, but the organisational efforts are worthwhile because the IST congresses, both regional and international, are the jewels in the IST crown.

The Congress also gave me the opportunity to reflect not just on my three years in office but on the development of the IST and toxinology in general. The IST has come a long way since its formation in 1962. Then, there were 79 founding members from 23 countries, while there are currently over 300 from 55 countries. Interestingly, the original annual subscription fee was US\$10, which is equivalent to \$80 today – the current subscription is clearly a bargain at \$55! The first world congress on animal, plant and microbial toxins was held in 1966 in Atlantic City, New Jersey; the Oxford congress was the 18th in the series – a remarkable continuity. The Society's official journal *Toxicon* was first published in 1962 with 256 pages in the first volume and was available to members at the reduced rate of \$10 (\$80 in today's equivalent). Last year, *Toxicon* published 2115 pages and was free to members of the IST. Of course, publishing has changed dramatically in recent years from hardcopy reprints to electronic copies: there were more than 500,000 full-text downloads of articles in *Toxicon* in 2014.

Many of the key topics in toxinology have remained throughout the history of the IST, although technologies have kept up with advances in related sciences. Key themes continue to be:

- improving the treatment of victims of snake envenoming
- improving the treatment of victims of scorpion stings
- dealing with toxins in the environment (mycotoxins, cyanobacterial toxins etc)
- dealing with dangerous bacterial pathogens
- finding and characterising new pharmacological tools
- contributing to drug discovery

An analysis of the topics of presentations at the Oxford congress gives a snapshot of where toxinologists are focussing on currently:

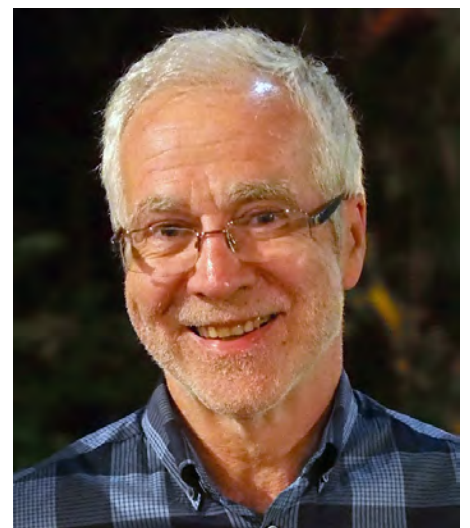


Recent articles in *Toxicon* broadly follow the same pattern. What this simple analysis does not show is the extent that the topics are being approached from an interdisciplinary perspective. That indeed is a great strength of the IST – being a forum to bring together scientists from many different disciplines and clinicians with experimental scientists.

In closing, I would like to thank members of the IST Council and members more generally for the support they gave me in the last three years. I am sure that our new President, Jay Fox, will also benefit from such willing support.

Best wishes

Alan Harvey



International Society on Toxinology

**Annual General Meeting
Sunday September 29th, 2015
St. Hilda's College, University of Oxford, UK**

MINUTES

1. Meeting opened: by Prof. Alan Harvey, IST President & Prof. Julian White, IST Secretary/Treasurer

42 members present

2. Apologies: M Kini, D Tambourgi, S Liang, L Possani

3. President's Report: delivered by Prof. Harvey

4. Toxicon Editor's Report: delivered by Prof. Alan Harvey, Editor in chief

5. Secretary/Treasurer's Report: delivered by Prof. Julian White

Motion: That Treasurer's report be accepted.

Moved: A Harvey

Seconded: R Harrison

Motion carried

6. Annual dues:

Motion: That the Annual Dues for the Society be maintained at US\$55.00

Moved: J White

Seconded: D Warrell

Motion carried

7. Election of Office Bearers and Council Members for the Society:

At conclusion of this section the incoming President, Prof. Jay Fox will be invited to assume his duties and continue running the meeting.

Nominations:

The President, Prof. Harvey, recommended to the meeting that nominations for the President and Secretary positions be delayed until the next World Congress in 2017, since the persons elected would not take up their positions until 2019. The meeting agreed with this proposal.

It should be noted that the following nominations had already been received:

President: Prof. M Kini (Singapore)

Secretary/Treasurer: Prof. J White (Adelaide)

General Council Members

Europe

Prof. D Warrell (UK)

Dr. N Casewell (UK)

Prof. J Tytgat (Belgium)

Pan-America

Prof. Gutierrez (Costa Rica)

Prof. Mari (USA)

Prof. L Possani (Mexico)

Asia-Pacific

Prof. Kini (Singapore)

Prof. G King (Australia)

Prof. S Weinstein (Australia)

In view of the multiple nominations for Council positions for all three regional Sections, an email vote of Members will be organised by the Secretary.

Vote of thanks to the outgoing President, Prof. Alan Harvey.

Moved: J White

Seconded: J Fox

Motion carried

8. The next IST World Congress:

A report on the 2017 World Congress planning was provided by Prof. Luo and the 2016 Pan-American Section congress by Prof. Mari. The 2017 congress will be in Haiku, Hainan, China, likely in November. The 2016 congress will be in Miami Beach, USA, likely in early September.

9. Other business:

- 9.1 Development of revised Objectives or a Mission Statement for IST and other matters pertaining to the future of the Society:
J Fox reported on the Council discussions about these matters, informing the meeting that Council will be examining possible new and revised actions to help the Society.
- 9.2 Prof. Koni raised the issue of payment methods for financial members, noting that the current PayPal system is difficult for some members. Several other members supported this view. Direct bank transfer was suggested, but Prof. Carl Vogel noted this would likely cause major administrative problems. The Secretary undertook to investigate alternative payment systems.
- 9.3 Prof. Habib requested that the Society make further moves to link with the African Toxinology Society and this was supported by Prof. Gopalakrishnakone and Prof. Warrell. The President and Secretary undertook to investigate possible actions to achieve this.
- 9.4 Dr. Straight moved for congratulations to be expressed by the membership to the organisers of the Oxford World Congress. This was resoundingly approved by members.

10. Close meeting: There being no other business, Prof. Fox closed the meeting.

INTERNATIONAL SOCIETY ON TOXINOLOGY

SECRETARY-TREASURER'S REPORT 2012-2015

Introduction

The 2012-2015 Triennium has been a period of further change for IST. The Society adopted a revised constitution at the 2012 World Congress and this has allowed a number of changes to occur.

The term for Executive Positions for the Society move to 4 years, from the previous 3 years (President, President-Elect, Secretary/Treasurer). Therefore our incoming President, Prof. Jay Fox, and myself as Secretary/Treasurer, will serve until 2019.

The Society now has a changed congress schedule, with only one congress per year, rotated around the three existing regional sections (Europe, Pan-America, Asia-Pacific), with every second year nominated as a World Congress. The next World Congress will be in Hainan, China, in 2017.

The Society has embarked on a journey to develop clinical toxinology as a recognised area of medical expertise. The revised constitution in 2012 enabled this journey to commence. Council then adopted a separate constitution to govern this process and through this, formed a Board of Clinical Toxinology and appointed an interim initial Board. This Board is in charge of developing and continuing the journey and I anticipate this will not be an easy or rapid process, but at least we have "left the station".

The Society has fully adopted the revised annual dues payment process that now requires all such dues to be paid via an online portal on the IST website. This has removed the confusing and problematic multiple payment options that previously existed and so diminished the number of "members" who were counted as financial, yet the Society received no payment. Inevitably this has seen a drop in the numbers of listed financial members.

At my last AGM report in 2012 I noted the Society had 314 financial members (Full members and Affiliate members) and 68 student members. As of this month, September 2015, I can report the Society has 224 financial members, plus a further 17 "special" members who are counted as financial because there are technical blocks to them paying, despite their best attempts, and 91 student members. Thus our membership has declined in the last 3 years. In part this reflects the significant number of "new" members who joined in 2012 to take advantage of special member registration rates for the Hawaii World Congress. I estimate there were about 112 in this category, of whom a significant number (at least 90) have not maintained their membership. This congress was combined with US Venom Week and we could expect many Venom Week participants, who just joined IST to gain the reduced congress registration fee, would not maintain their membership.

I think it is fair to say the Society may be heading for, or already in crisis over membership numbers. As stated in my last AGM report, I think that membership numbers from 5-10 years ago were considerably inflated by people who subscribed to Toxicon via Elsevier, using IST membership rates, but who made little or no contribution to the affairs of the Society. For many of these people the Society did not receive dues from Elsevier. However, that era is behind us and we must focus on our real membership and how we can maintain it, grow it, not just stop it from declining further.

One option we have considered is incorporating national toxinology societies into IST and the revised constitution has a potential way to achieve that, but so far our attempts to make this happen have been unsuccessful. I do not think that is a reason to give up on the idea and I urge members of IST who are also members of national toxinology societies to advocate within those societies for development of such linkages with IST. I think toxinology will be richer if we can organise together.

The Society newsletter has been a disappointment for me. I have been unable to convince members, even those on Council, to contribute to it. It could be a vital, alive communication vehicle for our Society, but that will only happen if many members, especially senior members, consistently make the effort to support it. If, as Secretary/Treasurer, I am virtually the only person contributing and I must repeatedly ask Executive and Council to provide at least reports on their areas of activity, often without ever receiving such reports, then I question the value of putting my time into producing the newsletter.

It is all too easy to say our Society is at a crossroads and I am not sure it is as clear as that, but I have to say that to me, our future looks distinctly uncertain, the road ahead shrouded in "mist". If we don't, collectively, do something soon to revitalise our Society, then I doubt we can look to the future with optimism. We all have busy lives, I suspect, but we increasingly focus on our own busyness, and use that as an excuse to avoid putting time and effort towards a broader objective, yet it could be argued that more than ever, toxinology needs a strong united voice, a voice that increasingly is missing or muted. It is not up to the Secretary/Treasurer to change that. It is up to you, the membership and, beyond you, the broader toxinology community, so many of whom are not part of our Society at this time.

On a brighter note, Society finances are improved over those I reported in 2012. Society funds are held in two bank accounts plus our PayPal account. Funds are currently listed in Aus\$, but for the PayPal account, the money is actually collected in US\$ and so held in US\$. It should be noted that varying exchange rates will significantly affect the value of funds held, depending on the currency in which any expense is incurred.

As of September 15th, 2015, the Society had Aus\$15,487.21 in bank accounts and Aus\$64,966.12 in the PayPal account (US\$47,594.72). In total, converted to Aus\$, this amounts to Aus\$80,453.33 in Society funds.

This compares to a total of Aus\$32,867.45 in Society funds at the time of the 2012 AGM, an increase of 245%.

The reasons for this substantial increase in funds is multifold. Firstly, the funds held in the PayPal account have been artificially inflated in Aus\$ because of the substantial fall in the Aus\$ exchange rate against the US\$ in recent months. Funds are collected by PayPal in US\$, not Aus\$.

Secondly, expenses for the Society have been tightly controlled. There are no postage or related expenses, since all communication is now by email, and this has removed a major recurrent cost for the Society. A number of other services such as the Society website (www.toxinology.org) are currently hosted free and the maintenance is also free. It should not be assumed this will always be the case, particularly once I am no longer Secretary/Treasurer and linked to the University of Adelaide.

The only expenses for the Society currently being billed are related to assisting Society congresses. Where requested, Council authorises financial grants to congress organisers. For World congresses, there is a further cost in funding travel expenses for the Redi Awardee. Since there have been no World congresses since 2012, until 2015, and the Awardee for 2015 has not yet submitted an invoice for travel expenses, this potential outlay has not occurred within the accounting term considered here.

The Society has provided funds to support the Oxford World congress, though the amount allocated by Council, US\$10,000, has not been fully invoiced by the congress at this time. At the request of the congress organisers, the bulk of this money was made available to them early in the organisation process.

Funds paid to support the Oxford World congress are as follows:

17-8-15 - Aus\$13.25

7-7-15 - Aus\$3,014.49 (£3,760.00 at the exchange rate operating at transfer date)

2013 - Aus\$6,649.65 (£3,760.00 at the exchange rate operating at transfer date)

Funds paid to support the Pan-American Section congress in Brazil:

2013 - Aus\$2,843.30 (US\$2,500.00 at the exchange rate operating at transfer date)

Funds paid to cover a portion of the budget overrun incurred by the organisers of the Hawaii World congress in 2012:

2013 - US\$2,500.00

There is a potential outstanding liability, the amount of which is uncertain. Our President, Alan Harvey, kindly negotiated with Elsevier to provide online access to Toxicon for all financial members of IST. This was originally to have been at a cost to the Society of about £2,500.00 per year, but to this date the Society has not received any accounts requesting this be paid and since this service is problematic for some members to access, I would think Council might query paying this, at least for past years.

Society funds have reached a point where they may be able to generate some income through interest, but this has not been activated because, at least in Australia, this may incur taxation-associated costs. I will be recommending to Council that a small subcommittee be established to investigate best options for maintaining Society funds into the future.

I also will be suggesting to Council that we should consider using the funds to more actively engage with running Society congresses, with a potential to earn further funds from running congresses. This will need careful consideration, to ensure the risks to Society funds do not outweigh potential benefits.

Our President, Alan Harvey and I have developed guidelines to assist members seeking to organise a congress on behalf of the Society, including an Excel budget template. There is more we could do, if we so choose, including establishing a congress section on the Society website and using this to provide information to potential registrants, collect congress registration fees, allow abstract submission and evaluation, and other standard requirements that otherwise might require congress organisers to employ a professional conference organiser. A number of societies run their congresses through their websites.

Lastly, at the AGM we usually consider annual membership dues. These were raised to US\$55.00 in 2012. It will be a matter for Council to decide if they should be altered, but it is my expectation they will remain unaltered until the next opportunity to consider changes, in 2017.

Julian White
Secretary/Treasurer
International Society on Toxinology
September, 2015

Message From 2015 Oxford IST World Congress Organisers



The Organisers of IST's 18th World Congress of Toxinology thank you for your appreciative messages and are delighted and relieved that you enjoyed our Congress.

We were blessed with marvellous weather, Oxford's beautiful buildings, outstanding plenary speakers and, most of all, tremendous international participants and contributors.

We hope that the attached will remind you of Oxford and will tempt you back here with your families on some future occasion.

Warmest best wishes for Christmas and The New Year,
David, Eddie and Sohail



IST 2015 Oxford Press Release (IST 2015 Oxford Press Release) 30 September 2015

INTERNATIONAL SOCIETY OF TOXINOLOGY – PRESS RELEASE – FOR IMMEDIATE RELEASE

Venom experts say death & disability from snakebite up to double current estimates WHO and governments need to correct data & prioritize snakebite as a killer disease

Oxford, 30 September, 2015 – Venom experts attending the International Society of Toxinology (IST) biennial [every 2 years] meeting presented new evidence showing that snakebite deaths, disability and DALYs lost are more than twice current WHO and Global Burden of Disease estimates. They called on WHO and governments to reinstate snakebite as a Neglected Tropical Disease (NTD). They warned that not only are antivenom stocks running dangerously low, but there is also a real crisis in the quantity and quality of antivenoms in rural areas, where they are needed most. Where there is antivenom, too often health staff do not have the training or know how to administer it safely or effectively to patients.

“Snakebite kills more people than other Neglected Tropical Diseases combined, but is almost completely ignored and grossly underestimated – WHO and governments need to adjust their data and rank snakebite where it belongs, as a very real public health and medical concern, which needs funding, training and focus.” Said Prof. Alan Harvey, President of the International Society of Toxinology.

Over 400 leading scientists, toxinologists and clinicians came together over five days to exchange research findings and information in Oxford. They showed how great improvements could be made quickly and cheaply in the treatment and management of snakebite – if there is the political will at a global and national level:

- They reaffirmed the size and severity of the clinical problem. A summation shows that snakebite kills up to 200,000 per year, this is twice the currently accepted estimates.¹ This includes new evidence that 46,000 people die of snakebite in India alone (WHO estimates 10,000) and 6,000 in Bangladesh.
- From Nigeria to Nepal to Papua New Guinea, there is a real crisis in the quantity and quality of antivenoms available. There is an urgent need to improve the training of medical staff to diagnose and treat snakebite.
- Anti-venom is produced using 100 year-old methods. New research promised improved understanding of the composition of venoms and design techniques to manufacture antivenoms – including proteomics.

Despite high mortality levels, in 2013, WHO demoted snakebite from an NTD to a “neglected condition” with no formal programme and in 2015 dropped it altogether. WHO no longer has staff or expertise allocated to snakebite. WHO needs to reinstate snakebite as a leading Neglected Tropical Disease. From a disease burden perspective, it should be ranked in the top three or four diseases, with a program to treat and prevent snakebite.

“We humans and our primate cousins have an innate fear of snakes and other venomous animals – so our instinct is to run away. Unfortunately this revulsion for snakes has clouded the judgement of Ministers, donors and WHO leadership to the point where they are ashamed to admit and do anything about the public health burden of snakebite.” Said Prof David Warrell, International Congress of Toxinology Co-Presidents and medical doctor. “The sad thing is that the evidence is

there – we can do so much with so little – but there needs to be a degree of political leadership and honesty about death and disability from snakebite.” He concluded.

The Global Burden of Disease report, published in the Lancet three weeks ago, also grossly underestimates the severity of the problem. Contact with venomous animals accounts for 3 million DALYs around the world – this includes snakebite, scorpion stings, spiders, stingrays, jellyfish, insects etc. One DALY can be thought of as one lost year of “healthy” life. New data presented in Oxford show that snakebite alone accounts for at least six million DALYs lost – including 320,000 in West Africa alone and 3 million in India – without factoring in chronic complications.²

Snakebite mainly affects people living in rural areas. With no health facilities nearby, and unable to afford expensive treatment, many either turn to traditional healers or don’t seek care at all. This suggests that the number of victims is probably higher than officially reported. If available, antivenom treatment can cost up to US\$250-500 per victim, representing the equivalent of four years of salary in the countries concerned. Subsidizing antivenom costs so that patients pay little to nothing is crucial to improve access to this life- saving treatment.

For further information or comment, please call:

Professor David Warrell cell: +44 7785242978, or email warrell@ndm.ox.ac.uk

Professor Alan Harvey cell: +353 87 210 7547, or email Harvey@dcu.ie

The 18th World Congress on Animal, Plant and Microbial Toxins (25-30 Sept) concludes today. It is the premiere scientific meeting for the International Society on Toxinology (IST) <http://www.toxinology.org>, to explore the structural, pharmacological, evolutionary and clinical aspects of “natural toxins”. Founded in 1962 by a group of scientists and clinicians interested in advancing the science of toxinology. The first international meeting was held in 1966 in Atlantic City, USA and its Journal, Toxicon, was first published in 1963.

1WHO currently estimates that annually at least 100,000 people die from snake bites, and around three times as many suffer from amputations and other permanent disabilities. <http://www.who.int/mediacentre/factsheets/fs337/en>

2Just published and presented at IST – estimates of lack of funding in snakebite and allocation of donor funds to Neglected Tropical Diseases <http://journals.plos.org/plosntds/article?id=10.1371/journal.pntd.0004088>

IST Nomenclature Committee

At the last IST World Congress held in Recife, Brazil in March 2009, a symposium devoted to the topic of toxin nomenclature received significant interest from IST members. The IST Council subsequently decided to form a nomenclature committee to examine the issue of toxin naming standards and recommend possible solutions. The mandate of this committee was to propose a nomenclature system, with interim reports to IST Council and a "final" report to be delivered at the IST World Congress in 2012. This deadline was not met, but it is hoped progress will be made in the following triennium. If you have any comments or suggestions on toxin nomenclature, could you please send them to a member of the nomenclature committee, which is currently comprised of the following members:

Dr Gerardo Corzo, Mexico (Email: corzo@ibt.unam.mx)

Dr Florence Jungo, Switzerland (Email: Florence.Jungo@isb-sib.ch)

Dr Evanguedes Kalapothakis, Brazil (Email: ekalapo@icb.ufmg.br)

Prof. Glenn King, Australia (Chairman; Email: glenn.king@imb.uq.edu.au)

Prof. Manjunatha Kini, Singapore (Email: dbskinim@nus.edu.sg)

Prof. Graham Nicholson, Australia (Email: graham.nicholson@uts.edu.au)

Prof. Toto Olivera, USA (Email: olivera@biology.utah.edu)

Prof. Jan Tytgat, Belgium (Email: jan.tytgat@pharm.kuleuven.be)

ArachnoServer spider toxin database

ArachnoServer is a manually curated database that provides detailed information about proteinaceous toxins from spiders. Key features of ArachnoServer include a new molecular target ontology designed especially for venom toxins, the most up-to-date taxonomic information available, and a powerful advanced search interface. Toxin information can be browsed through dynamic trees, and each toxin has a dedicated page summarising all available information about its sequence, structure, and biological activity. ArachnoServer currently manages 567 protein sequences, 334 nucleic acid sequences, and 51 protein structures. ArachnoServer is available online at www.arachnoserver.org.

The IST has established a special wiki site for members of this Nomenclature Committee to use to both communicate and develop information and recommendations. Members of the committee will soon receive an email detailing how they may access this site.

IST Snake Taxonomy Advisory Group

Keeping up with changes in taxonomy for venomous animals is always a challenge for toxinologists, but it is important to do so, if published research is to maintain viability longer term, as taxonomy evolves. To improve dissemination of information on taxonomic changes the IST has invited Assoc. Prof. Scott Weinstein (Australia/USA) to chair the snake taxonomy committee with a view to generation of regular taxonomy updates which can be made available to members.

We will consider making these updates available through the newsletter and, possibly, the IST website.

Julian White, Secretary IST

IST 2016

www.ist2016.com

XII Congress of the Pan-American Section of the International Society on Toxinology

Toxins by the Beach

September 18-23, 2016 Miami Beach, Florida, USA

Organizers:

Frank Bosmans

John Hopkins University
Baltimore, Maryland, USA

Frank Marí

Hollings Marine Laboratory
National Institute of Standards and Technology
Charleston, South Carolina, USA



*XII Congress of the Pan-American
Section of the International Society
on Toxinology*

September 18-23, 2016
Miami Beach, Florida, USA

Toxins by the Beach

The 12th Pan-American Congress of the International Society on Toxinology, will be held on 18th -23th September 2016 at the Deauville Beach Resort in Miami Beach, Florida, USA.

- Prominent international figures in Toxinology and related disciplines .
- Guest speakers who use toxins in an academic, industrial, or medical setting.
- High-quality seminars and lively first-rate poster sessions.
- Excellent networking opportunity.

Join us for what will be a most memorable meeting against the backdrop of South Beach, a lively Art Deco Historic district, and Latin music.





*XII Congress of the Pan-American
Section of the International Society
on Toxinology*

September 18-23, 2016
Miami Beach, Florida, USA

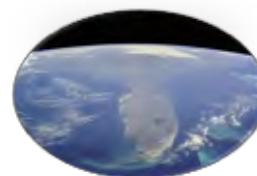
About Miami Beach

•Miami Beach is famous for having the largest collection of Art Deco architecture in the world, endless beaches, fantastic cuisine and nightlife, as well as being at the crossroads of the Americas.

•Easily accessed by three international airports (MIA, FLL, PBI).

•A tropical paradise, with year-round warm weather, turquoise waters, and world-class shopping.

•A sparkling and lively destination, Miami Beach encompasses an eclectic mixture of ethnic backgrounds.



*XII Congress of the Pan-American
Section of the International Society
on Toxinology*

September 18-23, 2016
Miami Beach, Florida, USA

Miami, FL, USA

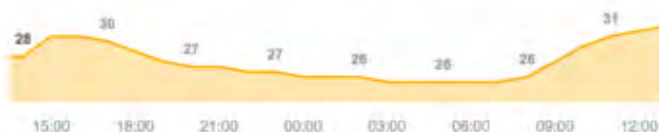
Saturday 14:00
Mostly Cloudy



28 °C | °F

Precipitation: 15%
Humidity: 78%
Wind: 12 mph

Temperature Precipitation Wind



Sat	Sun	Mon	Tue	Wed	Thu	Fri	Sat
31° 25°	32° 25°	32° 25°	32° 24°	32° 23°	31° 24°	30° 23°	31° 23°

Miami's Weather in September

•September is one of the wettest months in Miami. The city still enjoys mainly sunny skies, with some clouds and daily afternoon showers can be expected.

•The maximum temperature for September is between 88 and 90 degrees Fahrenheit (31 to 32 degrees Celsius), while the minimum temperature usually falls between 76 and 77 °F (24 to 25 °C).

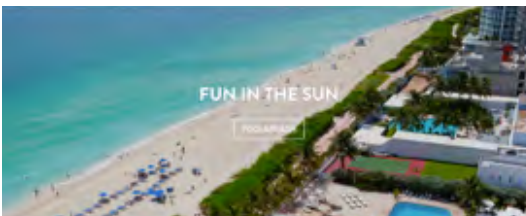


*XII Congress of the Pan-American
Section of the International Society
on Toxinology*

September 18-23, 2016
Miami Beach, Florida, USA

Deauville Beach Resort Miami

This contemporary beachfront hotel dating to the 1950s, where The Beatles stayed during their US tour in 1964, is right on the beach and only a 1.5-mile walk from the La Gorce Country Club, offering golf. Sleek rooms and suites with views of the ocean, Biscayne Bay or the city, offer 27-inch flat-screen TVs and minifridges. The property features a beach, an outdoor pool, a poolside tiki bar and a hot tub. Other amenities include a spa (fee), a fitness center, a casual restaurant and a jazz bar.



