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Short Communication

THE UNIQUE PROPERTIES OF CAMELID IgG HAVE POTENTIAL TO IMPROVE THE TREATMENT OF SNAKE BITE

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Systemic envenoming by snakes kills over 125,000 people each year, mainly in the rural areas of Africa and Asia. Injected venom that fails to enter the systemic circulation often irreversibly destroys the tissues local to the bite. While intravenous administration of antivenom, prepared from IgG of venom-immunised horses or sheep, is the sole effective treatment for systemic envenoming, it is ineffective against the effects of local envenoming that develop rapidly and include severe pain, oedema, haemorrhage and necrosis (Warrell *et al,* 1977) which can result in permanent scarring and deformity. The ineffectiveness of antivenom in treating local envenoming has been attributed to the inability of antivenom IgG (or $F(ab')_2$ and Fab fragment antivenoms) to cross the blood/tissue barrier (Lalloo and Theakston, 2003) and the rapid onset of venom-induced pathology. The development of a treatment for local envenoming is therefore a clinical priority.

Conventional antivenom treatment is also frequently associated with adverse affects. Antivenoms typically consist of 80+ mg/ml of equine or ovine IgG and between 30-200 ml of i.v. administered antivenom is required to neutralise the systemic venom effects. This volume of heterologous protein commonly causes delayed serum sickness (50% of treated patients) and more rarely (0.1%), life-threatening anaphylactic shock (Lalloo and Theakston, 2003).

Recent studies on the unique properties of camelid immunoglobulin provide several persuasive reasons to suggest that antivenoms developed in camelids may have significant clinical advantages over conventional equine and ovine antivenoms:

- Fifty percent of camelid IgG lacks light chains (Hamers-Casterman *et al,* 1993) and the 15 kDa antigen-binding domain of these heavy chain-only IgG (V_{HH}) has been shown to migrate across the blood/tissue barrier (Cortez-Retamozo *et al,* 2002). The rapid tissue-ingress of intravenously injected V_{HH} has obvious potential in the treatment of the local effects of snake envenoming.
- Camelid IgG is also less immunogenic and less prone to activate complement than most mammalian IgG (Herrera *et al,* 2005) indicating that intravenous administration of a camelid antivenom is less likely to induce the serum sickness-like and anaphylactoid adverse reactions associated with equine and ovine antivenom treatment.

The first author has recently completed a pilot study to explore the obvious potential of camelid IgG for antivenom development. This study demonstrated (i) that camelids respond to snake venom immunisation with high titre antibodies that neutralised venom-induced pathology and (ii) that the antibody responses of dromedary camels and llamas to venom immunisation were very similar (Harrison *et al,* 2006). A similar study in Tunisia demonstrated that scorpion envenoming could also be treated using a camel antivenom (Meddeb-Mouelhi *et al,* 2003). These studies importantly demonstrate that there are no obvious immunological reasons why camelid IgG should not be as efficacious as conventional equine and ovine IgG antivenoms.

In an exciting collaboration with second author Professor Gutierrez of the Instituto Clodomiro Picado, San Jose, Costa Rica, Harrison's group have collected sera from camels immunised with either a mixture, or individual, venoms of the three most medically important snakes in West Africa (the saw-scaled viper, *Echis ocellatus*; the puff adder, *Bitis arietans* and

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the spitting cobra, *Naja nigricollis*) that kill 20,000 people each year (Chippaux, 2002). The sera will be sent to Costa Rica where the polyspecific and three monospecific antivenoms will be manufactured. The pre-clinical efficacy of these four new camel antivenoms will be determined in the Liverpool School of Tropical Medicine and then submitted for human clinical trials in West Africa.

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