Snakebite Research in PNG

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Snakebite with envenomation is a significant medical problem worldwide, leading to many deaths, perhaps as many as 125,000 per year, with several times that number maimed by the results of the bite and/or subsequent surgery, necessary or not. Initial management of this injury is the responsibility of medical and nursing staff working in emergency departments, though in many countries snakebite is considered a surgical problem.

It is only relatively recently that "snakebite" was officially recognised by the World Health Organisation (WHO) as a Neglected Tropical Disease (NTD) (<u>http://www.who.int/neglected_diseases/diseases/snakebites/en/index.html</u>). The exact number of victims, worldwide, is elusive because snakebite is not a reportable injury in the vast majority of countries.

Thanks to the efforts and enthusiasm of a small team of dedicated people, led by Australian herpetologist, David Williams, the current Snakebite Research Project (SRP), a collaboration between the Australian Venom Research Unit (AVRU) of the University of Melbourne (UoM) and the School of Medicine & Health Sciences (SMHS) at the University of Papua New Guinea (UPNG) commenced in 2000. The project has many facets, including studies of snake systematics, venom composition, first aid training projects, clinical research into optimal management and collecting patient data from hospitals and health centres throughout most of Papua New Guinea to build a better epidemiological profile. The data collected so far indicates that, despite the purchase of Australian Commonwealth Serum Laboratory (CSL) snake antivenoms by the PNG government, there are probably at least 200 deaths per year following an estimated 3500 snakebites per year.

David and I jointly developed a comprehensive Snakebite Management Course in 2004, and we have run this course, in several forms in several centres in PNG since then, as one attempt to improve the mortality figures. While courses were run during the first few years with the assistance of lecturers from the UK and Australia, a small but increasing number of PNG national doctors and scientists have been involved in delivering the course, as well as being involved in associated research. In 2008 our efforts attracted the attention of the WHO Regional Office for the Western Pacific, and we were invited to assist the Cambodian Ministry of Health in assessing the extent of snakebite problems there and devising a strategy to address the issues. In 2009 we taught the first Snakebite Management Courses specifically developed for Cambodian doctors and health workers in Phnom Penh and Siem Reap, proving that expertise developed in PNG can be exported to the world.

The latest important achievement of the research group has been to develop, with the significant assistance of a government-funded research institute and antivenom manufacturer in Costa Rica, the Instituto Clodomiro Picado (ICP), a PNG taipanspecific whole IgG equine antivenom. In preclinical trials it has been proven to be equivalent to, or better than, the CSL monovalent product, according to a number of objective criteria. This work, published in PLoS NTD (http://www.plosntds. org/article/info%3Adoi%2F10.1371%2Fjournal. pntd.0001144) and the Journal of Proteomics (http://www.sciencedirect.com/science/article/pii/ S1874391912000231) represents the development of the first new snake antivenom intended for human use in Australasia for more than 50 years. It is also expected to cost the PNG government a tenth of the cost of the current CSL product. Additionally, it is hoped that technology transfer will allow this product to be produced in PNG, as well as this part of the SRP acting as a platform for training young scientists graduating from the UPNG.

In 2011 the National Health and Medical Research Council of Australia (NHMRC - www.nhmrc.gov.au)



for the first time made Global Health a special initiative area for Australian residents involved in research outside of Australia. Following a detailed application the AVRU-UPNG SRP was awarded in late 2011 a significant grant to enable us to run a Double Blinded Randomised Controlled Trial (DBRCT) of the new taipan antivenom against the current CSL monovalent taipan antivenom. This will be first ever RCT of any CSL antivenom against an alternative product. The grant is the second largest NHMRC grant awarded to the University of Melbourne in 2011 and the largest single grant ever awarded for antivenom research by the NHMRC.

Our trials of the new antivenom are being run in two stages – first, a small safety and dose-finding study, and secondly the DBRCT of the new product against the current CSL monovalent antivenom.

Supporting this NHMRC grant, the PNG Office of Higher Education has allocated our research group a large grant (by PNG standards) as co-funding for the project. This generosity has made it possible to establish a new Clinical Research Laboratory the Charles Campbell Toxinology Centre – at the UPNG Medical School. Construction of this new facility was completed in May 2012. The Centre will employ up to 16 PNG doctors, nurses and allied health workers during the clinical trials. Other projects commencing later in 2012 will build this workforce to a total of 20 personnel. The Centre is being equipped with state-of-the-art haemostasis, haematology and biochemistry analysers to enable us to conduct exacting investigations in snakebite patients, supporting the latest point-of-care (POC)

bedside analysers, which we will be using in the Port Moresby General Hospital Emergency Department where the clinical trials are taking place. Trial patients will be cared for with the aid of new state-of-theart monitoring and life support equipment. Also, a new immuno-diagnosis platform, developed by a collaborator in Australia, will be used to detect quantitatively measure plasma levels of specific taipan venom toxins.

The PNG taipan antivenom clinical trials project is strongly supported by the management of Port Moresby General Hospital (PMGH), the Director of the newly constructed Emergency Department, the Executive of the UPNG Medical School and both the UPNG Ethics Committee and the National Medical Research Advisory Committee (MRAC).

It is hoped that the trials will not only yield a positive result for the new antivenom, but that they will significantly benefit the development of medical science in PNG by training staff involved in the trials in various capacities.

Also, a new Memorandum of Agreement (MoA) has been established between the UPNG and the UoM for the next 5 years, encompassing both research and teaching.

Mounting a double-blinded, randomised controlled trial in PNG is an enormous challenge. A number of visiting toxinology experts, emergency physicians, and others are lending support to the project.

Anyone interested in hearing more about our work is most welcome to contact Simon Jensen at simondjensen@hotmail.com.