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Scientific Committee

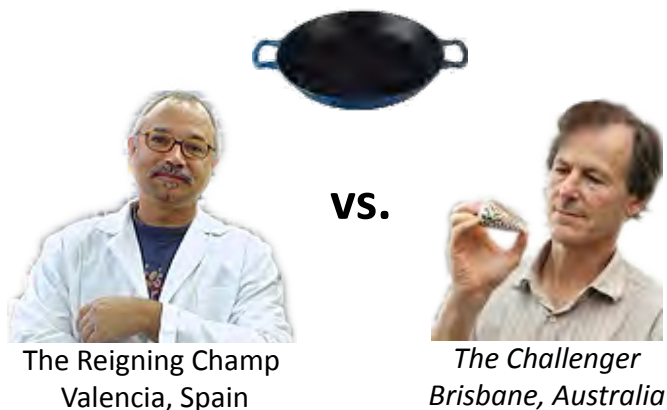
Yara Cury – Brazil
Denise Tambourgi – Brazil
Baldomero Olivera – USA
Jay Fox – USA
Kenton Swartz – USA
Richard J. Lewis – Australia
Marymeg Daly – USA

Juan Jose Calvete – Spain
Gilberto Domont – Brazil
Greta Binford – USA
Lourival Possani – Mexico
Michael Pennington – USA
Baltazar Becerril – Mexico
Jose Maria Gutierrez – Costa Rica



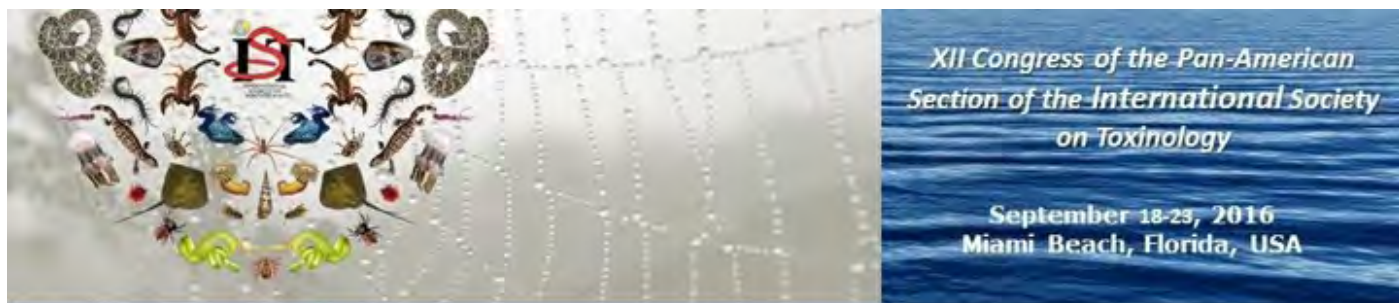
Networking, Team-Building and Entertainment

- Inaugural Reception
- Poster Mixers – Beer, Wine, Tapas
- Dinner Conference
- Music and Dance
- Paella Wars*



In a Nutshell

- Top Notch Speakers (50-60)
- No Parallels sessions (unless necessary)
- Rapid Fire Talks
- Posters – Where the action should be!



Join us!
More info at:

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Getting to Know Us

In this issue of the newsletter we introduce a new section called Getting to Know Us. The aim of this section is to introduce either an individual toxinology laboratory or an institute with a focus on venoms or toxins to the toxinology community. Each article will cover the history, major areas of interest, and primary research methods of the laboratory or institute. In this way we hope to foster collaborations between toxinology laboratories around the world.

We are delighted that Dr Robert Harrison agreed to write the inaugural article for this section covering the history and scientific objectives of the Alastair Reid Venom Research Unit at the Liverpool School of Tropical Medicine in Liverpool, England. You will find his fascinating article in this issue of the newsletter.

If you would like to contribute an article to this section on your laboratory or institute, or you have a suggestion about who we should contact for submissions, please email Glenn King at glenn.king@imb.uq.edu.au.

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The Alistair Reid Venom Research Unit

(<http://www.lstmed.ac.uk/research/centres-and-units/the-alistair-reid-venom-research-unit>)

A Brief History

Hugh Alistair Reid's interest in the medical problems of snake bite began after he joined Penang General Hospital, Malaya as the consultant physician in 1952. He conducted several epidemiological and clinical studies on bites by sea snakes (*Enhydrina schistosa*) and the Malayan pit viper (*Calloselasma rhodostoma*) and was soon a world authority. In 1961, he founded the Penang Institute of Snake and Venom Research, which amongst other activities, supplied venom from locally caught sea snakes to the Commonwealth Serum Laboratories in Melbourne to prepare the first antivenom against this particular snake venom.

The next year, Reid, together with Findlay Russell and Paul Saunders, founded the International Society of Toxinology. Coincident with the award of the Order of the



Dr Alistair Reid. OBE

British Empire in 1963, he joined the Liverpool School of Tropical Medicine and founded the Venom Research Unit, whose objective was 'research to improve the treatment of envenoming'. The recruitment of David Theakston in 1974 was the start of decades of research on biological, epidemiological, diagnostic and clinical aspects of snake bite in West Africa and elsewhere, and the designation of the Liverpool School of Tropical Medicine as a World Health Organisation (WHO) Collaborating Centre for the Control of Antivenoms. The Venom Research Unit was renamed the "Alistair Reid Venom Research Unit" in commemoration of Dr Reid who died in 1983.



Echis ocellatus: the most dangerous African snake?



Permanent disfigurement in a child victim of a cobra bite (DA Warrell)

Under David Theakston's leadership and the recruitment of key individuals (Gavin Laing and Paula Sells) the unit consolidated its reputation as a centre of excellence for efficacy testing of new antivenoms, immunodiagnosis, the pathophysiology of venom toxins and instigated enduring collaborative links with David Warrell, Aura Kamiguti, John Harris, Ana Moura-da-Silva, Jose-Maria Gutierrez, Steve Watson and Jay Fox, amongst many others. The recruitment of Paul Rowley in 1994 provided the Herpetarium with essential expertise in the safe handling of, and venom extraction from, highly dangerous snakes – a role that Paul maintains to this day with undiminished commitment and enthusiasm. In the early 1990s, David Theakston ensured that the unit was involved in the early use of genetic techniques for the molecular characterisation and expression of venom toxins, and later enthusiastically supported Rob Harrison's first



Professor RDG Theakston

project (2000) exploring venom toxin DNA immunisation to raise toxin-specific and pathology-neutralising antibody.

Rob Harrison assumed leadership of the Unit in 2006 on David Theakston's retirement and instigated a research program to develop 'next-generation' therapies to improve the efficacy, safety and affordability of snakebite treatment: for both the potentially lethal systemic effects, and the disfiguring tissue-destructive effects of snake venom. This Africa-centric research program was/is heavily reliant upon the recruited molecular and bioinformatics skills of Simon Wagstaff. This therapeutic research is increasingly informed by the phylogenetics/genomics skills that Nick Casewell's recruitment brings to the unit, and which has resulted in rapid accumulation of very high profile publications. Gareth Whiteley joined the Unit in 2012 and is exploiting his skills in molecular biology, database analysis and biochemistry on a variety of our basic biology projects. In combination, these diverse therapeutic and basic research provides the Unit with a wealth of data and material that has fuelled a succession of PhD projects (Fiona Bolton, Camila Renjifo, Maimonah Al Ghanmi, Rachel Currier, Nick Casewell, Darren Cook, Jennifer Oliver, Sidgi Hasson and Louise Affleck). All the Unit's staff and students have enthusiastically supported Rob Harrison's many efforts to raise awareness of the plight of tropical snakebite victims, whether it be through our publications, our new snakebite MSc module, our many public engagements or our hosting of over 4,000 visitors to the newly-refurbished herpetarium.



Her Royal Highness, the Princess Royal discusses the neglect of tropical snakebite victims

So while the technology and personnel may have changed substantially since Alistair Reid established the unit, our scientific objectives remain remarkably constant: research to improve the treatment of envenoming. Another constant



Drs Nasidi and Harrison of the EchiTab Study Group discuss the need for improved snakebite management with the Nigerian Federal Ministry of Health

has been the unit's outreach efforts to improve the availability of antivenom treatment for tropical snakebite victims. Thus, through the EchiTab Study Group, we were central to the provision of new antivenoms designed specifically to meet the needs of Nigerian snakebite victims – the type of medical benefit that we seek to extend to other rural, remote regions of Africa where snakebite remains a cause and consequence of poverty.



Drs Durfa, Ballah and Harrison of the EchiTab Study Group in Kaltungo, Nigeria

The Herpetarium

The Herpetarium is a UK Home Office accredited and inspected experimental animal facility and is a critical resource for all the activities of the Alistair Reid Venom Research Unit. Our lead herpetologist, Paul Rowley, and his assistant John Dunbar provide specialist care for what is the largest and most diverse collection of venomous snakes in the UK. There is a special emphasis on the African continent with the majority of our snakes being haemotoxic vipers such as Saw-scaled vipers (*Echis* spp.), Puff adders (*Bitis arietans*), Gaboon vipers (*Bitis gabonica*) and neurotoxic elapids such as the Black and Green mambas (*Dendroaspis* spp.) and several spitting and non-spitting cobras (*Naja* spp.). Paul Rowley, with the assistance of Rob Harrison and John Dunbar, extracts venom from our snakes at regular intervals and this venom is used for antivenom production, and for our therapeutic and basic science research.

The Venom Unit has worked assiduously to increase awareness of the neglect of tropical snakebite victims. Part of this includes providing talks about our research work and tours of the Herpetarium to visitors from the Armed Forces, the public, school and college pupils, and undergraduate & post-graduate University students (4,000 visitors in the past 4 years).



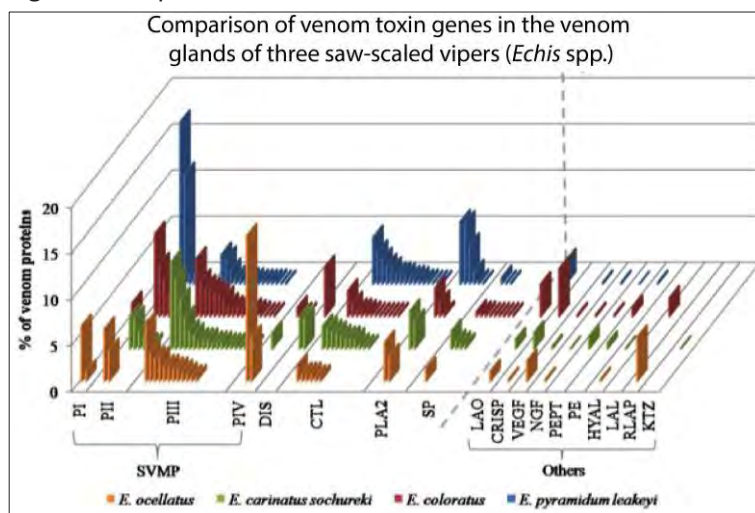
LSTM's Paul Rowley demonstrates the handling of gaboon vipers to school pupils

Our research

Throughout the 50 year history of the Unit, its objective has been to conduct a rich and diverse portfolio of research activity to investigate the basic biology of snake venoms and to improve the treatment of snakebite. Our research often employs multi-disciplinary approaches, and is funded by a variety of national and international agencies.

Venom composition and variation

A mainstay of our basic research involves characterising the toxic proteins found in the venom and the toxin-encoding genes found in the venom glands of medically-important venomous snakes. These characterisation studies provide us with essential information required to analyse how the venom composition of snakes varies from species to species and, in some cases, within a species. This is important because variation in venom composition can render specific snakebite therapies, known as antivenom, ineffective. This data also allows us to reconstruct how snake venoms and their toxins have evolved over time, which provides us with important insights into the likely pathologies caused by envenoming of different snake species.



Snake genomics

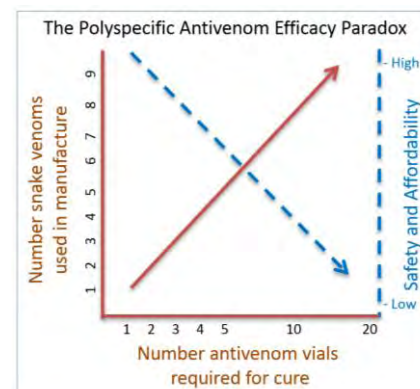
We were heavily involved in work leading to the recent publication in PNAS of the first snake genome sequences as members of the king cobra and Burmese python genome projects. These genome sequences provided us with the first complete genetic codes of any snakes, permitting us, and our collaborators, to investigate how a number of snake-specific adaptations, such as the loss of limbs, extreme digestion and venom, have arisen. Our main focus was investigating the evolution of the snake venom system and we demonstrated that venomous snakes have complex venoms as a result of a long history of duplicating toxin genes. We are currently involved in a number of other ongoing snake genome projects, including co-leading the Malayan pit viper genome project.



Therapeutic research

The ARVRU has been heavily involved in undertaking and publishing research on the development, testing and delivery of snakebite therapies known as antivenoms. These antibody-based therapeutics are the cornerstone of snakebite treatment, although their method of production has changed little over the past century: horses or sheep are hyper-immunised with harmless amounts of venom, and antivenom is prepared from the IgG antibodies isolated from the animals' blood.

Polyspecific antivenoms are required for regions like sub-Saharan Africa because of the diversity of venomous snakes, and are prepared by immunising horses with venoms from multiple snakes. This however creates a therapeutic paradox because the proportion of IgG in a vial that targets the venom of any one species is small, necessitating the administration of multiple vials to reverse effects of envenoming. However, each extra vial of polyspecific antivenom increases both the risk of severe antivenom-induced adverse effects (anaphylactic shock and serum sickness) and the cost to the patient. The focus of our therapeutic research is to dislocate the various factors causing this polyspecific antivenom paradox by developing next-generation of antivenoms designed to have unparalleled snake species efficacy, affordability and safety.



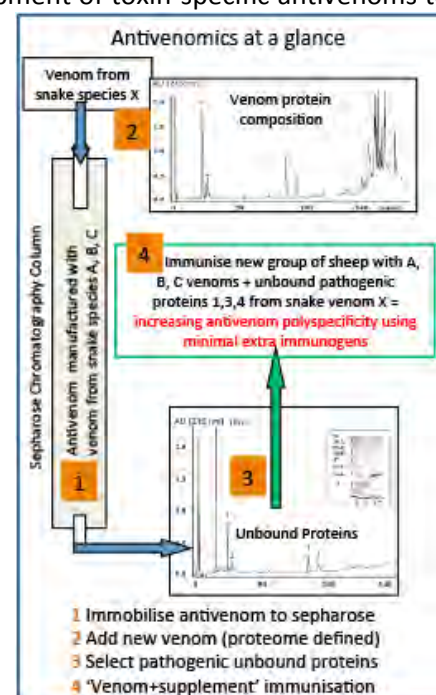
Next-generation snakebite therapies

Toxin-specific antivenoms

Using a genetic engineering approach, we are currently pioneering the development of toxin-specific antivenoms to treat envenoming by multiple snake species. By characterising the toxin genes expressed in the venom glands of different snakes, we can identify which venom proteins are common to all snake species and distinguish those that are (toxins), and are not, likely to be responsible for causing life-threatening pathology during snakebite. We interrogate these toxin DNA datasets to identify regions of these genes that are cross-species conserved and likely to generate an immune response, and then assemble these 'domains' into synthetic proteins for immunisation. The resulting antibodies are thus specific only to the pathological toxins in the venoms of multiple snake species. We anticipate that the improved toxin-specificity of these experimental antivenoms should confer greater dose efficacy over conventional antivenoms and thus greatly reduce both the risks of adverse effects and costs to the victim.

Antivenoms with extensive geographical clinical cover

Part of the reason that antivenoms are unaffordable to the rural poor is that each antivenom is specific to treating snakebite by relatively few snake species, and therefore sales and profit for the antivenom manufacturer are low. Producing a single antivenom for use in an entire geographical region should provide economies of scale to make antivenom manufacturing more amenable



to commercial entities. To this end we are using “antivenomic” approaches to improve the geographical cover of existing antivenoms. By first using proteomic technologies to identify which snake venom toxins are not neutralised by an existing antivenom, we can then isolate those toxins and add these to the immunising mixture. By doing so, the new version of the antivenom should show greater efficacy to additional snake species found in the region of interest. We are currently using this approach, in collaboration with Professors Juan Calvete (CSIC, Valencia) and Professor Jose-Maria Gutiérrez (ICP, San Jose) and their colleagues, to develop a new antivenom for the whole of sub-Saharan Africa.

A therapy for venom-induced local tissue pathology

Envenoming by many snakes causes extensive tissue death (necrosis). Antivenom IgG is administered intravenously to treat systemic envenoming, but is too large (150 kDa) to rapidly cross the blood/tissue barrier to neutralise the venom toxins responsible for causing necrosis. Surgical debridement or amputation of the affected tissue is therefore performed to prevent spread of life-threatening gangrene. This problem is so commonplace that 8,000 amputations are performed on snakebite victims every year in Africa alone. We were the first to demonstrate that the uniquely small parts of camelid IgG (VHH) provide the most dose-effective immunotherapy ever developed against the local tissue-destructive and systemic effects of snake venom. The research challenge is to modify this novel experimental result into a venom-necrosis therapy for Africa that is affordable, effective at ambient temperatures and easily applied as an immediate First Aid tool.

Collaborations

We are not a core-funded Science Unit graced with a large number of staff, however we have greatly enjoyed and benefited from the research that we have conducted with numerous friends and colleagues, many within IST, and some of our current, greatly valued collaborators are listed here:

Global Snakebite Initiative: <http://www.snakebiteinitiative.org/>

Health Action International: <http://www.haiweb.org/>

Institute of Primate Research (Kenya): www.primateresearch.org

Instituto Butantan (Brazil): www.butantan.gov.br

Instituto Clodomiro Picado (Costa Rica): <http://www.icp.ucr.ac.cr/index.php>

Prof. Juan Calvete (Instituto De Biomedicina De Valencia): <http://www3.ibv.csic.es/index.php/es/investigacion/genomica/upr>

A/Prof. Todd Castoe (University of Texas at Arlington): http://www.snakegenomics.org/CastoeLab/Castoe_Lab_Home.html

Snake Genomics website <http://www.snakegenomics.org/SnakeGenomics/Home.html>

Dr. Freek Vonk (Naturalis Biodiversity Centre): <https://science.naturalis.nl/en/people/scientists/freek-vonk/>

Prof. Michael K. Richardson (Leiden, Netherlands): <http://www.science.leidenuniv.nl/index.php/ibl/richardson>

Prof. Bryan Fry (University of Queensland): <http://researchers.uq.edu.au/researcher/540>

Prof. Glenn King (University of Queensland): <http://www.imb.uq.edu.au/glenn-king>

Dr. Wolfgang Wüster: <http://mefgl.bangor.ac.uk/staff/wuster.php>

Dr. David Gower (Natural History Museum): <http://www.nhm.ac.uk/our-science/departments-and-staff/staff-directory/david-gower.html>

Prof. Abdulrazak Habib (Bayero University, Kano, Nigeria):

Emeritus Prof. David A Warrell: <http://www.ndm.ox.ac.uk/principal-investigators/researcher/david-warrell>

Alistair Reid Venom Research Unit publications (selected papers over past 5 years)

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MYANMAR (BURMA) SNAKEBITE PROJECT

Report to IST by Prof. Julian White

In early 2014 I was approached by a colleague, Dr. Chen Au Peh, a renal physician based at the Royal Adelaide Hospital Dept. of Renal Medicine, in regard to the possibility of developing a foreign aid project to tackle the snakebite problem in Myanmar. On his frequent visits to Myanmar to assist with development of renal medicine services in that country, Dr Peh had noted the huge snakebite burden, with more than 70% of cases of renal failure being due to snakebite, specifically Russell's viper bite.

Dr. Peh, myself and Dr. Afzal Mahmood (a public health expert), all from the University of Adelaide, worked on developing an initial submission for funding from the Australian Government, Dept. of Foreign Affairs and Trade. We also involved Assoc. Prof. Scott Weinstein (the second clinical toxicologist in my dept. at the Women's & Children's Hospital, Adelaide) and Dr. Sam Alfred (an emergency physician from the Royal Adelaide Hospital and also involved with my dept.). Our "expression of interest" was one of those which were successful and we were then invited to submit a full submission for funding. This was completed in late September and at the end of October we were notified our submission was successful.

The project we had submitted had a combined value of nearly \$4 million, making it possibly the largest foreign aid grant to deal with snakebite ever made. It is important to note this is a foreign aid project, not a research project, and funds are for foreign aid purposes only, so that any "research" that might be involved is only in the direct service of the foreign aid objective for the project. It is clearly very clinically focussed, not venom research focussed. The total monetary value of the project is made up from a grant from the Australian government, matched by "in kind" contributions (mostly staff time) from government ministries in Myanmar and from participating Australian organisations.

Project Title

Improving the health outcomes for snakebite patients in Myanmar

Summary of Project

Snakebite is a major cause of mortality and morbidity, particularly among the farming poor in Myanmar. The central aim of this Project is to address this problem through the identification and implementation of achievable objectives. In response to requests from the Ministries of Industry and Health in Myanmar, the University of Adelaide will partner with CSL Limited and University of Sydney to improve the health outcomes for snakebite patients in Myanmar by applying a coordinated and systematic approach:

- (1) to improve the quantity and quality of antivenom production,
- (2) to increase the availability of antivenom to health centres especially in rural regions, and
- (3) to optimise the management of snakebite patients at the community level.

This Project intends to apply a comprehensive strategy to each of these areas through the use of a team of experts, supporting Myanmar colleagues to build local capacity and resolve local problems sustainably.

Key Implementation Steps

At a workshop in Myanmar (July 2014), a team comprising experts from Australia, the Ministries of

Industry & Health planned the following strategies (first 2 operating at a national level; the 3rd at regional level).

1. IMPROVING ANTIVENOM PRODUCTION:

Improving the quantity and quality of antivenom is a key to this Project. Current production is inadequate to meet the need. The Project will:

- 1.1 Improve the health and survival of horses used for antivenom production towards the standard benchmark of <1%.
- 1.2 Develop sustainable availability of venom used in immunisation of horses.
- 1.3 Establish quality control of production processes.
- 1.4 Determine the mix of venom used for immunisation.
- 1.5 Improve animal welfare (snakes & horses).

2. INCREASE THE AVAILABILITY OF ANTIVENOM:

2.1 The lack of electricity mandates a change from liquid to lyophilised (freeze dried powder) form of antivenom to avoid cold chain requirement. We will assist in establishing lyophilisation capacity in Myanmar.

2.2 Currently there is suboptimal distribution of antivenom. We will develop a trackable distribution system to reduce waste, to maximise availability of antivenom when and where needed, and to redress the supply-need mismatch.

3. OPTIMISE THE MANAGEMENT OF SNAKEBITE PATIENTS:

3.1 We will undertake clinical and epidemiologic surveys to establish the health system capacity to respond to snakebites, using selected Project townships.

3.2 Strategies will be implemented to improve responsiveness in terms of timely and appropriate management at community health centres to reduce morbidity and complications from snakebites.

3.3 Training programs will be developed using international experience, and implemented in Project townships to train front-line community health workers for timely and appropriate management of snakebites.

3.4 First-aid options will be examined, selected, and tested to ensure applicability in rural settings.

3.5 Strategies to strengthen primary prevention will be implemented in the Project townships.

The project commenced in late 2014 and is scheduled to complete the initial funded phase in mid 2018. It is likely that some project activities will continue past this time. The benefits produced through this project should be sustainable in the long term in Myanmar and the underlying aim of the project is to empower the people of Myanmar to sustain good outcomes for snakebite patients into the future.

ORGANISATIONS INVOLVED IN THE PROJECT

In Australia

Coordinating Organisation

University of Adelaide, Faculty of Health Sciences

Organisations linked through the University of Adelaide

Royal Adelaide Hospital; Departments of Renal Medicine and of Emergency Medicine

Women's & Children's Hospital; Toxinology Department

Veterinary School, University of Adelaide

Partner Organisations

bioCSL Ltd (Melbourne)

University of Sydney (Sydney)

Other participating organisations

Venom Supplies, Tanunda

Australian Animal Health Laboratories, Geelong

University of Frankfurt, Germany

In Myanmar

Government of Myanmar; Departments of Health, of Industry, of Forestry and of Livestock

Myanmar Medical Association

The Project Team

Project Team Leaders (Project Executive Committee)

Dr. Chen Au Peh; Renal Physician, Royal Adelaide Hospital (overall Project Leader)

Prof. Julian White; Clinical Toxinologist, Women's & Children's Hospital

Dr. Afzal Mahmood, Public Health Expert, University of Adelaide

Other Principal Team Members (outside of Myanmar)

Assoc. Prof. Scott Weinstein, Clinical Toxinologist, Women's & Children's Hospital

Dr. Sam Alfred, Emergency Physician/Toxicologist, Royal Adelaide Hospital

Prof. Bob Cumming, Epidemiologist, University of Sydney

Prof. David Warrell, Emeritus Tropical Medicine Consultant, University of Oxford

Prof. JM Gutierrez, Toxinologist/Antivenom Expert, University of Costa Rica

Mr. Keiran Ragas, Antivenom Expert, CSL Ltd

Dr. John Moody, Veterinarian/Antivenom Expert, CSL Ltd

Mr. Nathan Dunstan, Herpetologist/Venom Extraction Expert, Venom Supplies

Dr. Lucy Woolford, Veterinary School, University of Adelaide

Dr. Debbie Eagles, Australian Animal Health Laboratories, CSIRO, Geelong

Dr. Ulrich Kuch, Frankfurt, Germany

There may be other experts, including IST members, who we may approach to be involved in some way with this project, as project needs dictate.

In addition there are a number of colleagues in Myanmar who are critical to the success of the project. Our project executive group have made numerous trips to Myanmar where we had the privilege of interacting with both clinical colleagues and senior government officials and establishing the vital personal links that make the project possible. We received clear support from all four Myanmar Government ministries involved.

In 2015 the Project moved into full action and the following is a summary of achievements so far:

Antivenom production: Numerous improvements have been made in antivenom production, particularly in regard to snake and horse health and husbandry. All the snakes used to produce venom for antivenom production have been moved to the new snake farm facility. Most are now housed in special clear plastic individual containers, in a temperature-controlled environment, with records now kept for each snake. Snake survival has markedly increased and some breeding success has occurred, a first for the Myanmar antivenom production facility and another sign of improving snake health/husbandry. Several key Myanmar staff have undertaken training in snake husbandry at Venom Supplies in Australia under the guidance of Nathan Dunstan (an IST member).

More detailed records are being established to better track horse health on an individual basis. A database has been created to assist this process. Improved housing for horses, expanded paddock space, better food and other interventions have seen a dramatic improvement in horse health and survival rates, with most recent data showing the highest horse survival rates ever recorded by the

Myanmar antivenom facility. Key staff have undergone training in Australia to improve both horse husbandry and systems to determine causes of ill health and death, including specific autopsy training. Training has been supervised by Dr. John Moody and colleagues at bioCSL Ltd (now renamed Seqiris) in Melbourne, Dr. Lucy Woolford and colleagues at the Veterinary School, University of Adelaide, Roseworthy campus, and Dr. Debbie Eagles and colleagues at the Australian Animal Health Laboratories, CSIRO Geelong campus. Myanmar staff have also been trained in relevant laboratory techniques and have been guided through development of new ELISA-based assays for anti-snake venom antibody levels in production horses, to minimise the need for destructive live mouse assays. Foreign aid-funded equipment, notably haematocrit analysers, have allowed much improved monitoring of horse health and better selection processes for new stock animals.

The net result of these activities and interventions has been a significant increase in the efficiency of antivenom production, allowing the Myanmar antivenom production facility to approach a capacity filling the entire country antivenom requirements. This is a major step forward.

The project has contributed funding towards purchase of a commercial lyophiliser that will allow production of freeze dried antivenom. This will alleviate storage issues in remote health facilities, where power is often unreliable. This ties in with efforts to improve antivenom distribution and availability. Within Project pathfinder sites all available antivenom will soon be exclusively Myanmar product. This is possible because of the improved antivenom output, strong cooperation with staff in the Ministry of Health, and the Project sourcing a number of WHO-approved solar powered fridges, the latter avoiding some of the problems of poor power supply affecting many rural health facilities.

On the clinical side a series of visits to Myanmar and cooperative meetings with key medical colleagues there has enabled development of new patient record systems for snakebite patients, combined with newly developed diagnostic and treatment algorithms. These will shortly be trialled in pathfinder sites to determine their effectiveness. After visiting many potential pathfinder sites, both major and rural health facilities across the country, the Project, in concert with the Myanmar Ministry of Health, has selected key pathfinder sites. These are mostly based around the Mandalay General Hospital and two adjacent township regions, Kyaukse and Madaya, plus at a later stage, hospitals in and around Yangon. A number of the clinical expert team involved in this (and other) aspects of the Project are IST Members (Prof. Julian White, Prof. David Warrell, Prof. Scott Weinstein).

Training of consultant-level Myanmar doctors to become local trainers for health staff has commenced and these new trainers have commenced training of medical staff in Kyaukse and Madaya districts. This process is ongoing.

The public health aspects are at an advanced stage of organisation, with key staff employed in Myanmar and initial village-level surveys and education programs about to commence in early 2016. These will provide detailed data on the real rate and impact of snakebite in rural communities in Myanmar which, in turn, will allow more informed health system planning and resource allocation.

The Project has established a working relationship with internationally recognised herpetologist, Dr. Ulrich Kuch (Frankfurt, Germany) to link with his existing project to map the venomous snake fauna causing bites in Myanmar. Dr. Kuch is an IST Member.

The Project has ongoing funding kindly provided by the Australian Government Department of Foreign Affairs and Trade through till at least the middle of 2018. Project staff are very grateful for the continuing support and generosity of the Australian Government in enabling the Project to occur. Project staff are also grateful to our respected employing institutions for allowing us time to undertake this work, both in Myanmar and in Australia and in particular wish to acknowledge; the University of Adelaide, the Royal Adelaide Hospital, the Women's & Children's Hospital, bioCSL Ltd, CSIRO AAHL, the University of Sydney.

REPORT ON THE IST WORLD CONGRESS, OXFORD, SEPTEMBER 2015

Julian White

The following report is part of an internal report I prepared for my hospital on an extended overseas trip, which included my attendance at the IST World Congress. The views, opinions and comments are my own personal comments and do NOT represent any official IST opinions or comments. If any presenter I mention in this report is unhappy about my views, opinions or comments expressed herein, I hereby apologise in as far as appropriate, for any distress I may have inadvertently and unintentionally caused. Clearly it is the nature of scientific discourse that colleagues may not share the same views, opinions, comments or interpretations of scientific studies and I reiterate that while the views, opinions, comments expressed herein are mine, and I am entitled to them, they should be read as being my personal opinions etc, where opinions are expressed, not uncontested statements of fact. I have tried to provide an honest and, as far as practicable, factual portrayal of those presentations I was personally able to attend during the Congress.

I have not included anything about the very many valuable posters presented during the Congress. Possibly I will include a selection of these relating to clinical toxinology in a future edition of the newsletter.

The Congress was very busy, with concurrent sessions and a separate clinical stream, such that I had little opportunity to attend sessions on venom/toxin research, because the clinical stream sessions were so relevant to my work. If I had a disappointment with the Congress it was that inability to be in two separate sessions at once, so that I missed out on the many doubtless excellent venom/toxin research presentations. I hope other Congress attendees can put together reports on these venom/toxin sessions that can be published in future editions of this newsletter.

Please note that the full report contains information on other aspects of my trip, other meetings attended, and these sections have been excluded from the report presented here.

Lastly, I take this opportunity to thank the organisers of the Congress for presiding over such a worthwhile meeting and the many attendees who presented at the Congress, either via oral or poster presentations. To all of you your work is important and valued and it was a privilege to be exposed to it.

Julian White

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IST World Congress, Oxford, UK, September 24th to 30th

This is the major international congress for IST. Until this year it was held every 3 years, but from this year onwards it will be held every second year, with intervening years being a regional congress, on a rotating schedule.

This congress was held at the Examination School and the Sheldonian Theatre, University of Oxford, UK. The main congress ran from September 25th to 30th. There were 3 concurrent 1-day pre-congress workshops and I was involved in planning one of these, on clinical toxinology. This was the best attended workshop. I gave 4 lectures in this workshop, so was the busiest faculty member, together with my co-organiser, Prof. David Warrell (University of Oxford).

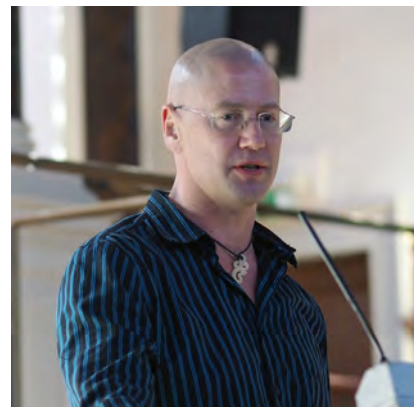
The main congress was attended by over 400 registrants, with a large number of abstracts accepted covering a broad spectrum of toxinology. Unusually for these congresses the exception being the congress in Adelaide in 2003), the program had a strong clinical track, such that it was essentially impossible to attend any basic toxin research sessions, except those scheduled as non-concurrent plenaries and debates. From my perspective this was a very useful congress. I presented 3 oral papers (all invited), a poster, plus was a coauthor on another oral presentation, given by my colleague Assoc. Prof. Scott Weinstein.



Scott also was one of 3 presenters on the opposing team in the major public debate in the Sheldonian Theatre. The proposition being debated was that venomousness has arisen only once in reptile evolution (the “toxicofera” hypothesis). The proponent team was led by Brian Fry and they seemed very confident of victory, but the opposing team mounted strong arguments against this theory, with Scott the outstanding speaker across both teams and the proposition was overwhelmingly defeated. This debate and defeat of this proposition was a rather important event, as this “toxicofera” theory has become dominant

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on the internet and across parts of the scientific literature, so such a convincing defeat by a premier collection of toxinology peers is most significant.



Assoc. Prof. Scott Weinstein Dr. John Mulley

Assoc. Prof. Brian Fry

A similar style debate, on the first day, considered the proposition that venomics will answer all future toxin research questions, championed by Prof. Juan Calvete (Vallencia, Spain). This proposition was also convincingly defeated.



Prof. Juan Calvete

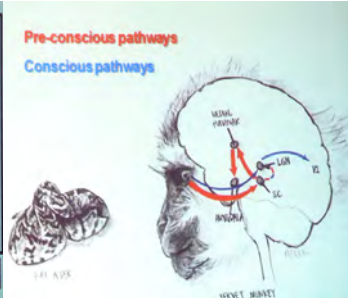
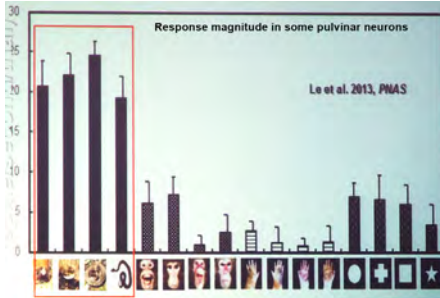
Prof. Gilberto Domonte

Audience in Sheldonian Theatre

Amongst the several plenary lectures the most memorable was the public engagement plenary by Prof. Harry Greene (Cornell University, US) titled “Primates & snakes: 80 million years of deadly dialogue?” This outstanding lecture by one of the global leaders in herpetology, presented fascinating evidence in support of the hypothesis that humans and venomous snakes have each influenced the others evolution to a great extent. For instance, in visual recognition, the snake like form has a recognition accuracy and speed for snakes, both in higher primates and human children, that is far faster than for other potential threats. From primitives tribes such as the Agta, attacks from large pythons are common and these snakes routinely feed on primates, so are a clear threat driving evolution of rapid recognition/response in our ancestors. Indeed it appears that early pythons ate large prey. With the evolution of venom and delivery mechanisms (fangs) snakes had a better mechanism to both subdue and pre-digest large prey. Venom could also be used to punish & teach potential predators, including human ancestors. As primates evolved intelligence, an upright posture and manipulative capacity they could develop strategies to avoid being bitten by snakes and kill snakes. The super-social capabilities of higher primates allows communication of potential threats, such as snakes. Amongst the Ecuadorian Waorani indians, 95% of adult males have been bitten at least once by a venomous snake during their lifetime, 50% more than once. White-faced capuchins have been recorded using clubs to kill venomous snakes. This ability may have

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pushed evolution of better defensive use of venom. The development of highly specific defensive strategies, particularly venom spitting by some cobras, appears to have arisen around the time our ancestors started to become a potential threat for venomous snakes on the ancient African savannah (“Lucy’s legacy”).



The most prestigious IST award, presented only at IST world congresses, is the Redi Award. In 2015 the Redi Awardee was Prof. “Chema” Gutierrez, from Costa Rica. He gave a very good lecture covering his lifetimes work in toxinology.



Prof. Gutierrez holding his Redi Award certificate, together with IST President Prof. Alan Harvey.

Chema used his Redi Lecture to cover the gamut of his research output, from understanding of local tissue destructive effects of viper venoms, to development of better antivenom production techniques.

Prof. David Julius presented the opening plenary lecture on the development of knowledge at the molecular level on pain sensing pathways and the major contribution of toxins as tools in this research effort.



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Prof. “Toto” Olivera (Salt Lake City, USA) provided an update on cone snail toxinology and biology.

He showed a series of new videos of cone snail hunting behaviour, while discussing the various strategies employed. The lightning strike cabal uses δ conotoxins (block Na channel in open position) & κ conotoxins (block K channel in closed position) to produce continuous action potentials resulting in excitogenic shock (“tazer & tether”). This strategy has clear advantages hunting fish, far faster than cone snails, but it is also used by snail hunting *Conus* to capture other snails, by forcing the stunned prey to remain outside the shell, so available for eating. The toxins of the motor cabal cause flaccid paralysis by affecting the Ca channel at the NMJ presynaptically (ω , ψ & μ conotoxins). Toto discussed several selected clades on *Conus*. The F1 clade of fish hunters uses a net strategy to acquire sleeping schools of fish at night, by opening the “mouth” wide and engulfing several fish, then stinging them. It releases toxins into the water which destroy the fish hair cell sensory system, preventing the fish from detecting movement, plus inject fish insulin rendering them hypoglycaemic. This combined approach was called the “net strategy” using the Nirvana cabal of toxins. From these a number of promising drug leads are emerging, including for analgesia and epilepsy control. The toxins are also proving invaluable in understanding normal ion channel structure and function.



Prof Oliver Dolly (Dublin, Ireland) on the use of botulinum toxin therapeutically titled “Molecular basis for the therapeutic efficacy of botulinum neurotoxins and new recombinant variants.

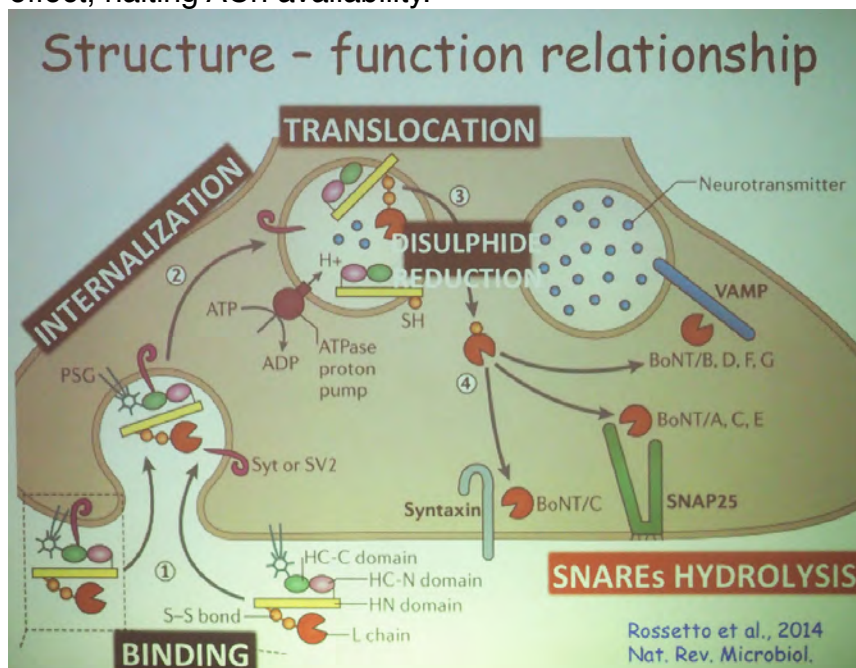
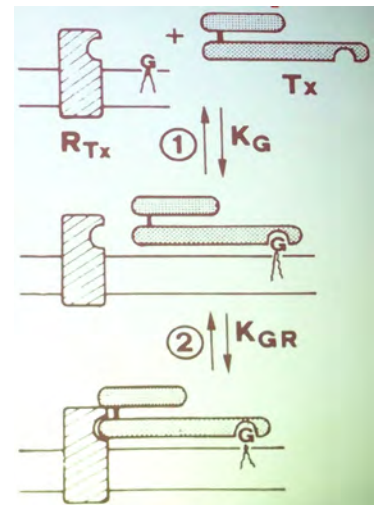
Prof. Dolly outlined the molecular mechanisms and target for botulinum toxins, noting their therapeutic efficacy is a combination of their targeting specificity (peripheral cholinergic neurons), their potency (amplification via protease activity of functional inactivation of SNAP-25 at transmitter release sites), prolonged action (stabilised intra-neuronally with persistent protease activity), tolerability and versatility (variety of neuronal target sites for specific recombinant variants).



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Prof. Cesare Montecucco (Padua, Italy) on neurotoxins acting at the neuromuscular junction.

Cesare provided an update overview of knowledge on toxin interactions at the NMJ, focussing on slow-acting enzyme toxins which inactivate all target molecules, examples being botulinum toxin & scorpion metalloproteases. Importantly, the NMJ is subject to stress and damage and so has retained an ability to regenerate. For Botulinum toxin, there are at least 75 types known, with likely many more to be described, all with a similar structure. These toxins have problems accessing their target site, but utilise a double receptor model to increase binding probability. Once bound they enter the axonal cytoplasm via ACh-releasing synaptosomes and thereafter exert their effect, halting ACh availability.



Prof. Juan Calvete (Valencia, Spain) on "the bright future of venomomics (an ironic title given his loss on the debate on venomomics).

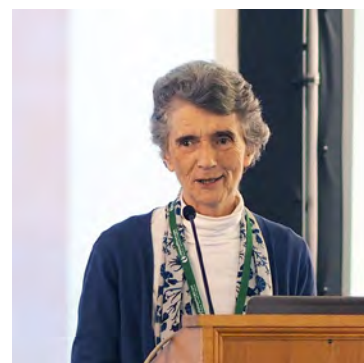
Juan presented a selected overview of his venomomics approach to toxinology research, suggesting it could deliver a profile of venoms for all ~600 species of venomous snakes within 3-4 years and that his work to date has elaborated on venom evolution and species diversification across both elapid and viperid snakes, notably in Central & South America. He used coral snakes (*Micrurus* spp.), rattlesnakes (*Crotalus* spp.) & lanceheads (*Bothrops* spp.) as examples.



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Prof. Angela Vincent (UK) on the use of animal toxins to define the human neuromuscular physiology.

Angela, from Oxford University, presented a summary history of the understanding of autoimmune neurological diseases and the vital role animal toxins have played as research tools used to define causes, through elucidation of normal and abnormal structures at the molecular level. The story starts in the 1970's, with myasthenia gravis and Lee & Chang's discovery of the post-synaptic neurotoxin α -bungarotoxin, in krait venom. This toxin targets the ACh receptor (AChR) at the NMJ and was instrumental in purifying and defining the AChR and thereby detect autoAb to it in myasthenia gravis, resulting in potential treatments. From this, an understanding of arthrogryposis in infants born to a small subset of mothers with myasthenia gravis became possible. Next was an understanding of voltage gated calcium (VGCC) and potassium (VGKC) channels in the terminal axon at the NMJ. Lambert Eaton myasthenic syndrome (LEMS), associated often with small cell lung carcinoma, and causing weakness, appeared to be associated with autoimmunity against VGCC. Using a cone snail toxins it became possible to isolate VGCC and develop Ab against them, to prove the pathophysiology of LEMS. Similarly, autoimmunity against VGKCs was demonstrated in acquired neuromyotonia using a mamba toxin against VGKC. More recently further autoimmune neurologic diseases such as limbic encephalitis, very frequent brief dystonic seizures and neuropsychiatric disturbance & movement disorders, have been elucidated using live cell-based assays, which are more problematic than toxin-based assays, but currently there are no suitable toxins known.



*OVERSEAS TRIP REPORT ~ Prof. Julian White ~ September-October 2015***Prof Peter Ratcliffe (UK) on oxygen sensing physiology**

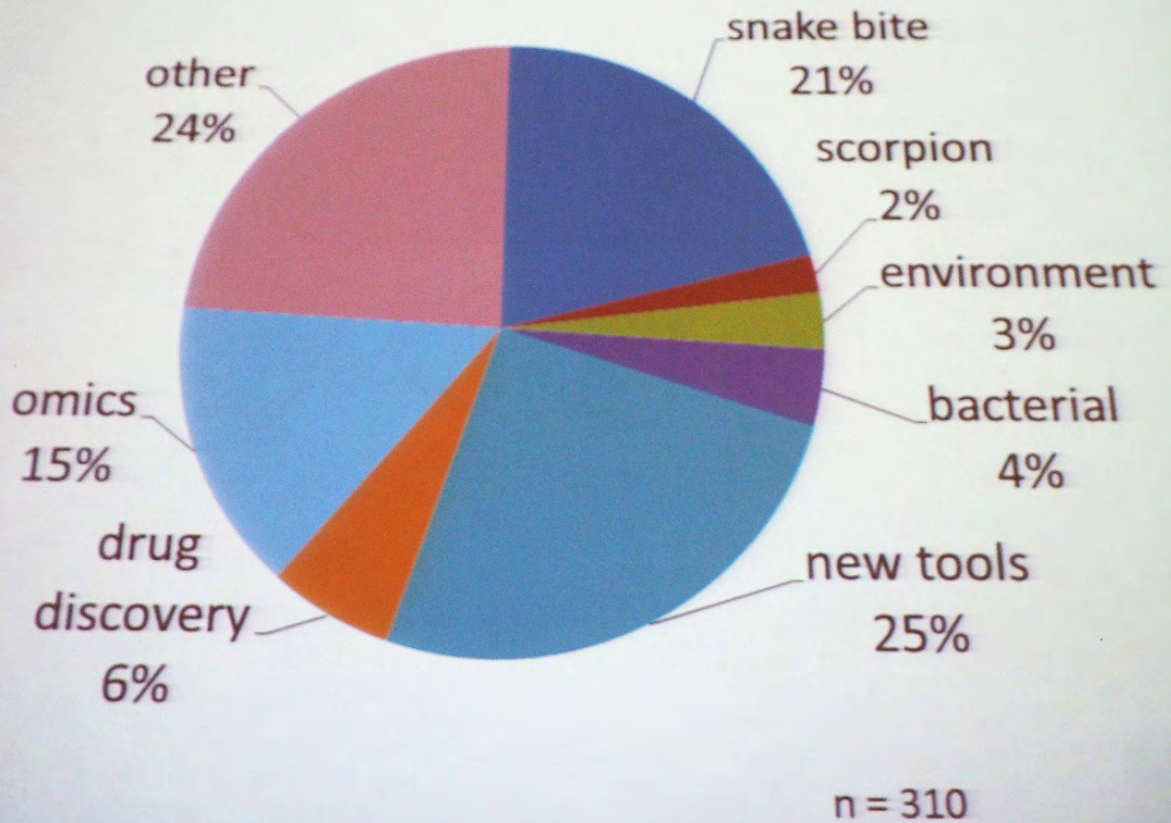
Sir Peter provided a history of research and understanding of the physiology of oxygen sensing. This commenced with an understanding of altitude physiology, with Haldane et al at Pike's Peak (Colorado, USA, ~4,400m), then understanding O₂ sensing in hypoxia and discovery of erythropoietin production in the kidney. From here the gene control of Epo developed and the key role of the hypoxia response element and HIF. HIF- α is regulated by O₂. HIF prolyl hydroxylases, a set of dioxygenases preserved throughout the animal kingdom, occupy a central role and act as sensors of O₂ level in tissues, leading to HIF transcription factors that result in Epo production. It appears that the HIF hydroxylase system is involved in many functions, not just O₂ homeostasis. Studies of Tibetans has revealed they have modified O₂ sensing at sea level, blunting responses to hypoxia. He also discussed translational medicine, predicting therapeutic responses, plus the co-opting of the HIF pathway by pathogens by both certain infections (*Leishmania donovani*) and tumours (Kaposi's sarcoma).



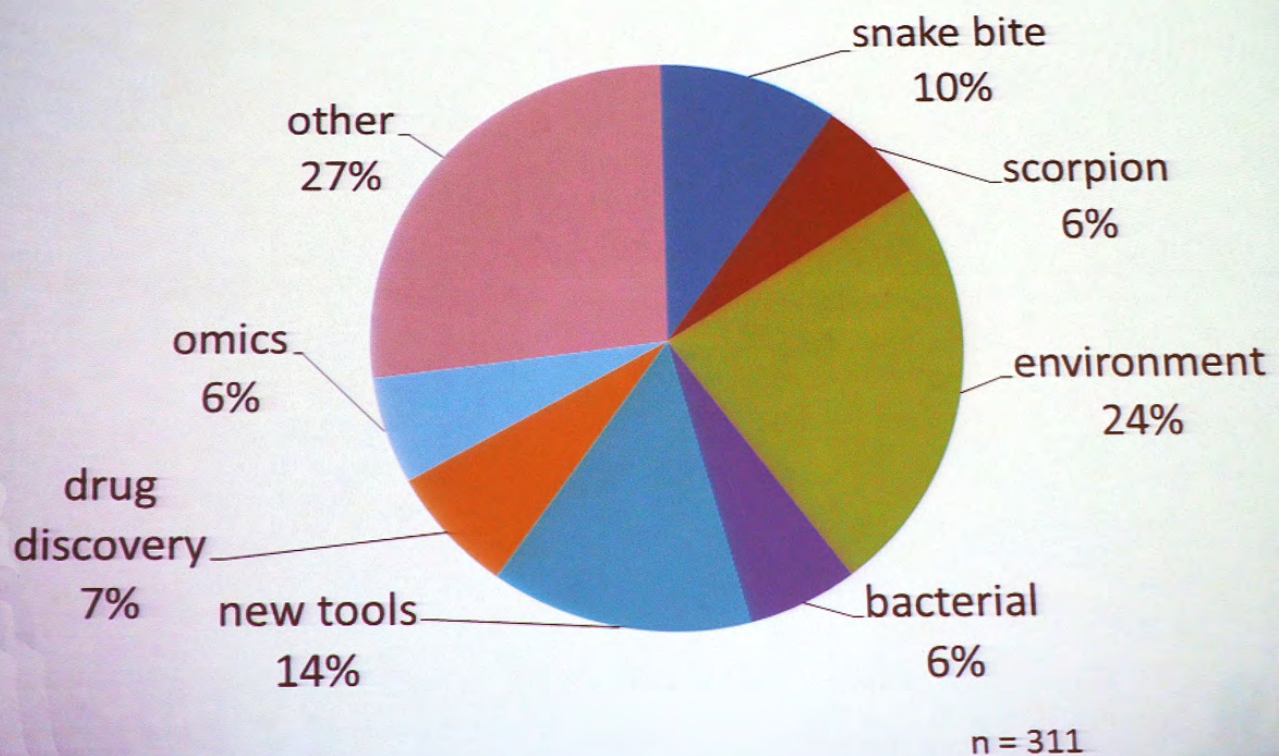
The Congress concluded with a lecture from the outgoing President of IST, Prof. Alan Harvey, who considered the progress of IST since foundation in 1962. In 1962 IST had 79 members from 23 countries, with annual subs of \$10 (\$80 in current values) and the Society journal *Toxicon* had 256 pages and cost members an extra \$80 to subscribe. In 2015 the corresponding numbers are > 400 members, 55 countries, 2115 pages, >500k article downloads/yr and free (online) to members. He listed outstanding issues as treating snakebite & scorpion sting patients, dealing with toxins in the environment, dealing with bacterial pathogens, finding new pharmacologic tools and contributing to drug discovery. He then indicated how areas of interest varied between congress abstracts versus *Toxicon* papers, finishing with a "report card" on IST progress.

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Level of interest - Oxford



Level of interest - Toxicon






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Progress?

Topic	Level of interest	Amount of progress?
treating victims of snake envenoming	6/10	4/10
treating victims of scorpion stings	2/10	1/10
dealing with toxins in the environment (mycotoxins, cyanobacterial toxins etc)	6/10	6/10
dealing with dangerous bacterial pathogens	3/10	2/10
finding and characterising new pharmacological tools	8/10	7/10
contributing to drug discovery	4/10	1/10

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APPENDIX 1: Summary of oral presentations at Oxford IST World Congress, related to clinical toxinology. These are based on my own notes on each presentation.

Speaker	Topic/Summary
José María (Chema) Gutiérrez (Keynote) 	<p>Improving the distribution of antivenoms through a knowledge-based approach: a neglected aspect of innovation</p> <p>Chema discussed equations developed for deciding on optimal distribution of antivenom, allowing decisions on how much AV is required at each location, matched against distribution of snakes and health centers. The relevant equation is $N = [(x.y) + (\alpha + \beta)] - \delta$ where N = number of AV vials to be distributed, x = number of snakebite cases, y = mean number of AV vials utilised per patient, α = subnotification, β = technical losses, δ = stocks of AV. For strategic stocks this should become $N = [(x.y) + (\alpha + \beta)] \times 2 - \delta$. He used experience in Costa Rica to demonstrate this, where mapping of problem areas for snakebite prevalence and poorer outcomes corresponded with areas of poverty. One conclusion was that placing AV in primary health care facilities and training personnel there to use AV was a viable strategy to improve outcomes, but a case-by-case analysis is required. His group are also investigating improving stability of liquid AV, using sorbitol, to avoid the need for lyophilisation. He emphasised the importance of staff training.</p>
Philippe Billiald (Keynote)	An update on the use of antibodies against envenomings
	<p>Philippe developed the idea of a “magic bullet” for development of new era AVs using monoclonal technology raised against synthetic “venom” antigens. This has been successfully developed against North African <i>Androctonus</i> scorpions and work is underway developing a similar anti-<i>Loxosceles</i> AV. He also canvassed the idea of humanising AVs to further reduce adverse reaction rates and the potential for industrialisation of AV production. He provided economic analysis indicating that for a 100,000 vial/yr output, cost would be <€8/vial, so highly competitive compared to current methodologies for polyclonal AV production.</p>
Abdulrazaq G Habib (Keynote)	Cost-effectiveness of Antivenoms for Snakebite Envenoming in 16 countries in West Africa
	<p>Abdul gave an introduction to the massive snakebite problem in West Africa, where only about 2.5% of patients currently receive AV treatment due to supply issues. His group have used a decision meta-analysis system to determine a number of factors and generate recommendations for AV use and supply. Their overarching conclusion is that AV is highly cost effective in this setting, justifying more efforts to secure good supply.</p>


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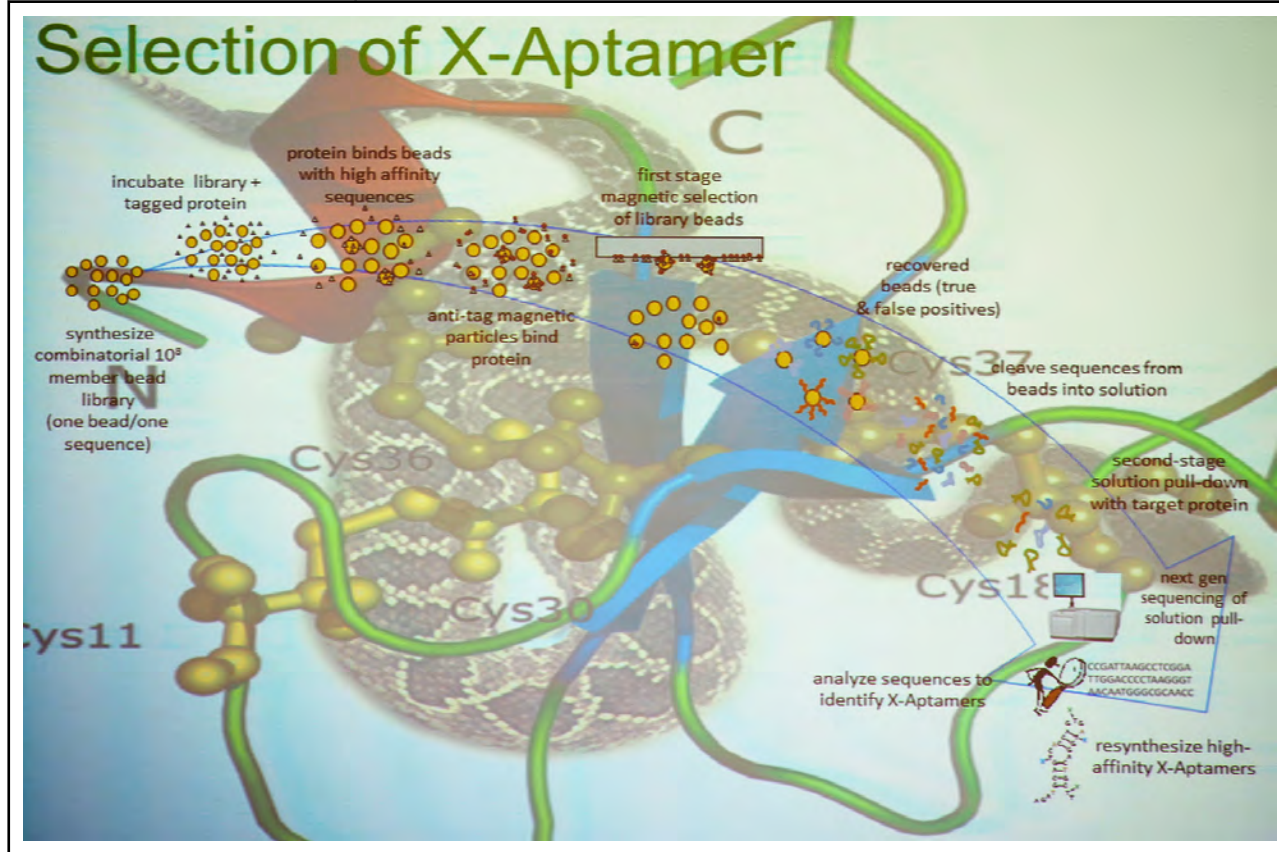
Speaker	Topic/Summary
Robert A Harrison (Keynote)	Approaches to improve the snake-species, dose and local tissue-necrosis efficacy of snakebite treatment: Next Generation Snakebite Therapies
	<p>Rob provided a review of the value of AV, noting it was generally effective against systemic effects, less so against local effects, the latter causing very significant morbidity and long term disability. However, AV availability in Africa is particularly poor, driven by factors such as cost, dose efficacy, adverse effects (anaphylactic reactions etc to poor quality AVs), plus the poor effectiveness against local venom actions. He then examined factors that reduce AV effectiveness and/or increase production cost. All current AVs are polyclonal, mostly equine, but as little as 10% of Abs in AV may be specific for major venom toxins. If this could be increased it would increase effectiveness and decrease cost. Polyspecific AVs are associated with decreased effectiveness (reduced Ab against each of the immunising venoms, declining as number of venoms used increases) and increased cost, with often increased adverse effects profile. His group are working on a different approach to providing immunogens, using molecular construction of artificial immunogens containing key conserved epitopes from a variety of toxins, so that the Ab/AV is raised against an epitope string antigen. It remains unclear if this approach will result in clinically usable AVs.</p>
David J Williams	Papua New Guinea's innovative Snakebite Research & Training Project: an international collaboration for sustainable change
	<p>David presented an outline of the large and ongoing snakebite project in PNG that has been running for some years now. Activities, coordinated from the Charles Campbell Centre in Port Moresby, include workforce training, community training (particularly use of correct first aid), research into the value of early IV fluid loading in snakebite patients, in the hope of reducing incidence of AKI, research into <i>Micropechis ikaheka</i> venom and clinical effects, improved infrastructure for managing snakebite at the Port Moresby Hospital, establishment of a specific snakebite clinic at the hospital, with dedicated resources, a rural support service including an ICU ambulance and a mobile phone based clinical advice service.</p>

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Speaker	Topic/Summary
<p>Jorge Kalil</p> 	<p>Reducing costs in antivenom production: present and future</p> <p>Jorge, who is Director of Instituto Butantan, Brazil's largest AV producer and also a major research institution, discussed factors affecting cost and innovation in AV production. Where venom is very expensive, as for arthropods (scorpions, spiders etc), then looking at newer technologies may be viable, especially if there is toxin homogeneity across target venoms/toxins, potentially allowing use of artificial immunogens. His group have used this with success for <i>Loxosceles</i> spider venom/AV and are looking at other opportunities. Coral snake venom is also hard to obtain in quantity, so may also respond to a multiepitope methodology. Monoclonal Ab is becoming attractive as synthetic immunogens with multi epitopes become practical and mAb costs drop.</p>
<p>Andreas H Laustsen</p>	<p>Rational design of snake antivenoms: Identification of key toxins targets and drug discovery via Next Generation Phage Display</p>
	<p>Andreas is a chemist/engineer currently undertaking a PhD in use of new mAb technology to produce AV. He is developing oligoclonal humanised Ab technology with up to 100 mAbs produced at once. His study is looking at African snake venoms. A key decision is selection of which toxins for Ab production and he is developing mathematical systems to help answer this question. One measure is the Toxicity Score = % of venom composition for a particular toxin / toxin LD₅₀. Using <i>Naja kaouthia</i> venom as a model, he determined that a particular α-cobratoxin was a dominant component, using venomomics. Then, using Next Generation Phage Display Screening he demonstrated how a discovered peptide-based antitoxin (not Ab) could block the toxin activity at the NMJ. He expressed enormous confidence that these new technologies can deliver complex polyvalent antivenoms using bioengineering methods that remove the need for access to either venoms/venomous animals long term, or animal hosts for Ab production, at the same time removing some of the allergy issues affecting existing equine etc AVs. It remains to be seen if his work will be successful, but it does seem to dovetail or take the next step from existing work in other labs.</p>

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Speaker	Topic/Summary
<p>Elda E Sánchez</p> 	<p>Neutralization of Snake Venom Myotoxins with a Chemically-Modified DNA Aptamer: An Approach to the Development of a Universal Antivenom</p> <p>Elda, now the Director of the Texas A&M University venom lab, discussed her work with the US military to develop a synthetic stable field use antidote for envenoming. Using X-aptamers she is developing non-AV antidotes that bind venom proteins specifically. Specific toxins are isolated and aptamers developed against them. Using crotamine (from rattlesnakes) as a toxin, she has made effective antidotes that show neutralisation in a mouse model, with dose dependency. This model may work best for some local rather than systemic effects, but may offer new and effective specific first aid/field treatment for certain types of envenoming.</p>



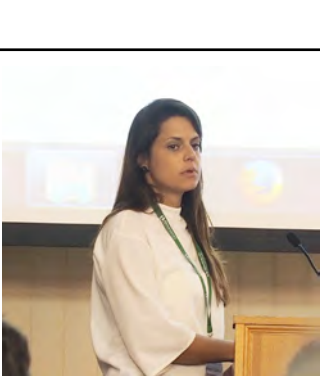

OVERSEAS TRIP REPORT ~ Prof. Julian White ~ September-October 2015

Speaker	Topic/Summary
<p>David G Lalloo (Keynote)</p> 	<p>Clinical evaluation of interventions in envenoming; the challenges</p> <p>This was just an overview presentation pushing the notion that DBRCT should be the “gold standard” in toxinology. He discussed the limits of pre-clinical testing of antivenoms, partly due to problems with animal models. Similarly clinical assessment of AV has many problems such as difficulty identifying the biting species and huge variation in the response to and degree of envenoming. There are few reported clinical trials of AV (32) and fewer registered trials (12), mostly of poor quality. Yet trials are needed to define the harm-benefit equation, optimise dose, determine efficacy. Dose finding is important to establish minimal effective dose. Phase 1 trials may not be needed, as can use in-vitro data, or could use small numbers of severely envenomed patients. Follow up with later randomised 2-dose trials comparing outcomes. He considered trials of AV require equipoise, good choice of comparator and endpoint, plus safety assessment. Control options include placebo, superiority and inferiority options, depending on what existing treatments are available. Endpoints must have clinical relevance, be easily measured and assessed over an appropriate time frame.</p>
<p>David J Williams (Keynote)</p> 	<p>Clinical trials of a new Papuan taipan antivenom in Papua New Guinea: opportunities, challenges and rewards</p> <p>David presented detail on his ongoing trial of the new ICP taipan AV versus CSL AV. The ICP AV is a research-funded product with the trial NHMRC funded. He is using a DBRCT to compare the AVs (non-inferiority) with primary endpoints being extent of neurotoxicity (progression to intubation), coagulopathy (time to reverse; INR <1.3, aPTT <40secs, fibrinogen >1.0g/L), and adverse reactions to AV.</p> <div data-bbox="512 1491 1426 2002"> <p>Phase I: Dose-finding & safety</p>  <pre> graph LR A[Phase I Recruitment] --> B[2 Vial Doses N=6] A --> C[1 Vial Doses N=12] B --> D[ICP Taipan N=3] B --> E[bioCSL Taipan N=3] C --> F[ICP Taipan N=6] C --> G[bioCSL Taipan N=6] </pre> <ul style="list-style-type: none"> • Double-blinded, randomised controlled trial involving patients bitten by Papuan taipan snakes ≤4 hrs prior to hospital admission; • divided equally into groups A or B by random allocation after informed consent. </div>



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Speaker	Topic/Summary
	<p>There are 18 patients enrolled in the Phase 1 trial, all confirmed taipan bites with defibrination. In the 2 vial arm no patients progressed to intubation, both AVs had similar rates of coagulopathy resolution, and neither caused serious ADRs. In the 1 vial arm, the CSL AV had a higher rate of neurotoxicity (1 intubation), both were again similar for coagulopathy resolution (ICP AV arguably more rapid response looking at graphs), and neither had serious ADRs. Both AVCs effectively removed procoagulant from serum (Ab measurement). In Phase 2 he plans for 86 patients, all <8hrs post-bite, given 1 vial of AV, the hypothesis being that ICP AV will decrease the rate of treatment failure from 20% to 10%.</p>
Julian White (Keynote)	Evidence versus experience; an antivenom dilemma
	<p>This was a discussion of the problems arising from some recent “evidence based” trials, focussing on problems with the RAVE II trial of CSL Red Back Spider AV versus placebo, IV, where the authors concluded AV was ineffective. Issues with choice of dose (uncertainty about dose used), selection of patients (including patients who normally would not receive AV and in whom treatment failure was certain given the parameters used), statistical interpretation, plus the huge gap between the RAVE II findings and those of 50+ years experience. A very lively Q&A occurred after the presentation.</p>
M S Bolton	Refinement of the WHO-recommended preclinical tests of antivenom efficacy
	<p>Ms. Bolton, a vet, was clearly passionate about reducing experimental animal suffering in toxinology-related research and AV control. She detailed the difficult path in developing reliable pain models in mice, relevant to toxinology. She modified the grimace method and developed a suit of neurological observations (visual placing, ear tickle, tail curl, righting reflex, blink reflex), but it was clear that no method is yet perfected. Similarly, the choice of analgesics to minimise pain has proved problematic. She noted it will be important to define specific endpoints for each venom being studied, rather than have a single model that fits all.</p>


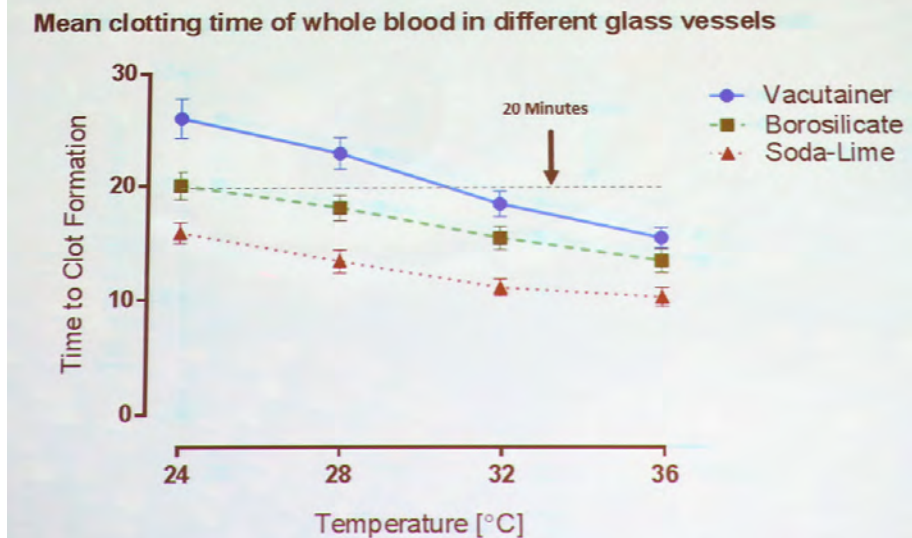
OVERSEAS TRIP REPORT ~ Prof. Julian White ~ September-October 2015

Speaker	Topic/Summary
<p data-bbox="167 309 359 342">Dan E Keyler</p> 	<p data-bbox="515 309 1428 421">The development of a new polyspecific antivenom for snake envenoming in Sri Lanka: A new model of international research collaboration</p> <p data-bbox="515 423 1428 943">Dan discussed his ongoing project to develop a snake AV specific for Sri Lanka, noting that existing Indian AVs cause high adverse reaction rates 81% for VINS, 43% for Haffkine) and appear of limited efficacy. His group have developed a new AV, made by ICP (Costa Rica), with a much higher ED50 than VINS AV. This will be trialled in 2016, with randomisation to Indian vs ICP AV for bites by species covered by the Indian AV in current use, while bites by Hypnale (not covered by any Indian AV) are randomised to different doses of the ICP AV (which does cover Hypnale). The ICP AV is caprylic acid purified whole IgG, lyophilised (with tested rapid reconstitution) and 3000 vials are now available. The plan, if the trial is successful, is to technology transfer to Sri Lanka so they can produce their own AV.</p>
<p data-bbox="167 974 459 1008">Larissa M Alvarenga</p> 	<p data-bbox="515 974 1412 1041">Engineered antibody fragments for the detection, quantification and neutralization of <i>Loxosceles intermedia</i> toxins</p> <p data-bbox="515 1075 1428 1444">Larissa detailed efforts to develop a <i>Loxosceles</i> MAb-based AV in Brazil, to overcome difficulties in sourcing enough venom and making polyclonal AV. One MAb is for diagnosis of loxoscelism, the other for treating patients. The treatment product is a diabody MAb which inhibits sphingomyelinase-D (cause of necrosis), and reduces venom-induced haemolysis (lethal effect; ?PLA2). The next step is humanisation of the AV and animal model testing, before clinical trials. Loxoscelism is a particular problem in SE Brazil, in areas of high urban population.</p>
<p data-bbox="167 1478 399 1512">Steven A Seifert</p> 	<p data-bbox="515 1478 1396 1624">A prospective, multicenter, double-blind, randomized, controlled, clinical trial comparing Crotalinae Equine Immune F(ab')₂ and Crotalidae Polyvalent Immune Fab (ovine) for the treatment of US Crotalinae envenomation</p> <p data-bbox="515 1626 1428 2145">Steve discussed a prospective DBRCT in US pit viper bitten patients comparing the existing CroFab AV (Fab ovine AV, partly made north of Adelaide) which has a significant envenoming recurrence problem (thrombocytopenia, coagulopathy, local effects) with a Mexican F(ab')₂ equine AV. The trial had 3 arms; Mexican AV control dose + maintenance dosing, Mexican AV control dose + placebo maintenance & CroFab control dose + maintenance dose. There were 41 patients in each arm, with enrollments from across southern US. His analysis of results indicated the Mexican AV was better at preventing recurrence and had higher mean nadir platelet counts, with much lower rates of late developing coagulopathy. Following this study the FDA has approved the Mexican AV for use in the US from 2018. The recommended dose of this AV will be 10 vials.</p>


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Speaker	Topic/Summary
Sanjib K Sharma	A randomized, double blind, clinical trial of two dose regimens of VINS polyvalent antivenom for the treatment of snake bite with neurotoxic envenoming in Nepal
	<p>Sanjib presented results of his prospective DBRCT of 2 doses (2 vials then follow up = Nepal guidelines; versus 10 vials initially, follow up as required = WHO/SEARO guidelines) of Indian (VINS) polyvalent AV in treating snakebite in the terai of Nepal (Damak, Charali, Bharatpur), which has a high snakebite case load. Currently very high AV doses are used (up to 250 vials!) with a high rate of ADRs. Patients already needing ventilation were excluded. Primary outcomes were death, respiratory paralysis or worsening neurotoxicity. They enrolled 154 patients and interestingly, more than half were female. Unfortunately they discovered the study was underpowered to show clear differences in subset populations, but it appears that the initial high dose delivers better outcomes and is more practical. Disturbingly the AV seemed poorly effective against krait envenoming. ADRs were similar in both arms. I know from other sources that amongst the 12 deaths, some appeared due to anaphylactic reaction to the AV.</p>
Steven A Seifert (Keynote)	Far From Home: The Challenges of Non-Native Snake Envenomations
	<p>Steve detailed his studies into the exotic envenoming problem in developed nations, noting this is no longer just snakebite, but also envenoming from scorpions, spiders, fish etc and for many of these there may be no AV available. Over 11 years in Germany & France there were 404 cases reported, 39% snakes, 30% marine, 27% spiders, scorpions & other arthropods, though all severe cases were snakebites. UK data indicates even higher rates and emerging data confirms rates of keeping exotic venomous animals are rising. The US alone imports up to 2 million exotic reptiles/yr with >10% being snakes. Health systems and staff are not equipped to deal with such exotic envenomings (lack of accurate treatment information, staff training & AV). Studies in the US show that many academic institutions work with venomous animals, but most lack either emergency protocols or staff training on how to handle envenoming accidents. PIC (AAPCC) data on exotic envenomings are not accurate, with frequent miscoding of species and case duplication. Some European nations (Netherlands, France, Germany, Switzerland) have established response systems and AV banks, the Netherlands being the best developed and resourced system. In the US federal law prohibits hospitals from keeping exotic AVs, which limits availability of supplies, zoos being the usual resource for the community, though not funded for this.</p>


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Owen K Paiva	Clinical evaluation of the 20 Minute Whole Blood Clotting Test (20WBCT) and reliability at different temperatures and types of glassware																				
	<p>Owen, from the PNG snakebite unit, presented preliminary research on the use of the 20WBCT to determine snakebite coagulopathy in a resource-poor environment. This test remains the only available method of detecting coagulopathy in most of the world, but its validity has been recently questioned. This PNG study aimed to determine which variations of the method were most reliable, looking at type of glassware etc. Careful technique standardisation was used. Exactly 2ml of venous blood was used, placed in a variety of container types and incubated at different temperatures, with results compared to proper coagulation testing methodology (Coaguchek + iStat). Both glass type and ambient temperature influenced results, with only soda-lime glass giving reliable clotting by 20 min at all tested temperatures. The PNG unit has now standardised its 20WBCT protocol; they use 10ml soda-lime glass penicillin vials, scrubbed & autoclaved (no detergent used), at room temp (25-28°C), adding 10 drops of fresh venous blood, swirled once, then wait 20 min, tilt once & record if clotted or not. Testing this in 240 snakebite patients, against Coaguchek results, showed good correlation in detecting significant coagulopathy, with high specificity and sensitivity for detection low fibrinogen levels (<0.5 g/L). They found borosilicate or silica-coated vials/tubes are likely to give false positives.</p> <div><h3>Results: Glass Type and Temperature</h3><p>Mean clotting time of whole blood in different glass vessels</p><table><thead><tr><th>Temperature [°C]</th><th>Vacutainer (min)</th><th>Borosilicate (min)</th><th>Soda-Lime (min)</th></tr></thead><tbody><tr><td>24</td><td>25</td><td>20</td><td>16</td></tr><tr><td>28</td><td>22</td><td>18</td><td>14</td></tr><tr><td>32</td><td>18</td><td>15</td><td>11</td></tr><tr><td>36</td><td>15</td><td>13</td><td>10</td></tr></tbody></table></div>	Temperature [°C]	Vacutainer (min)	Borosilicate (min)	Soda-Lime (min)	24	25	20	16	28	22	18	14	32	18	15	11	36	15	13	10
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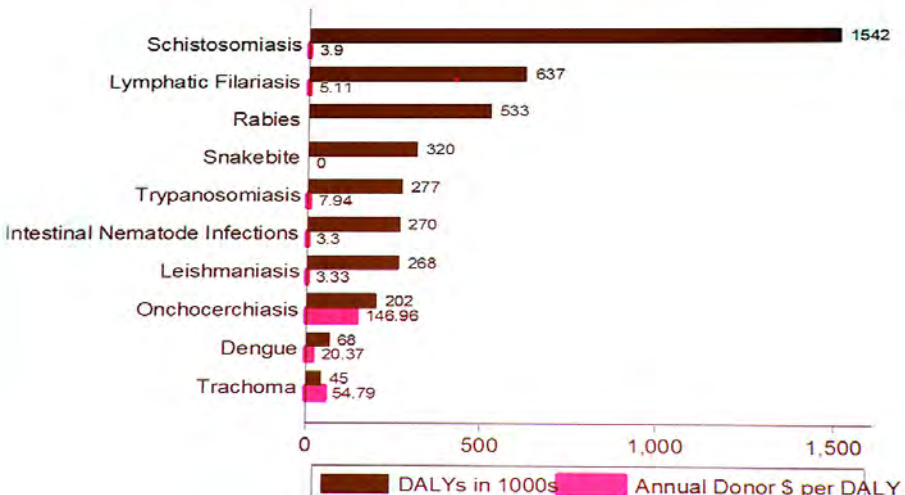

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Speaker	Topic/Summary
<p>Joerg Blessmann</p> 	<p>Snakebites in Lao PDR: Community-based surveys disclose high incidence of an invisible public health problem</p> <p>Joerg presented his recently published work on the epidemiology of snakebite in Laos. His team first looked at hospital case data on snakebite (2012-2014), which showed a low incidence, but rapidly rising in 2014 (26, 36, 127 cases/yr for 2012, 2013, 2014 respectively), attributable to his team's work and new availability of AV (previously unavailable). They also conducted a community level survey in Champone (river plain, rural, agricultural) and Phin (mountainous, poorer, forested), with nearly 17,000 people interviewed. Discovered rates of snakebite per 100k population were 355 (high) for Champone and 1105 (very high) for Phin. This places Phin amongst the highest rates of snakebite ever recorded, in stark contrast to the low incidence from hospital data (which is what WHO bases epidemiologic predictions on). In both communities no patients sought hospital treatment, nearly all relying on traditional healers, despite a number of fatalities and long term morbidity. This important study clearly documents the hidden burden of snakebite in the poor rural tropics.</p>

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<div>Abdulrazaq G Habib</div> <div></div>	<p>The Public Health Burden of Snakebite Envenoming in 16 Countries in West Africa</p> <p>Abdul presented a detailed analysis of the measurable economic & social burden of snakebite in West Africa, compared to other “neglected” tropical diseases. Using the DALYs methodology (Disability Adjusted Life Years = [number of deaths x years of life lost due to premature deaths] + [number of amputations x years of life lived with disability x disability weighting]), a globally recognised tool, and a meta-analytic approach to 40 yrs of all available literature, an average incidence was calculated for different parts of Africa. The annual rural mortality was 2.23/100k pop., vs 0.15 in urban areas and the amputation rate was 3% with a disability weight of 0.13. Data for each country was individually examined and results presented. The methodology was deliberately conservative, so that results can be considered at the lowest end of the likely range; their study showed 320k DALYs/yr in West Africa, while applying similar methods to the Kasturiratne WHO global estimates study, just for West Africa yields 1.2 million DALYs. For India, using the best current data yields 2.97 million DALYs and so globally at least 6 million DALYs. This now allows comparison of funding vs DALYs as a measure of actual burden of disease. Looking at all “neglected” tropical diseases, only schistosomiasis, lymphatic filariasis and rabies exceed the DALYs burden caused by snakebite, but all NTDs receive more funding than snakebite. This detailed study shows starkly why snakebite should be included amongst the major NTDs by WHO and why it requires significant funding. Essentially, in my opinion, this study documents a scandal of funding priorities for NTDs.</p> <p>Snakebite Burden in Western Africa</p> <table><tr><th>Country</th><th># Deaths (95% Confidence Interval)</th><th>#Amputations (95% Confidence Interval)</th><th>Local remaining life expectancy at time of bite [i,(years)]</th><th>DALYs from YLL [ii]</th><th>DALYs from YLD [iii]</th><th>Total DALYs (= DALYs from YLL + DALYs from YLD)</th></tr><tr><td>Benin</td><td>117(93-142)</td><td>143(90-244)</td><td>44</td><td>7558 (6008-9173)</td><td>818(515-1396)</td><td>8376 (6523-10569)</td></tr><tr><td>Burkina Faso</td><td>299(236-365)</td><td>352(208-600)</td><td>43</td><td>19315 (15246-23579)</td><td>1968(1163-3354)</td><td>21283 (16409-26933)</td></tr><tr><td>Cameroun</td><td>263(208-320)</td><td>319(198-544)</td><td>41</td><td>16990(13437-20672)</td><td>1700(1055-2900)</td><td>18690 (14492-23572)</td></tr><tr><td>Chad</td><td>198(156-240)</td><td>234(140-399)</td><td>38</td><td>12791(10078-15504)</td><td>1156(692-1971)</td><td>13947 (10770-17475)</td></tr><tr><td>Cote d'Ivoire</td><td>264(209-320)</td><td>322(203-550)</td><td>39</td><td>17054(13501-20672)</td><td>1633(1029-2789)</td><td>18687(14530-23461)</td></tr><tr><td>Gambia</td><td>31(24-38)</td><td>37(22-63)</td><td>44</td><td>2003(1550-2455)</td><td>212(126-360)</td><td>2215 (1676-2815)</td></tr><tr><td>Ghana</td><td>310(246-376)</td><td>379(240-648)</td><td>45</td><td>20026(15892-24290)</td><td>2217(1404-3791)</td><td>22243 (17296-28081)</td></tr><tr><td>Guinea Bissau</td><td>24(19-29)</td><td>28(17-48)</td><td>41</td><td>1550(1227-1873)</td><td>149(91-256)</td><td>1699 (1318-2129)</td></tr><tr><td>Guinea Conakry</td><td>159(126-193)</td><td>192(118-327)</td><td>43</td><td>10271 (8140-12468)</td><td>1073(660-1828)</td><td>11344 (8800-14296)</td></tr><tr><td>Liberia</td><td>37(30-45)</td><td>47(31-81)</td><td>44</td><td>2390(1938-2907)</td><td>269(177-463)</td><td>2659 (2115-3370)</td></tr><tr><td>Mali</td><td>238(188-289)</td><td>284(172-484)</td><td>43</td><td>15375(12145-18669)</td><td>1588(961-2706)</td><td>16963 (13106-21375)</td></tr><tr><td>Niger</td><td>264(208-322)</td><td>311(183-529)</td><td>44</td><td>17054(13437-20801)</td><td>1779(1047-3026)</td><td>18833 (14484-23827)</td></tr><tr><td>Nigeria</td><td>1927(1529-2333)</td><td>2368(1506-4043)</td><td>41</td><td>124484 (98773-150712)</td><td>12621(8027-21549)</td><td>137105 (106800-172261)</td></tr><tr><td>Senegal</td><td>192(152-232)</td><td>232(145-397)</td><td>45</td><td>12430(9819-14987)</td><td>1357(848-2322)</td><td>13787 (10667-17309)</td></tr><tr><td>Sierra Leone</td><td>92(73-112)</td><td>111(69-190)</td><td>37</td><td>5943(4716-7235)</td><td>534(332-914)</td><td>6477 (5048-8149)</td></tr><tr><td>Togo</td><td>78(62-95)</td><td>94(57-160)</td><td>43</td><td>5039(4005-6137)</td><td>525(319-894)</td><td>5564 (4324-7031)</td></tr><tr><td>Total</td><td>4494(3557-5450)</td><td>5454(3398-9306)</td><td>Not applicable</td><td>290,275 (229,911-352,135)</td><td>29599(18446-50519)</td><td>319874(248357-402654)</td></tr></table>	Country	# Deaths (95% Confidence Interval)	#Amputations (95% Confidence Interval)	Local remaining life expectancy at time of bite [i,(years)]	DALYs from YLL [ii]	DALYs from YLD [iii]	Total DALYs (= DALYs from YLL + DALYs from YLD)	Benin	117(93-142)	143(90-244)	44	7558 (6008-9173)	818(515-1396)	8376 (6523-10569)	Burkina Faso	299(236-365)	352(208-600)	43	19315 (15246-23579)	1968(1163-3354)	21283 (16409-26933)	Cameroun	263(208-320)	319(198-544)	41	16990(13437-20672)	1700(1055-2900)	18690 (14492-23572)	Chad	198(156-240)	234(140-399)	38	12791(10078-15504)	1156(692-1971)	13947 (10770-17475)	Cote d'Ivoire	264(209-320)	322(203-550)	39	17054(13501-20672)	1633(1029-2789)	18687(14530-23461)	Gambia	31(24-38)	37(22-63)	44	2003(1550-2455)	212(126-360)	2215 (1676-2815)	Ghana	310(246-376)	379(240-648)	45	20026(15892-24290)	2217(1404-3791)	22243 (17296-28081)	Guinea Bissau	24(19-29)	28(17-48)	41	1550(1227-1873)	149(91-256)	1699 (1318-2129)	Guinea Conakry	159(126-193)	192(118-327)	43	10271 (8140-12468)	1073(660-1828)	11344 (8800-14296)	Liberia	37(30-45)	47(31-81)	44	2390(1938-2907)	269(177-463)	2659 (2115-3370)	Mali	238(188-289)	284(172-484)	43	15375(12145-18669)	1588(961-2706)	16963 (13106-21375)	Niger	264(208-322)	311(183-529)	44	17054(13437-20801)	1779(1047-3026)	18833 (14484-23827)	Nigeria	1927(1529-2333)	2368(1506-4043)	41	124484 (98773-150712)	12621(8027-21549)	137105 (106800-172261)	Senegal	192(152-232)	232(145-397)	45	12430(9819-14987)	1357(848-2322)	13787 (10667-17309)	Sierra Leone	92(73-112)	111(69-190)	37	5943(4716-7235)	534(332-914)	6477 (5048-8149)	Togo	78(62-95)	94(57-160)	43	5039(4005-6137)	525(319-894)	5564 (4324-7031)	Total	4494(3557-5450)	5454(3398-9306)	Not applicable	290,275 (229,911-352,135)	29599(18446-50519)	319874(248357-402654)
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OVERSEAS TRIP REPORT ~ Prof. Julian White ~ September-October 2015

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Chamara Wijesinghe	Development and assessment of a brief psychological intervention for snakebite victims																																	
	<p>Chamara, a psychiatrist from Sri Lanka, presented background information demonstrating that snakebite has now been shown to cause significant psychiatric illness in multiple studies, mainly depressive disorder and PTSD. He then detailed results from a prospective single blind randomised study of psychiatric intervention in snakebite patients, delivered by non-psychiatrist medical officers (ie a practical solution) at Polonnaruwa Hospital, Sri Lanka. 225 patients were enrolled (more than statistically required). Local doctors were trained in psychological education and intervention for snakebite. The former involved dispelling myths and advocating appropriate responses to snakebite, while the latter was based on trauma focussed cognitive behavioural therapy. There were 3 arms ([A] no intervention = control; [B] psycho-education and first aid at time of discharge; [C] education + brief psycho-intervention at 1 month post discharge). All participants were then expertly assessed 6 months later, with 89% completing the trial. The study showed a decrease in symptoms of depression in group B, more pronounced in group C. The rate of depression was similar across all groups (Beck depression scale), but the rate of severe depression was highest in the control group (A = 10.3%; B = 1.5%; C = 0%). Similarly, psychiatric disability (Sheehan disability inventory) showed a decreasing trend from group A to C. However, the proportion with PTSD was similar across all groups. They concluded that the combined psychiatric intervention delivered by trained non-psychiatrists reduced psychiatric symptoms, improved overall family and social life functionality, but did not alter the rates of depression and PTSD caused by snakebite.</p>																																	

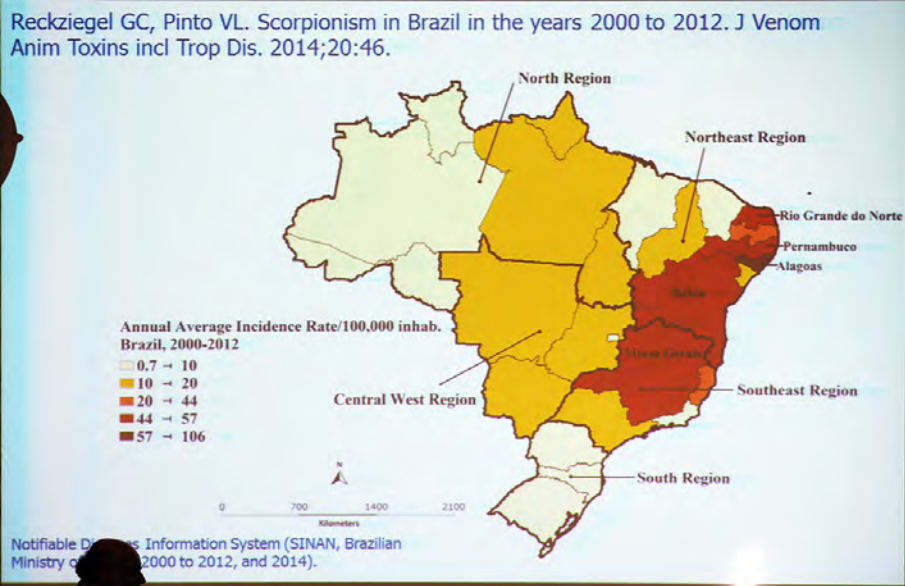

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Speaker	Topic/Summary
Jeremy N Day	Space, time and species trends in snake envenomation in the south of Vietnam 1997 – 2012
	<p>Jeremy detailed studies conducted at Cho Ray Hospital (Ho Chi Minh City = Saigon, southern Vietnam) by the Wellcome Trust/ University of Oxford Tropical Medicine unit there. A retrospective review of snakebites (1997-2012) found 9433 cases with a 1.14% mortality rate, the dominant causes of bites being (in order of frequency - fatality rate as % of cases in []), green pit vipers (<i>Trimeresurus</i> spp.) [0.2%], Malayan pit vipers (<i>Calloselasma rhodostoma</i>) [1.5%], spitting cobras (<i>Naja siamensis</i>) [2.8%], monocled cobras (<i>N. kaouthia</i>) [0.4%], unidentified cobras [1.8%], kraits (<i>Bungarus</i> spp.) [15%], king cobras (<i>Ophiophagus hannah</i>) [4%], rear-fanged Homalopsid aquatic snakes (<i>Enhydris</i> spp.) [0%], red necked keelbacks (<i>Rhabdophis subminiatus</i>) [13%], the remainder being unidentified snakes. Trends in presentation rates were fairly static except for green pit vipers, which showed a marked upward trend in incidence. He then discussed problems with the study and with managing snakebite, specifically mentioning the lack of AV for <i>Rhabdophis</i> bites, despite their comparatively high fatality rate.</p>
Dirk F van Helden	A pharmacological approach to snakebite first aid
	<p>Dirk outlined knowledge on lymphatic flow as a major venom transport factor in snakebite patients. Fear increases lymphatic flow rates, but tested venoms do not. Tested elapid venoms (mulga & tiger snakes) contain a muscarinic antagonist that “probably protects lymphatic delivery in the event of acetylcholine (ACh) release from damaged muscle nerve terminals.” Viper venom (<i>Crotalus atrox</i>) does not have this toxin. ACh inhibits the intrinsic lymph flow through release of endothelial NO. Applying an NO-donor topical cream (0.2% glyceryl trinitrate = GTNO) slows lymphatic flow in humans (no venom) and in a rat model (hind limb injection of venom) where it also increases survival time. Similar effects are seen with application of either cold (2°C) or topically applied nifedipine, lignocaine, or nitroprusside. However, in the rat model application of a cuff at 50mm Hg (mimicing PBI first aid) is far more effective at minimising measured plasma venom levels than either topical GTNO, or cold. Any movement of the bitten limb, despite PBI (cuff), decreases effectiveness. His studies also show that a local pressure pad is as effective as whole limb PBI. He therefore proposes consideration of a simplified snakebite first aid using topical GTNO + pressure pad & limb immobilisation.</p>



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Speaker	Topic/Summary
<p>Fábio Bucarechi (Keynote)</p> 	<p>Scorpion stings in Brazil</p> <p>Fabio presented an overview of scorpion stings in Brazil, where <i>Tityus</i> spp. (notably <i>T. serrulatus</i>, <i>T. stigmurus</i>, <i>T. obscurus</i>, <i>T. bahiensis</i>) have a significant medical impact. <i>T. serrulatus</i>, the parthenogenetic species, in particular, is expanding its range and impact and is a big problem in urban areas. In Brazil scorpion stings are clinically graded (0 = no envenoming; 1 = only local effects; 2 = systemic effects; 3 = life-threatening systemic effects including shock, cardiac failure, respiratory failure; F = fatal cases). In the Campinas region proportions for each grade are: 0 = 3.4%, 1 = 79.6%, 2 = 15.1%, 3 = 1.8%, F = 0.1% (all grade 3 & F cases caused by <i>T. serrulatus</i>). Main local clinical features, in order of frequency, are pain (near 100% of cases), erythema, radiating pain, swelling, parasthesia, sting mark & sweating. In grade 2 & 3 cases there is hypokalaemia & hyperglycaemia, and in grade 3 cases mildly elevated CK and markedly elevated troponin, with decreased ejection fraction (<54%) on echocardiography and sometimes pulmonary oedema. Pain relief is the predominant treatment used (analgesics ± local anaesthesia) with AV used in only 6.8% of cases. The rapid progression of severity in major cases requires early recognition and use of AV, PICU support, and when indicated, dobutamine for myocardial depression and ventilation for pulmonary oedema/compromise. Fabio also noted a study from Israel with <i>Leiurus quinquestriatus</i> stings in children, where early echocardiography appeared instrumental in detecting and successfully managing patients developing venom-induced cardiac failure. He also noted a case of Takotsubo-like stress-induced cardiomyopathy following a <i>T. serrulatus</i> sting. As more case data is collected, so distinct envenoming profiles are emerging for each species. <i>T. obscurus</i> causes generalised parasthesiae, ataxia, dysarthria, myoclonus, dysmetria and electric-shock-like sensations body-wide, so a neurotoxic picture quite distinct from <i>T. serrulatus</i> stings. <i>T. stigmurus</i> and <i>T. bahiensis</i> cause effects similar to <i>T. serrulatus</i>, with fatalities in children <5 yrs now recorded for <i>T. stigmurus</i>. Lastly, he noted that when needed, AV should be given as a rapid undiluted bolus as the catecholamine-storm like effects of envenoming make acute ADRs to AV unlikely and there is a need to achieve therapeutic AV levels rapidly.</p>




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Speaker	Topic/Summary
	<p>Reckziegel GC, Pinto VL. Scorpionism in Brazil in the years 2000 to 2012. <i>J Venom Anim Toxins incl Trop Dis.</i> 2014;20:46.</p>  <p>Annual Average Incidence Rate/100,000 inhab. Brazil, 2000-2012</p> <p>0.7 → 10 10 → 20 20 → 44 44 → 57 57 → 106</p> <p>Notifiable Diseases Information System (SINAN, Brazilian Ministry of Health) 2000 to 2012, and 2014).</p>
Richard C Dart (Keynote)	Efficacy of F(ab) ₂ Antivenom for the Treatment of <i>Latrodectus mactans</i> Envenoming in the United States
	<p>Rick presented his opinions on the use of AV to treat latrodectism, relating back to the RAVE II study and my earlier presentation on this topic, but Rick concentrated on other good clinical trials and studies from North America to question RAVE II. First he noted the Clark et al paper detailing 163 cases, some with AV treatment, which showed those given AV had much shorter duration of symptoms and few required admission, compared to non-AV treated patients. However, there was a single AV-associated fatality in this series. The AV used was the still available Merck equine whole IgG product. His analysis of RAVE II noted the poor methodology (poor pain score and inclusion of cases in the AV arm that should not have received AV and could not show benefit, thus skewing results) and that reanalysis of results could arguably conclude clear benefit for AV. He further noted the RAVE II conclusion that the “only other placebo controlled randomised trial ... also had negative results”. Rick conducted that trial and indicated this statement in RAVE II was incorrect. His trial, DBRCT of a “new” equine F(ab')₂ AV vs placebo, showed that AV was effective. The phase III trial of this AV, with far more patients, is showing similar results in favour of AV. Therefore the evidence does not support the RAVE II conclusion that AV is ineffective and should not be used.</p>

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Speaker	Topic/Summary
<p data-bbox="169 315 416 349">Ronelle E Welton</p> 	<p data-bbox="518 315 1401 387">Hospitalisations and deaths due to venomous bites and stings in Australia from 2000 to 2013</p> <p data-bbox="518 392 1426 1021">Ronelle, from AVRU Melbourne, presented her study of retrospective hospital admission (principle diagnosis) and coronial data for venomous bites & stings Australia-wide, 2000-2013. 64 fatalities were recorded (0.024/100k pop./yr), 81% male and 44% were prior to reaching medical care. Of these 34 were due to anaphylaxis to an arthropod sting/bite (bee 25; wasp 2; ant 2; tick 3), particularly common in SA & WA. In comparison, there were 27 snakebite deaths, 74% of whom reached health services and Qld & NT dominated state of origin. There were just 3 box jellyfish fatalities. Overall, most deaths occurred in urban or inner regional areas with few in remote areas. For all cases (not just fatalities) males predominated with stable numbers over the study period. This study shows that arthropod sting allergy is a more frequent cause of deaths than snakebite and that both are predominantly in areas of higher population with good health system access, rather than remote areas.</p>
<p data-bbox="169 1055 384 1088">David A Warrell</p> 	<p data-bbox="518 1055 1426 1126">Severe neurotoxic scorpion envenoming (<i>Parabuthus leiosoma</i>) in East Africa</p> <p data-bbox="518 1160 1417 1939">David presented a case of severe envenoming with a new envenoming syndrome, in a 63 yr old game warden in Kenya. There was immediate pain, extending within 30 min, then generalised numbness (+1 hr), skin hypersensitivity & painful muscle spasms (+1.5 hrs), bilateral ptosis & limb weakness, increased salivation (+2 hrs), dyspnoea, tongue/throat swelling (+2.5 hrs), tachycardia, generalised weakness, severe skin hypersensitivity & touching others skin felt like sandpaper (+4 hrs), severe dyspnoea, wheezing (+4.5 hrs), but then given O2 with rapid improvement in breathing, HR, but hypertensive. No AV available at that time, so symptomatic treatment only, with gradual resolution of symptoms over 2 days, other than tight, swollen numb stung finger. At 2 weeks he had generalised joint pain and stiffness in muscles. The scorpion was kept and expertly identified as <i>Parabuthus leiosoma</i> (African black tailed scorpion). There is limited data on the venom of this species. The related <i>P. granulatus</i> & <i>P. transvalicus</i> in South Africa cause severe neurotoxic & paralytic envenoming, also neuroexcitatory effects (salivation, sweating, urinary retention, hypertension, though cardiac dysrhythmias, pulmonary oedema, cardiac failure appear uncommon to rare).</p>

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Speaker	Topic/Summary
<p>John Rathbone</p> 	<p>Use of emergency transport by patients with envenomation injury in Queensland, Australia: a retrospective longitudinal study from 2007 to 2014</p> <p>John presented a retrospective review of envenoming cases presenting to Qld Ambulance Service (2007-2014). There were 12,800 records during this period, with just 202 related to envenoming, with a male predominance and overwhelmingly snakebite (60.8%). Most cases occurred in or around the home (46%). For cases with allergic reactions to stings/bites (18%), most reactions were local or non-specific systemic, similarly for snakebite, with only 5 having acute LOC & 1 seizure. There were 5 cases of box jellyfish sting with cardiac arrest; all survived with a "good outcome".</p>
<p>Thomas Junghanss and Mauro Bodio</p>	<p>"VAPAGuide – The free access Emergency Guide to Venomous and Poisonous Animals"</p>
 	<p>Mauro & Thomas presented their online VAPA Guide, funded by Swiss organisations and basically taking their 1996 book and making it into an interactive website. As with the book, it lacks any photos, so no colour illustrations of the animals or their envenoming effects. They claim their system allows ready access to key diagnostic information for clinicians. In my opinion the level of detail is low compared to the WCH/ University of Adelaide CTRW site. They organised a live internet session to demonstrate site features.</p>


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Speaker	Topic/Summary																																	
<div>Fábio Bucarechi (Keynote)</div> <div></div>	<p>Coral snake (<i>Micrurus</i> spp.) bites in Brazil: A review of literature reports over the last 147 years</p> <p>Fabio reviewed coral snake (<i>Micrurus</i> spp.) bites in Brazil. Though there are 31 species, few cause bites and even these are a small proportion of all snakebites. The venom is principally neurotoxic, causing flaccid paralysis, either pre- & post-synaptic (eg <i>M. corallinus</i>), or purely postsynaptic (eg <i>M. frontalis</i>, <i>M. lemniscatus</i>). Fabio reviewed every available report of coral snake bites in Brazil, finding 194 cases, of which 150 were distinct cases with some clinical detail, spanning 1933-2014. Local pain, often severe, was the commonest finding, while the major systemic effect was neurotoxic paralysis (59% of cases) and there were only 3 cases with myolysis detected, all mild (highest CK 1766 U/L). Review of the literature found only 4 cases with myolysis, never severe, all from bites outside Brazil (<i>M. fulvius</i>, USA; <i>M. lemniscatus helleri</i>, Ecuador; <i>M. laticollaris</i>, Mexico). Antivenom was given in 77% of cases (10 vials of IB soro antielapidico bivalente). Neostigmine was used in 9 cases, with a positive response in 5 and overall only 5 patients required ventilation. He presented one case where AV provided no improvement, but there was a good apparent response to later neostigmine. Finally he showed a treatment algorithm for coral snake bites.</p> <div><p>Micrurus spp snakebites in Brazil: Review. N= 150</p><div><table><thead><tr><th>Snake identification</th><th>n</th><th>%</th></tr></thead><tbody><tr><td>M. corallinus</td><td>36</td><td>24.0</td></tr><tr><td>M. frontalis</td><td>12</td><td>8.0</td></tr><tr><td><i>M. lemniscatus</i></td><td>5</td><td>3.3</td></tr><tr><td><i>M. hemprichii</i></td><td>2</td><td>1.3</td></tr><tr><td><i>M. filiiformis</i></td><td>1</td><td>0.7</td></tr><tr><td><i>M. ibiboboca</i></td><td>1</td><td>0.7</td></tr><tr><td><i>M. spixii</i></td><td>1</td><td>0.7</td></tr><tr><td><i>M. surinamensis</i></td><td>1</td><td>0.7</td></tr><tr><td><i>Micrurus</i> spp.</td><td>22</td><td>14.7</td></tr><tr><td>Total</td><td>81</td><td>54.0</td></tr></tbody></table></div></div>	Snake identification	n	%	M. corallinus	36	24.0	M. frontalis	12	8.0	<i>M. lemniscatus</i>	5	3.3	<i>M. hemprichii</i>	2	1.3	<i>M. filiiformis</i>	1	0.7	<i>M. ibiboboca</i>	1	0.7	<i>M. spixii</i>	1	0.7	<i>M. surinamensis</i>	1	0.7	<i>Micrurus</i> spp.	22	14.7	Total	81	54.0
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Speaker	Topic/Summary
	<p>paresthesia 52.0% local pain 48.0% fang marks 45.0% ptosis 32.0% dizziness 28.0% blurred vision 22.0% weakness 20.0% dysphagia 15.0% dyspnea 12.0% myalgia 10.0% inability to walk 10.0% salivation 8.0% death 14.0%</p> <p>Dry bites: 14%</p> <p>0.0 10.0 20.0 30.0 40.0 50.0 60.0</p> <p>%</p> <p>Suspected OR confirmed coral snake (<i>Micrurus</i> spp.) bite</p> <p>Suspected OR confirmed envenomation: monitoring required</p> <p>Only local manifestations</p> <p>Acute myasthenia WITHOUT PARALYSIS</p> <p>Acute myasthenia WITH PARALYSIS</p> <p>Observation (24 h)</p> <p>Onset of MYASTHENIA</p> <p>AV: 5 vials IV</p> <p>Onset of PARALYSIS</p> <p>NO MYASTHENIA</p> <p>Discharge</p> <p>Effective treatment</p> <p>AV: 10 vials IV Provision of respiratory support Consider tests with anticholinesterase drugs</p> <p>Algorithm for the treatment of patients bitten by coral snakes in Brazil (Brazilian Ministry of Health, 2014).</p>


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Speaker	Topic/Summary
<p data-bbox="167 309 416 342">Joseph K Joseph</p> 	<p data-bbox="513 309 1401 383">Morbidity and Mortality Related to Capillary Leak Syndrome in Daboia russelli Bite</p> <p data-bbox="513 387 1428 1727">Joseph, a nephrologist from the Little Flower Hospital, Kerala, India, first presented a case of Russell's viper bite with AKI who, despite AV treatment, developed capillary leak syndrome (CLS) and subsequently died from pulmonary haemorrhage. He then outlined the diagnostic criteria for CLS as defined by Clarkson in 1960 and characterised by severe hypotension, hypoalbuminaemia, haemoconcentration without albuminuria and leukocytosis. The clinical progression is from a prodromal phase (irritability, fatigue, myalgia, nausea, abdominal pain, thirst, syncope), then the initial phase (generalised oedema, ascites, pericardial & pleural effusion, rhabdomyolysis, AKI/ARF, conjunctival chemosis (important clinical sign), parotid swelling ("viper head", important new sign), hypotension, followed by the "recruitment" phase (pulmonary oedema, polyuria, reversal of vascular leak and return of leaked fluids to the circulation, leading to acute intravascular fluid overload, potentially fatal. Joseph then detailed a prospective observational study over 2 years of CLS, with 25 cases (vasculotoxic snakebite + CLS - Clarkson criteria) + 25 matched controls (envenoming without CLS). Cases with pre-existing diseases were excluded (such as chronic renal failure, congestive heart disease etc). In addition to clinical criteria, lab criteria (\uparrowHb, \downarrowalbumin, \uparrowHCT, albuminuria, \uparrowCK) and radiologic findings (pleural effusion or pulmonary oedema) were used. Some key differentiators between CLS cases and controls were myalgia, thirst, parotid swelling, conjunctival chemosis and hypotension. around half of CLS cases had pleural effusion, none amongst controls. Nearly half of CLS cases died, but only one of the controls. He concluded that CLS patients require higher AV doses and early recognition of CLS with measures to prevent AKI are important, but no clear treatment pathway was outlined. During questions David Warrell queried whether poor AV might be a factor, Scott Weinstein suggested prednisolone, Abdul Habib queried if this was nephrotic syndrome (no according to Joseph), Chema Gutierrez queried if this was a secondary inflammatory effect.</p> <div data-bbox="513 1731 1125 2159">  </div>

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Speaker	Topic/Summary
Paula R Oliveira	Epidemiology of Snakebites in Angola
	<p>Paula gave an overview of the relatively new Angolan PIC, noting snakebite was the 4th most common cause of “poisoning”, with most cases in rural farm workers. However, there was scant detail and no clear attribution of cases to particular snake species, though she stated <i>Bitis arietans</i> was a leading cause of bites. Much of the presentation was on the PIC educational work and establishment of a local herpetarium to collect venom.</p>
Lois Armstrong	Snakebites in rural northern Bihar, India – A one year, prospective study on snakebite epidemiology and risk factors for bad outcomes
	<p>Lois, an Australian nurse working in Raxaul, rural Bihar, India, presented findings of her 1 yr prospective study of snakebite. She had collected snakes causing bites, including the common cobra (<i>Naja naja</i>), common krait (<i>Bungarus caeruleus</i>), and wolf snake (<i>Lycodon aulicus</i> - not medically significant), but so far had found no Russell’s vipers or other cobra species. Over 12 months she collected 609 cases; 386 with history of snakebite, 214 with unknown bite, 6 with envenoming without observed bite, 14 dead on arrival after snakebite. There were 77 envenomed patients (29 neurotoxic only; 38 neurotoxic + local necrosis; 1 haemotoxic, 9 where symptoms not recorded because died too soon), so an envenoming rate of 12.6%. Most bites (67%) were on a lower limb. 46% of patients arrived at hospital “late” due to a variety of causes (difficulty finding transport, long distance, referral from another hospital, treated initially by traditional healer, etc). 22 patients died (14 dead on arrival) with a strong correlation with delay in reaching hospital and no fatalities if seen within 1 hr of bite. The strongest odds ratio for bad outcome was initial treatment by traditional healers. Factors reducing bad outcomes included use of motor bikes for rapid patient transport. Recommendations included better public education about prevention and risk factors causing bad outcomes.</p>



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Speaker	Topic/Summary
<p>Marieke A Dijkman</p> 	<p>The clinical presentation of an Aruban rattlesnake bite is comparable with bites by snakes belonging to the <i>Crotalus durissus</i> complex</p> <p>Marieke presented a case of Aruba Island rattlesnake bite (<i>Crotalus unicolor</i>) in a 57 yr old keeper bitten on his finger while feeding the snake. He developed local pain, nausea, “fainted” and on arrival at hospital had clear bite marks with slight swelling, BP 154/84, HR 95, RR 23, 99% O2 sats on room air. The Netherlands exotic snakebite protocol was activated and AV sent to the hospital. Initial labs were normal, but by 3.5 hrs his whole hand was swollen and repeat labs showed hypofibrinogenaemia (0.6 g/L). At 9 hrs post-bite he was given 9 vials of Antivipmyn AV. 3 hrs later his swelling had extended and fibrinogen was undetectable, with prolonged coag tests (PT = 38.7 secs; aPTT 40 secs), normal platelets, CK 1427 U/L. More AV was sourced, and at 7 hrs post AV, though fibrinogen was still undetectable, coag tests had normalised, CK now 1868 U/L. At 19 hrs post-bite a further 6 vials of AV was given. No further labs were presented, but he stayed in ICU for 3 days, then 2 days in ward, being discharged without sequelae. There was no evidence of AKI. In discussion Marieke queried whether the second AV dose was helpful. In questions I suggested that possible the Venezuelan AV might be more appropriate, or even the Brazilian AV, rather than Mexican Antivipmyn.</p>

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Speaker	Topic/Summary
<p data-bbox="167 309 395 342">Sadanand Raut</p> 	<p data-bbox="515 309 1380 342">Snake Bite management experience in western Mah (INDIA)</p> <p data-bbox="515 347 1428 1496">Sadanand who, with his medico wife (both have attended the Adelaide clinical toxinology course), runs a hospital (Vighnagar Nursing Home) in Maharashtra, India, where they treat snakebite. In the 5 yr period to Sept. 2015 they managed 376 cases, the most common causes being Russell's viper > cobra > krait > saw scaled viper > "pit viper", plus some scorpion stings. There were also numerous bites by non-venomous snakes (127/376). He provided detail on several cases, plus series data for major species. For cobras (55 cases studied), most bites occurred during daytime working hours, particularly June-September. Within his district 16 snake "rescuers" were fatally bitten by cobras, none treated at his hospital, which recorded no cobra fatalities, though 25% of cases required ventilation (3-12 hrs), 36% developed local necrosis & 11% needed skin grafting. For krait bites (53 cases studied), 22% of cases had no discernable bite marks, most bites occurred in the "early morning", with symptoms developing 1-8 hrs later. While most had minimal or no local effects, systemically most experienced abdominal pain, vomiting and 47% developed paralysis requiring ventilation. A few patients presented with convulsions, pulmonary oedema, or stroke and there were 2 fatalities. Russell's viper bites (93 cases studied) occurred mainly June-August, 53% on lower limbs, and mostly in the afternoon to evening. Symptoms included severe local pain, swelling, coagulopathy & shock. 6 developed neurotoxicity, requiring ventilation. Only 2 cases with local necrosis occurred, while 6 developed AKI, 3 needing haemodialysis. There were no fatalities. 26 patients had (non-fatal) anaphylactic ADRs to AV and they don't use adrenaline premedication. Bamboo pit viper bites were associated with severe local pain, swelling, but normal 20WBCT and did not receive AV.</p>
<p data-bbox="167 1527 418 1561">Scott A Weinstein</p> 	<p data-bbox="515 1527 1359 1601">An instructive case of presumed brown snake (<i>Pseudonaja</i> spp.) envenoming</p> <p data-bbox="515 1606 1412 2123">Scott presented a recent case of presumed brown snake bite in outer Adelaide in an elderly woman who was unaware of being bitten, while rescuing her dog from a snake encounter. She presented the dog, who was envenomed, to a vet, but while there became unwell, collapsed. She was transported to hospital and found to have classic brown snake defibrination coagulopathy plus right-sided weakness and was given 2 vials of brown snake AV. A CT head revealed subacute infarction of the left corona radiata. Though her ECG was normal, she had mild troponin elevation (39 ng/L). Persistent bleeding/bruising ceased about 3 hrs post-AV. Her troponin peaked (639 ng/L) about 3.5 hrs post-AV and a diagnosis of non-ST elevated myocardial infarction (NSTEMI) was made. She continued to improve with resolution of neurological abnormalities.</p>

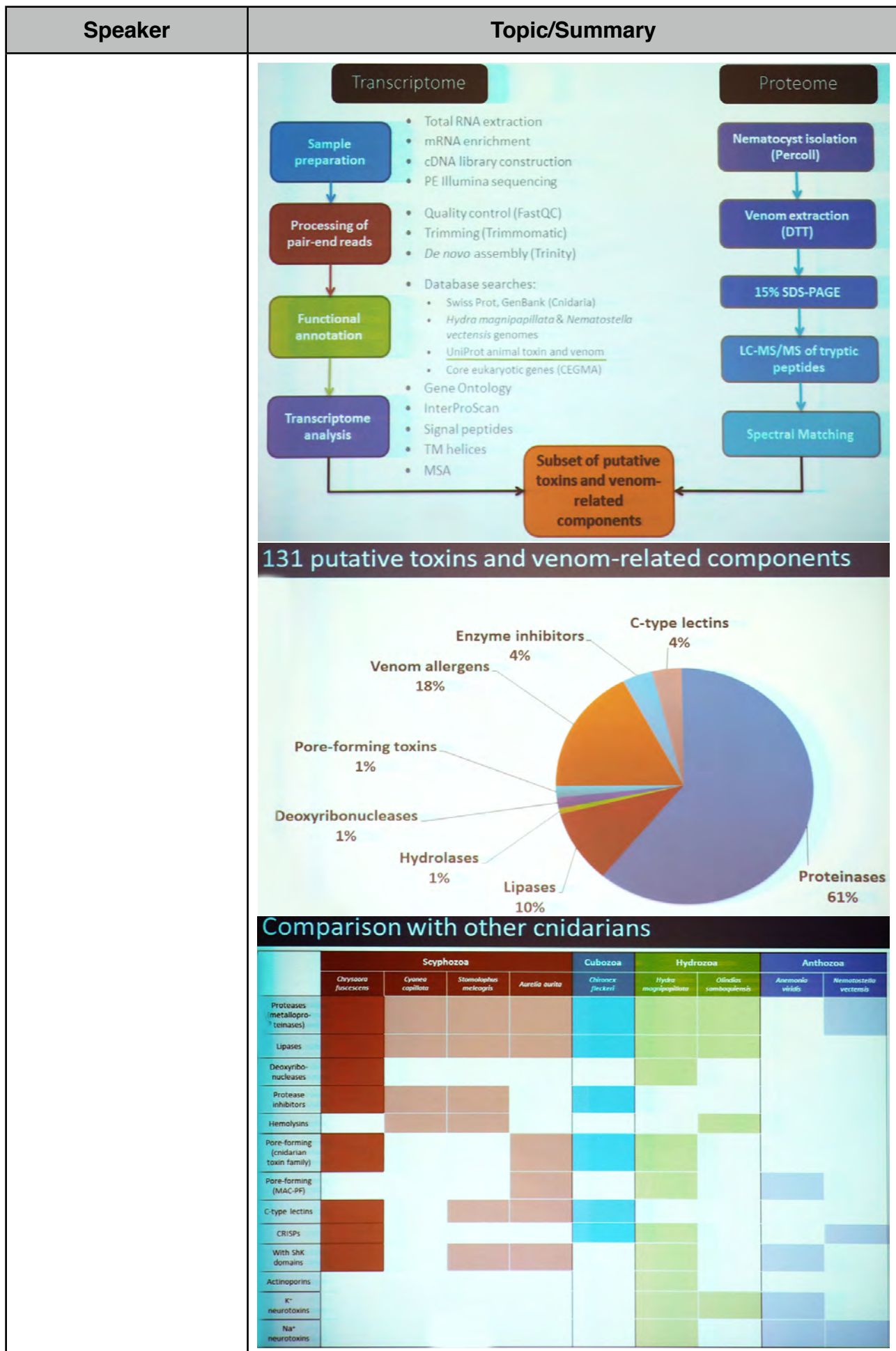
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Speaker	Topic/Summary
<p data-bbox="167 309 391 342">Dileep P Punde</p> 	<p data-bbox="513 309 1061 342">Crusade against Snake Bite poisoning</p> <p data-bbox="513 376 1417 1227">Dileep, who runs the Punde Hospital, India, first presented some data on bite cases (2535 cases in 14 yrs; 89% of snakebites from venomous species; scorpion stings). Amongst the snakebites, the most common were Russell's viper (420) > cobra (332) > saw scaled viper (158) > krait (97). Anaphylaxis to AV occurred in 17% of cases, though severe in only 18/187. Snakebite fatality rate was 1.8% (Russell's viper 14; cobra 4, krait & saw scaled viper 1 each). Most cases occurred in poor rural farmers (occupational disease). He then presented more detail on specific snake groups, with illustrative cases. Kraits had a 37% rate of respiratory paralysis. Russell's vipers had a 12.9% rate of AKI/ARF, 7% shock, 1.4% CLS, & 3.3% fatality. Mean AV requirement was >20 vials. He included a case with CLS (ascites, pleural effusion, thrombocytopenia, AKI), successfully treated with AV, frusemide, prednisolone, vasopressor support & dialysis. Cobra bites had a 36% rate of paralysis, 8% local necrosis, 1.2% fatality. Saw scaled vipers were a rare cause of death (1/158). He presented a case of a farmer with multiple bite episodes, all while working (cobra with paralysis; Russell's viper, mild envenoming; saw scaled viper, mild envenoming). He concluded by presenting examples of unusual bite locations and then his ongoing public education program on snakebite.</p>
<p data-bbox="167 1261 347 1294">Gus A Gross</p> 	<p data-bbox="513 1261 783 1294">"Size Does Matter"</p> <p data-bbox="513 1328 1417 1731">This was a rather strange dual presentation, first by a young "physician" (Trevor) who presented a <i>Crotalus atrox</i> bite to the leg of a snake keeper, who was given CroFab AV (20 vials overall), never developed coagulopathy, but despite doppler-detectable pedal pulse was surgically treated with a fasciotomy, then further surgery, resulting in a below knee amputation and later an above knee amputation. The message appeared to be, he needed more AV. I think he needed to be kept away from surgeons! Dr. Gross then further discussed this case, emphasising the inappropriateness of surgical intervention unless clearly demonstrated compartment syndrome present.</p>


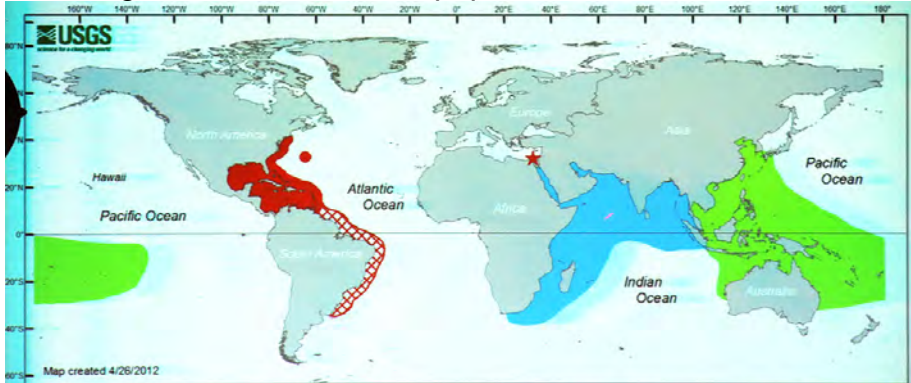
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Speaker	Topic/Summary
<p>Aniruddha ("Joy") Ghose</p> 	<p>Russell's Viper (<i>Daboia Russelli</i>): A Newly Recognized Cause of Neuro-Myo-Renal toxic envenomation in Bangladesh</p> <p>Joy presented a description of a new snakebite syndrome for Bangladesh, following Russell's viper bite. First he summarised a recent community survey of snakebite, which revealed an annual incidence of 710,159 cases, or 623/100k/yr, a very high rate, with around 6000 fatalities/yr. The leading causes of venomous snakebites are cobras, kraits & green pit vipers, but it was thought, not Russell's viper, though this was noted a century ago. A recent study found 3 confirmed Russell's viper bites and Joy detailed these. The first, a 20 yr old man, developed coagulopathy, active bleeding, compartment syndrome, "rhabdomyolysis" (CK 9800 U/L), AKI/ARF & shock (no documented neurotoxicity). Despite adequate AV (coagulopathy resolved), haemodialysis, ICU care, he died. Case 2, a 46 yr old man, developed coagulopathy, mild neurotoxicity, myalgia, oedema (periorbital, leg), hypotension, then melaena, conjunctival chemosis, retinal haemorrhages, AKI/ARF, thrombocytopenia, then DIC & shock, ending fatally, despite AV. Case 3, a 22 yr old man, developed marked bitten limb swelling, coagulopathy, AKI/ARF, "rhabdomyolysis" (CK 5500 U/L), gangrene of leg requiring amputation, worsening ARF and died, despite AV. Joy considered these cases showed 2 distinct envenoming syndromes; (A) mild oedema + neurotoxicity + classic RV features, (B) severe oedema + myotoxicity (not sure this was proven, given local tissue injury), that may represent regional intraspecific venom differences.</p>
<p>Dalia Ponce</p>	<p>Unravelling the venom complexity of the jellyfish <i>Chrysaora fuscescens</i> (Cnidaria, Scyphozoa) by an integrated transcriptome and proteome approach</p>
	<p>Dalia presented her research into jellyfish venom, using a transcriptomic & proteomics approach, with <i>Chrysaora fuscescens</i> venom. This jellyfish causes adverse, generally non-lethal effects in humans (Increased upper airway secretions, coughing, rhinorrhoea, lachrymation, local pain & blistering, cramps). After first isolating and fractionating venom, 131 putative toxins were identified (see slide) in 9 major classes/functional groups. She then dissected each class into subtypes. Within the protease class there were metalloproteases, disintegrins, endothelin converters, serine proteases & chymotrypsin-like enzymes. While the pore forming toxin class represented only 1% of venom, it contains toxins considered by some researchers to be key contributors towards pathologic reactions in humans (haemolysis, dermonecrosis, cardiovascular collapse & lethality). She then provided a chart comparing her findings with previously published data for other cnidarians.</p>


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Speaker	Topic/Summary
Vidal Haddad Junior	The lionfish in the New World: dissemination, ecological impact and risks to humans
	<p>Vidal, who uniquely at this congress, insisted no photos or recording of his presentation be made, discussed the growing environmental and consequent medical problems caused by the expanding distribution of the venomous lionfish, <i>Pterois volitans</i>, a favourite of aquarists, but introduced into wild environments. As the map shows, it has now spread widely and outcompetes native species of fish. While stings do not cause serious (life threatening) envenoming, they do cause intense pain and frequent secondary infection. Primary necrosis is not reported. Hot water immersion appears the most effective first aid and consider routine antibiotics. There is no clear solution to removing these exotic lionfish populations.</p>  <p>Map of native range of <i>Pterois volitans</i> (green) and <i>P. miles</i> (blue) adapted from Schultz (1986) and Randall (2005). Star in Mediterranean Sea denotes Lessepsian migration of <i>P. miles</i> via the Suez Canal (Golani and Sonin 1992). Non-native range of <i>P. volitans</i> and <i>P. miles</i> in the Americas is shown in red (from Schofield et al. 2012). Predicted future distribution of lionfish along coastal South America is shown in red hatching (Morris and Whitfield 2009).</p>


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Speaker	Topic/Summary
<p data-bbox="165 315 448 349">Angel A Yanagihara</p> 	<p data-bbox="513 315 1353 383">Cubozoan Envenomations: Pathogenetic Mechanisms and Clinical Management Implications</p> <p data-bbox="513 389 1417 1240">Angel, from the University of Hawaii, presented an overview of her recent work on jellyfish venoms, particularly from <i>Alatina</i> spp., using her self-developed methodology to extract venom from nematocysts. She compared this with other published methods, suggesting they were inferior. She then concentrated on her hypothesis that pore-forming toxins (“porins”) are the principle cause of pathologic reactions in stung humans. These haemolytic toxins appear to cause similar cardiotoxic effects in animal models as seen with whole venom, unlike other toxin isolates. Since box jellyfish fatal envenoming is associated with very rapid cardiotoxicity and cardiac arrest, she considers this indicates porins are the key toxins responsible. Her studies on <i>Chironex</i> venom demonstrated porins at equivalent lethal dosage induced rapid (5 min) release of K⁺ from RBC, then haemolysis at 20 min. This may indicate, according to Angel, that severe rapid hyperkalaemia, induced by porin damage to RBC, may be the cause of cardiac toxicity. EM studies showed numerous porin-induced pores in the RBC membrane. Zinc gluconate inhibits porin activity and prolongs survival of envenomed mice. She encapsulated these ideas/findings into hypotheses on how <i>Chironex</i> and irukandji stings induce pathology. Finally she presented information on her patented jellyfish sting cream, “Sting No More”.</p>


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Speaker	Topic/Summary
	<p>Hypothetical Model of Envenomation Induced Acute Cardiovascular Collapse</p> <p>ACC Post Envenomation Time line</p> <p>T_0 T_{3min} T_{10min}</p> <p>Pore formation</p> <p>Yanagihara Working Hypothetical Model to Account for Constellation of Irukandji Syndrome Symptoms</p> <p>Pathophysiology of Cubozoan Envenomations</p>


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Speaker	Topic/Summary
<p>Luis M Botana</p> 	<p>Presence of tetrodotoxin in an increasing number of vectors, and the real value of TEF (toxic equivalent factor)</p> <p>Luis discussed the increasing frequency of marine poisoning as a medical, social & economic problem, focussing on the wider distribution of tetrodotoxin (TTX), in more animals capable of vectoring it to humans. It can coexist with and therefore be masked by other toxins, such as with PSP, illustrated in the 2007 poisoning series in Malaga where consumption of a single shellfish killed several people. It has been found in starfish, echinoderms, several shellfish species, holothurians, in addition to a variety of fish in European/UK waters. Indeed, TTX poisoning must now be added to the list of types of shellfish poisoning. TTX analogues appear to be associated with bacterial contamination of shellfish, particularly by <i>Vibrio</i> spp. & <i>Pseudomonas</i> spp. and especially <i>V. alginolyticus</i> & <i>V. parahaemolyticus</i>.</p>
<p>Julian White</p>	<p>The Clinical Toxinology Resources Website; An Update On 13 Years Experience</p>
	<p>I presented an update on the design, functioning, content and usability of arguably the most comprehensive clinical toxinology internet resource, now running for 13 years. The underlying database driven model and nature of data stored was covered, then challenges around maintaining, updating and expanding the huge dataset. I canvassed to possibility of making the website a global project within toxinology, opening up data upkeep and expansion to experts outside the core group, with some form of oversight committee, possibly supported through IST, to manage quality assurance of new uploaded data. This stimulated considerable interest from the audience.</p>

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Speaker	Topic/Summary
<p data-bbox="167 313 414 380">Wolfgang Wüster (Keynote)</p> 	<p data-bbox="517 313 1425 380">Snakes behaving badly: evolution of venom spitting in cobras in its historical context</p> <p data-bbox="517 387 1425 1350">Wolfgang expanded on a subject touched on in Harry Greene's plenary lecture, the evolution of venom delivery mechanisms under the influence of escalating threat from evolving predators such as proto-humans. He noted that the key function of venom is subduing/killing prey, driving evolution of venom composition, while the role of venom in pre-digestion is controversial with limited supportive evidence. The defensive role of venom is documented mostly from snake-human interactions. The only clear example of defence-specific adaptations is venom spitting by cobras, with their modified fangs to allow long range spitting with high accuracy. He then detailed research to determine if the 3 separate clades of spitting cobras arose independently, or from a common origin, using DNA methodology. These studies strongly support independent evolution of spitting in the 3 cobra groups, but why did it arise in Africa 6 Mya and then separately in Asia 2-4 Mya? There is a clear correlation between the arrival of early hominids and development of spitting cobras, but why just against hominids? Possibly because hominids are known to kill snakes (as a threat) and using tools that blunt more intimate defensive contact such as a standard snake bite. Spitting as a long-distance defence, could confer substantial evolutionary advantage. Further, the evolved tendency to accurately target eyes, with painful, disabling, but non-lethal effects (ie teaching to avoid confrontation in future) could also be considered advantageous evolution.</p>


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Speaker	Topic/Summary
<p>Nicholas R Casewell (Keynote)</p> 	<p>Extreme convergence in toxin resistance by predictable parallel molecular evolution</p> <p>Nick, who usually presents on molecular aspects of venom, here presented on plant-based cardiac glycosides as a poisoning agent. These toxins inhibit the Na-K pump, preventing Na export from cells, so inhibiting Ca export, resulting in intracellular Ca accumulation which, in cardiac muscle cells, causes increased force of cardiac contraction, ventricular tachycardia and fibrillation. Cardiac glycosides are found in a variety of plants (foxglove, oleander, milkweeds) plus in Bufonid toads. A classic example is digoxin. A number of animals have evolved resistance to these toxins so that these plants (& toads) can be eaten safely. Alterations in molecular structure of receptor molecules can confer resistance to toxins and this appears to have arisen independently a number of times, even within reptiles (eg African & Asian varanid lizards; some Bitis vipers; a few cobras; numerous natricine snakes) and this can be linked to coexistence/exposure to bufonid toads. Similar findings have been demonstrated in insects, allowing consumption of these plants, and in rodents, hedgehogs, and anurans. It appears that in all cases it is the same molecule (α-subunit of Na/K-ATPase) undergoing subtle change, but at different structural positions, the common theme being absence of critical hydrogen bonding in resistant molecules.</p>


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Speaker	Topic/Summary
	<div><p>The top diagram illustrates a membrane protein with two α helices spanning a membrane. The extracellular side shows various charged residues: R^+ (x6), V, T, L, E^- (x1), D^- (x3), R^+ (x3), Q, G, N, H^+ (x4), and L (x3). The cytoplasmic side shows NH_2 and $COOH$ groups. Below the membrane, a row of icons represents different animal groups: insects, lizards, snakes, rodents, and hedgehog. The bottom diagram is a phylogenetic tree titled "Charged replacements underpin resistance". It shows the evolutionary relationships between various animal groups, with isoelectric point (pI) values indicated at the nodes. The groups include crocodiles, birds, squamates, mammals, snakes, lizards, rodents, hedgehog, Leptodactylus, bufonids, insects, anurans, bony fish, cartilaginous fish, lampreys, sea urchins, crustaceans, nematodes, molluscs, annelids, and cnidarians. A color scale on the right indicates the isoelectric point scale from 3.2 to 4.3.</p></div>


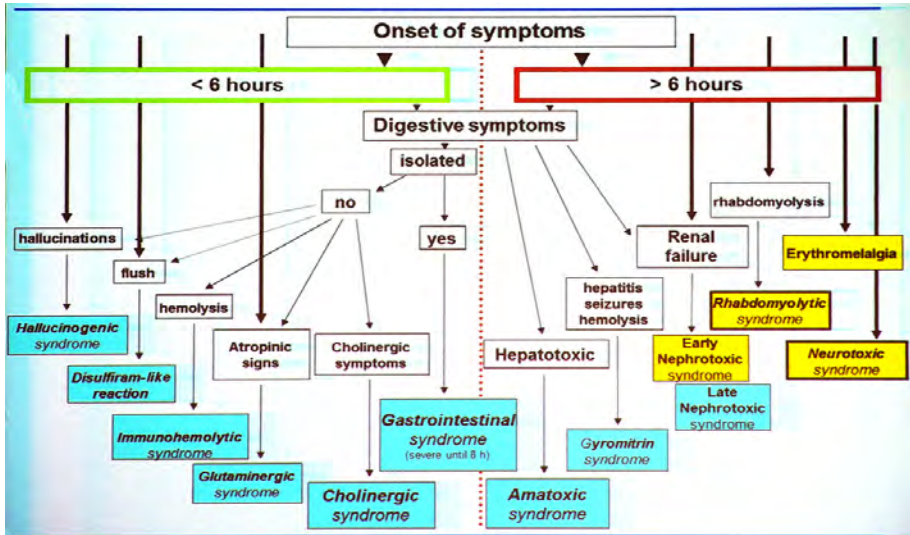
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Speaker	Topic/Summary
<p>Michael Eddleston (Keynote)</p> 	<p>Epidemiology and management of plant self-poisoning in South Asia</p> <p>Michael provided an overview of plant poisoning globally, noting 3 major types of poisoning (unintentional, recreational, intentional self-poisoning) and the major problem of lack of antidotes for most types of plant poisoning. In South Asia plant poisoning has long been recognised. Castellani & Chalmers in 1919 noted key criminal and suicide use of <i>Nerium oleander</i>, <i>Cerbera manghas</i>, <i>Cascabela thevetia</i> & <i>Gloriosa superba</i>, all causing GIT effects and the first 3 causing digoxin-like cardiac effects, lethal in 12-15 hrs. <i>Cascabela thevetia</i> (formerly <i>Thevetia peruviana</i>), yellow oleander, is a very commonly used poison in Sri Lanka & India with 10,000+ cases and 500+ deaths/yr. It causes severe cardiac glycoside-type poisoning with hyperkalaemia & cardiac toxicity and treatment can be problematic, including atropine, pacemaker, insulin/dextrose and, when available/affordable, DigiFab, the latter being the most effective and life saving treatment. (case fatality rate with DigiFab 3.1%; without, 9.3%). Pink oleander, <i>Nerium oleander</i>, also very common, can cause similar problems, as can sea mango fruit, <i>Cerbera manghas</i>, but the latter is not responsive to DigiFab. Oduvan, <i>Cleistanthus collinus</i>, causes severe hypokalaemia and cardiac dysrhythmias, metabolic acidosis, ARDS, shock, rhabdomyolysis and neuromuscular weakness. There is no antidote, though K⁺ and NAC may help. <i>Colchicum autumnale</i> & <i>Gloriosa superba</i>, containing colchicine, cause GIT upset, perioral paraesthesiae/numbness, abdominal pain, bloody diarrhoea, then seizures, coma, ascending polyneuropathy, coagulopathy & multi-organ failure, with alopecia in survivors.</p>
<p>Julian White (Keynote)</p>	<p>Mushroom poisoning: a proposed new clinical classification</p>
	<p>I presented detail on our new classification scheme for mushroom poisoning which we hope will become the new global standard, being co-authored by many of the world's leading mushroom poisoning experts. The scheme includes a detailed diagnostic algorithm.</p>


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Speaker	Topic/Summary
<p>Thomas R Zilker</p> 	<p>Management of Amanita poisoning</p> <p>Thomas, a global expert on amanita poisoning and ex-Director of the Munich PIC, first noted edible mushrooms causing confusion with amatoxic species (<i>Russula cyanoxantha</i>, <i>R. aeruginea</i> vs <i>Amanita phalloides</i>; <i>Agaricus silvicola</i> vs <i>Amanita virosa</i>; <i>Kuehneromyces mutabilis</i> vs <i>Galerina marginata</i>). Near 100% of amatoxins (α, β, γ - amanitins) are absorbed, but without being metabolised or protein bound, and 80% are eliminated via kidneys within 6 hrs, bile 7%, faeces 10%. Amatoxins are transported to hepatocytes, enter cell nucleus, bind to RNA-polymerase II and so inhibit transcription from DNA to mRNA thus leading to hepatocyte necrosis/apoptosis. There is “treacherous” latency; GIT phase 6-18 hrs, then lasting 1-2 days, followed by liver damage 2+ days, ending in terminal liver failure at 5-7 days. Thomas described treatment as “polypragmasia”, involving elimination (gastric lavage, forced diuresis, charcoal etc), antidotes (silibinin, NAC, prednisolone etc), treating coagulopathy (FFP, AT III, heparin), treating hepatic failure (paranomycin, lactulose). He noted that the best survival is associated with silibinin and combining this with penicillin increases the fatality rate, while penicillin alone has more than twice the fatality rate. NAC alone is almost as good as silibinin. In predicting severe cases likely to die unless they have a liver transplant, combining the prothrombin index + creatinine level had 100% sensitivity & 98% specificity. Also, if the latency period between ingestion and onset of GIT effects is <12hrs there is a 6 fold increased risk of fatal outcome. Commencing silibinin > 24 hrs after ingestion increases risk of fatal outcome 3 fold.</p> <p>Thomas then summed up issues using his devised poems viz:</p> <p>(1) On problems of polypragmasia; Tell me how many drugs you have seen; To get rid of amatoxin; But if you use many; We don't know any; Of which we could really be keen. (2) My plea; Evidence based medicine can fool; If there is no way or tool; To get a treatment registration; Leading to deepest resignation; Many patients meet their fate; Because the studies come too late; Hence, this is my real plea; Overcome bureaucracy. (3) To be or not to be depends on early therapy; Before we start a therapy; We think of a decision tree; We hope for the laboratory; And there we sit and wait and see; And there we sit and we debate; So long till everything is late; Because the toxin doesn't wait; It hits the liver rather straight; Please treat as promptly as you can; To be that woman or that man; That saves the mushroom's eater life; And all his children and his wife; With mushroom eaters who are hit; By belly cramps and lot of shit; You have to take at once the lead; Just take the antidote and treat.</p>


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Speaker	Topic/Summary
Régis Bédry	The "new" mushroom syndromes
	<p>Régis, from the Bordeaux PIC, France, discussed the growing number of mushroom poisoning syndromes being described from Europe (some may have been described earlier in other regions). However, to place in perspective, the well established causes of fatal poisoning, amatoxins & <i>Cortinarius</i> spp. (delayed renal failure) remain the most important. He emphasised the importance of the 6 hr rule to capture potentially severe poisonings such as by amatoxins (onset of first symptoms >6 hrs post-ingestion) and provide a management algorithm.</p>  <pre> graph TD A[Onset of symptoms] --> B[< 6 hours] A --> C[> 6 hours] B --> D[hallucinations] B --> E[flush] B --> F[hemolysis] B --> G[Atropinic signs] B --> H[Cholinergic symptoms] B --> I[Gastrointestinal syndrome (severe until 8 h)] B --> J[Cholinergic syndrome] B --> K[Amatoxic syndrome] C --> L[Digestive symptoms] L --> M[isolated] L --> N[yes] L --> O[no] M --> P[Hallucinogenic syndrome] M --> Q[Disulfiram-like reaction] M --> R[Immuno-hemolytic syndrome] M --> S[Glutaminergic syndrome] M --> T[Cholinergic syndrome] M --> U[Gastrointestinal syndrome (severe until 8 h)] M --> V[Amatoxic syndrome] N --> W[hepatitis seizures hemolysis] N --> X[Hepatotoxic] N --> Y[Gyromitrin syndrome] N --> Z[Renal failure] N --> AA[Rhabdomyolytic syndrome] N --> AB[Early Nephrotoxic syndrome] N --> AC[Late Nephrotoxic syndrome] N --> AD[Neurotoxic syndrome] O --> AE[rhabdomyolysis] O --> AF[Erythromelalgia] </pre>

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Speaker	Topic/Summary
	<p>He noted 4 “new” syndromes. Note all of these are within the new classification of mushroom poisoning presented in my earlier lecture.</p> <p>(1) Acromelagia syndrome (<i>Clytocybe acromelagia</i>, <i>C. amoenolens</i>): Originally described from Japan, now in France, patients develop painful hands, feet, ± swelling, often as paroxysmal nocturnal crisis, relieved by cold, developing 1-3 days after ingestion & lasting weeks to months. There is no definitive treatment.</p> <p>(2) Rhabdomyolysis (<i>Tricholoma equestre</i>, <i>Russula subnigrans</i>): Described from SW France (coastal pine forests sth of Bordeaux; Nth America, Japan, Poland). Delayed type (<i>T.e</i>) develops 1-6 days post ingestion, with fatigue, myalgia, sweating, nausea, myoglobinuria, but not AKI. In some cases progresses to myocarditis, ARF, hyperkalaemia, death. Rapid type (<i>R.s</i>) presents with GIT effects 2hrs post-ingestion, then in a few cases, electrolyte disturbance, hyperkalaemia, severe rhabdomyolysis, AKI/ ARF, pulmonary oedema, shock, death.</p> <p>(3) Early acute renal failure (<i>Amanita proxima</i>, <i>A. smithiana</i>): Onset of GIT effects 8-14 hr post-ingestion (much less if eaten raw), then hepato-renal syndrome at 1-4 days. Only mild hepatotoxicity, but acute tubulointerstitial nephritis & ARF, generally reversible.</p> <p>(4) CNS involvement (<i>Hapalopilus rutilans</i>, <i>Pleurocybella porrigens</i>, <i>Morchella esculenta</i>): For <i>H.r</i> (polyporic acid) onset of GIT effects 12 hr post-ingestion, then vertigo, ataxia, drowsiness, purple urine (diagnostic), resolves over 2-4 days. For <i>P.p</i> patients with pre-existing renal failure develop convulsive encephalopathy 1-31 days post-ingestion. Significant mortality, few fully recover. For <i>M.e</i> onset of GIT effects 6-12 hrs post-ingestion, ± ataxia, tremor, visual disturbance, resolves within 1 day.</p>
M Abul Faiz	Challenges of diagnosis of fatal plant related acute intoxication in Bangladesh
	<p>Abdul noted PIC data from Bangladesh, where plant poisoning is principally from <i>Datura</i>. However, he presented mass poisoning after consumption of <i>Xanthium strumarium</i> (ghagra shak - standard part of diet) in NE Bangladesh, with 24% mortality, mostly children. Prominent features included fever, diarrhoea, dyspnoea, fatigue/weakness, convulsions (32%), altered mental status (54%), coma (35%), abdominal pain. In the outbreak year drought had forced villagers to eat immature plants. He then discussed yellow oleander poisoning and herbal medicine poisoning, both associated with fatalities.</p>

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Speaker	Topic/Summary
<p data-bbox="167 309 387 342">David A Warrell</p> 	<p data-bbox="515 309 1406 342">Supping with the Panará: a case for Inspector Morse in Oxford</p> <p data-bbox="515 347 1422 1126">David provided an interesting and theatrical case of poisoning involving a 28 yr old academic anthropologist who presented with deafness, blindness, loss of smell & taste, altered sensation in limbs & face, ataxia, which had progressively developed over 2 months. He and his partner had been living in the Panara region of Amazonia with natives, Brazil, including through the annual dry season epidemic of painful blistering stomatitis. For natives this lasted 4-6 weeks, but the patient continued for 14 weeks. In Rio de Janeiro, prior to coming to Oxford, he was diagnosed as multiple sclerosis and placed on prednisolone. This diagnosis was dismissed in Oxford, but all lab tests were normal (CSF, B12, thiamine, folic acid), though on electrophysiology there was polyneuropathy with axonal degeneration. The key question on history was had he been eating cassava. He had, but with his stomatitis he resorted to cassava drink which tasted bitter. This contains cyanogenic glycosides and is known to cause tropical ataxic neuropathy and Konzo (acute spastic paraparesis). This condition is well described from Africa, less so from Sth America. Placed on a normal diet + vitamins including hydroxycobalamin, he progressively improved over several months.</p>



University of Adelaide
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CLINICAL TOXINOLOGY SHORT COURSE 2016

Women's & Children's Hospital
Adelaide, Australia
March 14-19, 2016



The Premier Clinical Training
Course in Toxinology at an
International Level

Courses Co-ordinator
Prof. Julian White
Head of Toxinology

Women's & Children's Hospital

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Website: www.toxinology.com



IMPORTANT COURSE INFORMATION

COURSE RELATED QUESTIONS:

Who is this course designed for?

Primarily for doctors/health professionals requiring detailed and practical information on snakebite, spiderbite, scorpion stings, marine envenoming, poisonous plants & mushrooms and related topics with a global and Australian perspective. It is particularly relevant for those working in emergency medicine, toxicology, intensive care, or in rural practice. Throughout there will be an emphasis on practical clinical issues and development of clinically relevant skills. It will also be of interest to poisons information pharmacists and graduate nurses in emergency medicine and toxinology scientists. You should be fluent in English, as no language translation will be available.

When and where are the courses held?

The course runs over 6 days; Monday March 31st to Saturday April 5th, 2014. The venue is the Women's and Children's Hospital, North Adelaide, SA, Australia

What does the course cover?

We cover terrestrial & marine animals, plants & mushrooms, including extensive sessions on venomous snakes by region. Detailed sheets on course content will be available on the web at <http://www.toxinology.com>.

Is the course accredited in any way?

The course is a University of Adelaide postgraduate training course. We are seeking formal accreditation of continuing education points with relevant colleges and possible incorporation within some college specialist training schemes.

How many people can attend the course?

The maximum course capacity is 50 registrants, to ensure a chance for interactions with faculty. Previous courses filled early, so early registration is advisable.

How much does the course cost and what does this cover?

The course costs Aus\$2,200 (+GST for Australians only); the fee covers the full course, course notes, field trip, morning and afternoon teas and light lunches. It does not cover the course dinner or accommodation.

Are there any course notes or reading material available prior to the course?

We produce course notes for registrants prior to the course, which will include recommended textbooks and reading list. You are still strongly advised to take notes during all sessions. (The 2012 Course Handbook exceeded 500 pages.)

What sort of practical clinical sessions are included?

The programme includes many interactive sessions discussing "clinical evolving problems" (CEPs) to develop registrant's understanding of clinical skills in toxinology and test those skills in a group setting. These are all based on real patients contributed by faculty members, drawn from their own clinical experience.

Is there any formal evaluation of my performance on the course?

Yes! Faculty will be evaluating all registrants on their interactions, especially during the clinical evolving problem sessions. On the Saturday there will be a written examination.

For further information contact Prof. White (julian.white@adelaide.edu.au) or Dr. David Bates (david.bates@adelaide.edu.au).

University of Adelaide

CLINICAL TOXINOLOGY SHORT COURSE

ENROLMENT FORM

First Name: Last Name: Title: (Dr., Prof. etc)

Qualifications:

Your position/job:

Institution:

Postal Address:

Suburb/City: Postcode:

Country:

Telephone: Fax:

Mobile phone:

Email:

Clinical experience with cases of envenoming?:

Arrival Date:

Departure Date:

What accommodation have you arranged?:

Have you checked to see if you need a VISA to enter Australia?:

Course Fees includes full course, course notes, field trip, morning & afternoon teas and light lunches, but do not include the Course Dinner (approx. Aus\$100.00 - to be confirmed). The Course runs from about 8.00/9.00am till 5.30/6.00pm daily.

Course fee is Aus\$2,200.00 (plus Aus\$220.00 GST if registrant is from Australia; may be claimable as tax refund).

Course venue: Women's and Children's Hospital, North Adelaide

Accommodation: This is the responsibility of course participants to find and pay for. A number of hotels/motels are close to the hospital and a few of these are listed in the information sheet for the course.

To confirm a booking for the Course you must promptly pay the Invoice we will send you once we receive your enrolment form. Cancellation must be made at least ten (10) weeks prior to commencement of the course to ensure refund of your deposit. Refunds will NOT be available for non-attendance without adequate notification. Full payment is required by February 1st, 2016.

You will be sent an Invoice once we receive your enrolment form. Please indicate below how much you wish to pay at this time:

(1) Deposit only (Aus\$400 plus GST if applicable) ☐

(2) Full course fee (Aus\$2,200 plus GST if applicable) ☐

The invoice should be paid immediately on receipt, to secure your place on the course. Payment options include credit card (VISA, MasterCard, AMEX), bankers cheque, or internet banking transfer (Australian residents only).

Please email your completed form to tox.members@adelaide.edu.au OR fax to +61-8-81618024

Signature: Date:/...../.....



1961 West Brichta Dr.
Tucson, AZ 85745, USA
Tel: 1 520 884-9345
Fax: 1 520 884-9345
ponerine@dakotacom.net

Southwest Venoms

CATALOGUE OF INSECT VENOMS (2012-2013)

Prices in U.S. dollars. All venoms are pure venoms (not venom sac or apparatus homogenates) collected according to the methods of Schmidt (1986. *In: Venoms of the Hymenoptera* [T. Piek, ed.], pp. 425-508. Academic Press: London.).

Prod. No.	VENOM	(LD ₅₀ mg/kg, mice)	VENOM PRICE			
			1 mg	5 mg	25 mg	100 mg
	SOCIAL WASPS	(LD ₅₀)				
	Yellowjackets -- <i>Vespula</i>					
W-10	<i>V. pensylvanica</i>	(6.4)	50	225	1000	*
W-19	other species**		*			
	Hornets -- <i>Vespa</i>					
W-20	<i>V. mandarinia</i>	(4.1)	50	225	1000	*
W-21	<i>V. tropica</i>	(2.8)	50	225	1000	*
W-29	others **		*			
	Paper wasps -- <i>Polistes</i>					
W-30	<i>P. comanchus navajoe</i>	(5)	40	180	800	*
W-31	<i>P. flavus</i>	(3.8)	40	180	800	*
W-32	<i>P. canadensis</i>	(2.5)	50	225	*	
W-33	<i>P. erythrocephalis</i>	(1.5)	50	225	*	
W-39	<i>Polistes</i> sp. as available**		30	135	600	2100
	New World Polybiine wasps					
W-40	<i>Brachygastra mellifica</i>	(1.5)	60	270	1200	*
W-50	<i>Synoeca septentrionalis</i>	(2.7)	60	270	1200	*
W-60	<i>Parachartergus fraternus</i>	(5)	70	300	1400	*
W-70	<i>Polybia sericea</i>	(6)	80	350	*	
W-71	<i>P. simillima</i>	(4.1)	80	350	*	
W-72	<i>P. occidentalis</i>	(5)	100	*		
W-80	<i>Agelaia myrmecophila</i>	(5.6)	140	*		
	Old World Polybiine wasps					
W-90	<i>Belonogaster juncea colonialis</i>	(3)	80	350	*	
	SOCIAL BEES					
	Honey bees -- <i>Apis</i>					
B-10	<i>A. mellifera</i>	(2.8)	20	90	400	1400
B-11	<i>A. mellifera</i> Africanized bees	(2.8)	20	90	400	1400
B-12	<i>A. mellifera</i> queens		40	180	800	2800
B-13	<i>A. dorsata</i>	(2.8)	50	225	1000	3500
B-14	<i>A. cerana</i>	(3.1)	55	245	*	
B-19	others (<i>A. florea</i> , etc.)**		*			
	Bumble bees -- <i>Bombus</i>					
B-20	<i>B. sonorus</i>	(12)	50	225	1000	*
B-21	<i>B. impatiens</i>	(12)	50	225	*	
B-29	other species**		30	*		

Prod. No.	VENOM	(LD ₅₀ mg/kg, mice)	VENOM PRICE			
			1 mg	5 mg	25 mg	100 mg
ANTS -- FORMICIDAE						
		(LD ₅₀)				
	<i>Pogonomyrmex</i> -- harvester ants					
A-10	<i>P. barbatus</i>	(0.6)	50	225	1000	3500
A-11	<i>P. maricopa</i>	(0.12)	60	270	1200	4200
A-12	<i>P. occidentalis</i>	(0.5)	70	315	1400	*
A-13	<i>P. rugosus</i>	(0.7)	50	225	1000	3500
A-15	<i>P. desertorum</i>	(0.7)	160	*		
A-19	<i>Pogonomyrmex</i> sp. as available		45	200	900	3200
	<i>Myrmecia</i> -- bull ants					
A-20	<i>M. gulosa</i>	(0.18)	60	270	1200	4200
A-21	<i>M. tarsata</i>	(0.18)	60	270	1200	*
A-22	<i>M. browningi</i>	(0.18)	70	315	*	
A-23	<i>M. rufinodis</i>	(0.35)	70	315	*	
A-24	<i>M. simillima</i>	(0.21)	70	315	*	
A-25	<i>M. pilosula</i>	(5.7)	100	*		
A-30	<i>Pachycondyla (Neoponera) villosa</i>	(7.5)	60	270	*	
A-31	<i>P. (Neoponera.) apicalis</i>	(> 16)	70	*		
A-32	<i>P. crassinoda</i>	(2.8)	80	*		
A-33	<i>P. (Megaponera) foetens</i> (Metabele ant)	(130)	70	315	*	
A-34	<i>P. (Paltothyreus) tarsatus</i> (stink ant)	(64)	50	225	1000	3500
A-35	<i>P. (Bothroponera) strigulosa</i>	(9)	70	*		
A-36	<i>Termitopone commutata</i>	(10)	70	315	1400	*
A-40	<i>Platythyrea lamellosa</i>	(11)	70	315	*	
A-50	<i>Diacamma</i> sp.**	(35)	100	450	*	
A-60	<i>Dinoponera gigantea</i>	(11)	60	270	1200	4200
A-70	<i>Paraponera clavata</i> (bullet ant)	(6.0)	60	270	1200	4200
A-80	<i>Ectatomma tuberculatum</i>	(1)	60	270	*	
A-81	<i>E. quadridens</i>	(17)	60	270	*	
A-90	<i>Odontomachus</i> sp.**	(33)	60	275	*	
A-110	<i>Tetraponera</i> sp**	(.35)	140	600	*	
A-120	<i>Streblognathus aethiopicus</i>	(8.0)	80	360	*	
SOLITARY WASPS AND BEES						
	Spider wasps -- Pompilidae					
SW-10	<i>Pepsis</i> sp.**	(65)	60	270	1200	4200
	Mutillid wasps -- Mutillidae					
SW-20	<i>Dasymutilla</i> sp.**	(71)	70	315	1400	*
SW-39	Other wasps (Scoliidae, Tiphiidae, Sphecidae, Eumenidae, etc.)**		*			
	Carpenter bees -- <i>Xylocopa</i>					
SB-10	<i>X. californica</i>	(21)	50	225	1000	*
SB-11	<i>X. veripuncta</i>	(33)	55	245	*	
SB-20	<i>Proxycopa rufa</i>	(11)	100	450	*	
SB-39	Other bees**		*			

*Inquire for prices and availability.

**Available species provided; exact determinations usually included.

Natural Toxins

Research Center
(NTRC)

TEXAS A&M UNIVERSITY
KINGSVILLE

VENOM QUALITY GUARANTEE

Authenticity of Species • Purity of Venom
Maximum Biological Activity • Our Venom is Never Pooled

Snake venoms contain important molecules which are valuable for researching the treatments of strokes, heart attacks, and cancer.

The Natural Toxins Research Center (NTRC) at Texas A&M University-Kingsville is dedicated to providing high quality snake products for biomedical research. We are committed to the procurement and distribution of venoms, venom fractions and tissue for biomedical research. Venoms from the same species can be different, and therefore extracted venoms are never pooled. Each vial contains venom from a single snake, and venoms of the same species are never mixed. The vials are labeled with the snakes' scientific and common names, ID tag number and sex. The ID tag number can be traced back to the NTRC Internet Database (ntrc.tamuk.edu/cgi-bin/serpentarium/snake.query) for additional information about each snake.

Southern Copperhead - <i>Agkistrodon contortrix contortrix</i>	\$75. ⁰⁰ /1g	\$50. ⁶³ /500mg	
Broad-Banded Copperhead - <i>Agkistrodon contortrix laticinctus</i> ..	\$100. ⁰⁰ /1g	\$67. ⁵⁰ /500mg	
Northern Copperhead - <i>Agkistrodon contortrix mokasen</i>	\$50. ⁰⁰ /1g	\$33. ⁷⁵ /500mg	
Trans-Pecos Copperhead - <i>Agkistrodon contortrix pictigaster</i>	\$75. ⁰⁰ /1g	\$50. ⁶³ /500mg	
Florida Cottonmouth - <i>Agkistrodon piscivorus conanti</i>	\$60. ⁰⁰ /1g	\$40. ⁵⁰ /500mg	
Western Cottonmouth - <i>Agkistrodon piscivorus leucostoma</i>	\$56. ⁰⁰ /1g	\$37. ⁸⁰ /500mg	
Eastern Diamondback Rattlesnake - <i>Crotalus adamanteus</i>	\$50. ⁰⁰ /1g	\$33. ⁷⁵ /500mg	
Western Diamondback Rattlesnake - <i>Crotalus atrox</i>	\$45. ⁰⁰ /1g	\$30. ³⁸ /500mg	
Sonoran Sidewinder - <i>Crotalus cerastes cercobombus</i>	\$125. ⁰⁰ /1g	\$84. ³⁸ /500mg	
Timber Rattlesnake - <i>Crotalus horridus</i>	\$70. ⁰⁰ /1g	\$47. ²⁵ /500mg	
Mottled Rock Rattlesnake - <i>Crotalus lepidus lepidus</i>	\$125. ⁰⁰ /1g	\$84. ³⁸ /500mg	
Blacktail Rattlesnake - <i>Crotalus molossus molossus</i>	\$400. ⁰⁰ /1g	\$270. ⁰⁰ /500mg	\$72. ⁹⁰ /100mg \$49. ²¹ /50mg
Great Basin Rattlesnake - <i>Crotalus oreganus lutosus</i>	\$125. ⁰⁰ /1g	\$84. ³⁸ /500mg	
Grand Canyon Rattlesnake - <i>Crotalus oreganus abyssus</i>	\$250. ⁰⁰ /1g	\$168. ⁷⁵ /500mg	\$45. ⁵⁶ /100mg \$30. ⁷⁵ /50mg
Texas Coral Snake - <i>Mircrurus tener tener</i>	\$2000. ⁰⁰ /1g		
Florida Coral Snake - <i>Mircrurus fulvius</i>	\$1800. ⁰⁰ /1g		
Southern Pacific Rattlesnake - <i>Crotalus oreganus helleri</i>	\$400. ⁰⁰ /1g	\$270. ⁰⁰ /500mg	\$72. ⁹⁰ /100mg \$49. ²¹ /50mg
Northern Pacific Rattlesnake - <i>Crotalus oreganus oreganus</i>	\$400. ⁰⁰ /1g	\$270. ⁰⁰ /500mg	\$72. ⁹⁰ /100mg \$49. ²¹ /50mg
Mohave Rattlesnake - <i>Crotalus scutulatus scutulatus</i> (A)	\$250. ⁰⁰ /1g	\$168. ⁷⁵ /500mg	\$45. ⁵⁶ /100mg \$30. ⁷⁵ /50mg
Mohave Rattlesnake - <i>Crotalus scutulatus scutulatus</i> (B)	\$1000. ⁰⁰ /1g	\$675. ⁰⁰ /500mg	\$182. ²⁵ /100mg \$123. ⁰² /50mg \$33. ²² /10mg
Prairie Rattlesnake - <i>Crotalus viridis viridis</i>	\$70. ⁰⁰ /1g	\$47. ²⁵ /500mg	
Red Spitting Cobra - <i>Naja pallida</i>	\$100. ⁰⁰ /1g	\$67. ⁵⁰ /500mg	
Desert Massasauga - <i>Sistrurus catenatus edwardsii</i>	\$1000. ⁰⁰ /1g	\$675. ⁰⁰ /500mg	\$182. ²⁵ /100mg \$123. ⁰² /50mg \$33. ²² /10mg
Western Massasauga - <i>Sistrurus catenatus tergeminus</i>	\$1000. ⁰⁰ /1g	\$675. ⁰⁰ /500mg	\$182. ²⁵ /100mg \$123. ⁰² /50mg \$33. ²² /10mg
Bushmaster - <i>Lachesis muta muta</i>	\$2000. ⁰⁰ /1g	\$1350. ⁰⁰ /500mg	\$364. ⁵⁰ /100mg \$246. ⁰⁴ /50mg \$66. ⁴³ /10mg

(A) - neurotoxic venom
(B) - non-neurotoxic venom
*Subject to availability

Venom is collected under stringent laboratory conditions using disposable labwear for each extraction. Venom is collected in new, non-reusable plastic cups with parafilm coverings. Snakes are allowed to bite into the parafilm diaphragm and the venom glands are not massaged. Immediately following collection, each venom sample is clarified by centrifugation at 500 x g for 5 minutes to remove cellular debris and frozen at -90° C until lyophilized.

Foreign Investigators: Please note that your order may be subject to import duties, taxes, tariffs, customs charges, DDP, VAT, and the like, once your package reaches your country. It is your responsibility to pay for these charges. The Natural Toxins Research Center will not be responsible for paying these charges, and we will not bill you for such charges when you place your order.

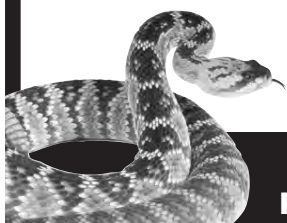
Venom glands and fractions also for sale - call for pricing & availability

**If you're interested in study or research opportunities
at the NTRC, call us at the number below!**

www.ntrc.tamuk.edu

Please Contact Us for More Information:

Phone: (361) 593-3082 • Fax: (361) 593-3798 • Email: kanmd00@tamuk.edu





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Email: venoms@venomsupplies.comWeb: www.venomsupplies.com

Lyophilised Venoms

Snakes

Scientific name

Price(US\$)/200mg

Price(US\$)/gm

<i>Acanthophis antarcticus</i>	\$170	\$745
<i>Acanthophis praelongus</i>	\$210	\$845
<i>Agkistrodon billineatus</i>	\$50	\$200
<i>Austrelaps superbus</i>	\$400	\$1,600
<i>Austrelaps labialis</i>	\$700	\$3,000
<i>Bitis arietans</i>	\$70	\$300
<i>Bitis rhinoceros</i>	\$75	\$340
<i>Bitis nasicornis</i>	\$75	\$340
<i>Bothriechis schlegelii</i>	\$200	\$850
<i>Crotalus adamanteus</i>	\$100	\$450
<i>Crotalus unicolor</i>	\$200	\$900
<i>Crotalus vegrandis</i>	\$160	\$700
<i>Hoplocephalus stephensii</i>	\$220	\$900
<i>Hoplocephalus bitorquatus</i>	\$220	\$900
<i>Naja kaouthia</i>	\$60	\$250
<i>Naja melanoleuca</i>	\$50	\$200
<i>Naja mossambica</i>	\$60	\$250
<i>Naja siamensis</i>	\$60	\$250
<i>Notechis ater humphreysi</i>	\$350	\$1,600
<i>Notechis ater niger</i>	\$350	\$1,600
<i>Notechis ater serventyi</i>	\$350	\$1,600
<i>Notechis scutatus</i>	\$300	\$1,445
<i>Ophiophagus hannah</i>	\$200	\$850
<i>Oxyuranus microlepidotus</i>	\$300	\$1,300
<i>Oxyuranus scutellatus</i>	\$260	\$1,250
<i>Oxyuranus scutellatus canni</i>	\$400	\$1,500
<i>Pseudechis australis</i>	\$110	\$520
<i>Pseudechis butleri</i>	\$160	\$700
<i>Pseudechis colletti</i>	\$110	\$500
<i>Pseudechis guttatus</i>	\$110	\$500
<i>Pseudechis porphyriacus</i>	\$140	\$650
<i>Pseudechis papuanus</i>	\$288	\$1,380
<i>Pseudonaja affinis</i>	\$800	\$3,900
<i>Pseudonaja aspidorhyncha</i>	\$800	\$3,990
<i>Pseudonaja inframacula</i>	\$800	\$3,990
<i>Pseudonaja nuchalis</i>	\$800	\$3,990
<i>Pseudonaja textilis</i>	\$760	\$3,700
<i>Tropidechis carinatus</i>	\$300	\$1,500

Spider Venom

Lampona cylindrata

\$360 / 10sac contents \$720 / 25sac contents

Latrodectus hasseltii

\$500/50 sac contents.

Bee Venom

Pure bee venom (*Apis mellifera*)

250mg

\$58

(1-5gm)

\$130/gm

(6-10gm)

\$116/gm

(60gm and over)

\$95/gm

Amphibian Venoms

Bufo marinus

\$95/200mg

\$450/gm

5% discount will apply for all orders over 5 gm and 7% will apply to orders over 15gm for venoms produced at Venom Supplies Pty Ltd.

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Dendroaspis polylepis	\$550.00
Dendroaspis angusticeps	\$400.00
Dendroaspis viridis	\$750.00
Naja nivea	\$205.00
Naja melanoleuca	\$205.00
Naja nigricollis (Tanzania)	\$205.00
Naja nigricollis (Ghana)	\$205.00
Naja h. annulifera	\$125.00
Naja kaouthia	\$205.00
Naja naja (Pakistan)	\$250.00
Ophiophagus hannah	\$150.00
Micrurus f. fulvius	\$2100.00
Bitis arietans	\$150.00
Bitis g. gabonica	\$150.00
Bitis g. rhinoceros	\$150.00
Crotalus adamanteus	\$150.00
Crotalus atrox	\$150.00
Crotalus h. atricaudatus	\$150.00
Crotalus h. horridus	\$150.00
Crotalus s.scutulatus	\$450.00
Crotalus d. terrificus	\$450.00
Sistrurus m. barbouri	\$450.00
Agkistrodon c.contortrix	\$190.00
Agkistrodon c. laticinctus	\$190.00
Agkistrodon c. mokasen	\$100.00
Agkistrodon p. conanti	\$100.00

Many other venoms available in limited quantity, please inquire
 Special orders to meet research needs

Exact locality data on most species available, Species are guaranteed

Prices are quoted per gram in U.S. dollars, subject to change without notice

Payment terms net 30 days check, money order, or wire transfer

Shipping is free in the U.S. may be extra for international orders

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HIGH QUALITY VENOMS & TOXINS

Lyophilized and
crystallized venoms

Bothrops alternatus	1440,00 US\$
Bothrops jararaca	220,00 US\$
Bothrops jararacussu	264,00 US\$
Bothrops moojeni	300,00 US\$
Bothrops neuwiedi	340,00 US\$
Crotalus durissus terrificus	220,00 US\$
Crotalus durissus collineatus	300,00 US\$

Lachesis muta muta 600,00 US\$

Bufo marinus / schneideri 264,00 US\$

All venoms collected in a sterile manner

Blood cells and freeze dried blood plasma from snakes

We have also other proteins, aminoacids and toxin polyclonal antibodies from Brazilian snakes

We trade or sell our products only with CITES from the IBAMA (Brazilian Environment Agency & Wildlife)

Prices quoted per gram in US\$. Transport FOB

Brazilian Contact:

Sanmaru Serpentarium,

Rod. Brig. Faria Lima km 365

14765-000 Taquaral SP, Brazil

herpetoscience@hotmail.com

taquaral@gmail.com

Fone (55) 14 9731 2436

(55) 16 3958 7269

Kentucky Reptile Zoo

Venom Price List 2009-2010

200 L and E Railroad

Slade, KY 40376

Tel:606-663-9160

Fax: 606-663-6917

Web: www.kyreptilezoo.orgEmail: reptilezoo@bellsouth.net**Crotalidae**

<i>Agkistrodon contortrix contortrix</i>	\$60.00
<i>Agkistrodon contortrix mokasen</i>	\$55.00
<i>Agkistrodon contortrix laticinctus</i>	\$70.00
<i>Agkistrodon contortrix phaeogaster</i>	\$70.00
<i>Agkistrodon contortrix pictigaster</i>	\$70.00
<i>Agkistrodon piscivorus leucostoma</i>	\$45.00
<i>Agkistrodon piscivorus piscivorus</i>	\$45.00
<i>Bothrops asper</i>	\$100.00
<i>Bothrops atrox</i>	\$100.00
<i>Bothrops moojeni</i>	\$100.00
<i>Crotalus adamanteus</i>	\$60.00
<i>Crotalus atrox</i>	\$70.00
<i>Crotalus basiliscus basiliscus</i>	\$200.00
<i>Crotalus cerastes</i>	\$100.00
<i>Crotalus durissus cumanensis</i>	\$300.00
<i>Crotalus durissus durissus</i> (fmr. <i>C. d. dryinas</i>)	\$200.00
<i>Crotalus durissus terrificus</i>	\$175.00
<i>Crotalus horridus</i>	\$100.00
<i>Crotalus horridus</i> (type A neurotoxin)	\$100.00
<i>Crotalus molossus</i> (Texas origin)	\$70.00
<i>Crotalus scutulatus scutulatus</i>	\$250.00
<i>Crotalus viridis viridis</i>	\$70.00
<i>Protobothrops flavoviridis</i>	\$200.00
<i>Trimeresurus borneoensis</i>	\$200.00

Elapidae

<i>Dendroaspis angusticeps</i>	\$350.00
<i>Dendroaspis jamesoni kaimosae</i>	\$400.00
<i>Dendroaspis polylepis</i>	\$400.00
<i>Micrurus tenere</i>	\$1000.00
<i>Naja kaouthia</i>	\$100.00
<i>Naja kaouthia</i> (Suphan province)	\$100.00
<i>Naja melanoleuca</i>	\$80.00
<i>Naja naja</i> (India)	\$85.00
<i>Naja naja</i> (Pakistan)	\$80.00
<i>Naja nigricollis nigricollis</i>	\$80.00

<i>Naja nivea</i>	\$100.00
<i>Naja pallida</i>	\$100.00
<i>Naja siamensis</i>	\$60.00
<i>Ophiophagus hannah</i>	\$95.00
<i>Pseudechis colletti</i>	\$320.00

Viperidae

<i>Bitis arietans</i>	\$120.00
<i>Bitis gabonica rhinoceros</i>	\$130.00
<i>Daboia (Vipera) russelli</i>	\$200.00
<i>Daboia (Vipera) siamensis</i>	\$200.00
<i>Echis carinatus</i>	\$350.00
<i>Echis pyramidum</i>	\$350.00

Helodermatidae

<i>Heloderma horridum</i>	\$600.00
<i>Heloderma suspectum</i>	\$600.00

Terms

- All venoms are collected in a sterile manner and frozen at -70C before lyophilization.
- Other venoms are available upon request in small quantities; please contact us for more information on other venoms
- CITES papers available on all CITES listed species. Extra costs apply for permits and inspection fees.
- Locale information available for most species.
- Payment may be made by check, money order, wire transfer, PayPal, MC, Visa, and Discover. All prices are listed per gram in US dollars. Shipping and packing charges are extra.
- Discounts on standing orders and orders of 10g or more.
- KRZ makes every effort to stay current regarding nomenclature and taxonomy. Our listing reflects current trends, with former names in parentheses. If you have questions, please feel free to contact us.
- Scale clippings for DNA analysis available at an extra charge. Please contact us for more information.

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ALPHA BIOTOXINE



Laboratoire de production de venin
Fournisseur en venin
Négociant en toxines purifiées

Venom production laboratory
Venom supplier
Pure toxins dealer

Venins cristallisés, venins lyophilisés, bases pour teintures mères, plasma,...

Crystalised venom, lyophilised venom, mother tincture bases, plasma,...

ALPHA BIOTOXINE est une jeune société spécialisée dans la production de venin.

Nous mettons à votre service plus de 20 ans d'expérience dans l'étude des animaux venimeux et la production de venin.

Notre laboratoire s'adapte à tout type de demande. Contactez nous.

ALPHA BIOTOXINE is a young society specialised on venom production.

We offer you more than 20 years of experience on study of venomous animals and venom production.

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Barberie 15
7911 Montroeuil-au-Bois
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