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# Neurophysiological findings in patients 1 year after snake bite induced neurotoxicity in Sri Lanka

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ABSTRACT

Snake bite causes significant morbidity and mortality in Sri Lanka. Snake venoms contain neurotoxins that block neuromuscular junction transmission. Presynaptic neurotoxicity most commonly causes destruction of nerve terminals with recovery by regrowth, whilst postsynaptic neurotoxicity usually involves competition at the acetylcholine receptor. The aim of this study was to investigate whether there were long-term clinical or neurophysiological changes in snake bite survivors 1 year after their envenoming. Detailed neurophysiological tests and clinical examinations were performed on 26 snake bite victims who had presented with neurotoxicity 12 months previously, and their results were compared with controls recruited from the same communities. Significant differences were observed in some nerve conduction parameters in some snake bite victims compared with controls, predominantly in those thought to have elapid bites, including prolongation of sensory, motor and F-wave latencies and reduction of conduction velocities. There was no evidence of any residual deficits in neuromuscular junction transmission. These results suggest a possible demyelinating type polyneuropathy. None of the cases or controls had abnormalities on clinical examination. This is one of the few studies to report possible long-term neurological damage following systemic neurotoxicity after snake bite. The clinical significance of these neurophysiological abnormalities is uncertain and further studies are required to investigate whether the abnormalities persist and to see whether clinical consequences develop.



## 1. Introduction

Sri Lanka has a high incidence rate of snake bite, with around 30 000 bites and 100 deaths occurring annually.[1] More than 97% of these deaths are due to bites from elapids [cobras (*Naja naja*) and common kraits (*Bungarus caeruleus*)] or Russell's viper (*Daboia russelii russelii*). The venoms of these snakes contain powerful neurotoxins causing a progressive neuromuscular paralysis by blockade of neuromuscular transmission at the nerve terminal and neuromuscular junction. The venom of the common krait has neurotoxins that act both pre and postsynaptically, whilst those of the Indian cobra act on the postsynaptic terminal and those of the Russell's viper are most likely to exert their effect presynaptically, although postsynaptic toxins have also been identified.[2–6] Postsynaptic neurotox-

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icity normally involves competition at the acetylcholine receptor, whereas presynaptic neurotoxicity most commonly occurs after irreversible binding and destruction of the nerve terminal, with recovery by regrowth of the nerve terminal.[7,8] In addition, the venom of Russell's viper contains toxins causing coagulopathy.

The clinical manifestations of neurotoxicity following envenoming include ptosis, ophthalmoplegia and respiratory failure that may require ventilation. Most patients will make a full clinical recovery within days of the bite if supported during the acute phase after receiving antivenom. The aim of this study was to investigate whether there were any long-term clinical or neurophysiological changes in snake bite survivors 1 year after their envenoming. Cases who had previously been enrolled in an antivenom study in 2007 after presenting with features of systemic neurotoxicity and who had been treated with antivenom at that time were recruited. Detailed neurophysiological testing was performed on all these cases and the results were compared with a control group.

## 2. Methods

### 2.1. Participants and study location

Cases were identified from the records of an antivenom study that had taken place between March 2005 and April 2008 investigating the role of different pre-medications in patients about to receive antivenom following envenoming. All the patients included in this study had presented to the Teaching Hospital, Kurunegala, Sri Lanka, approximately 100 km north of the capital city Colombo, in 2007, with features of neurotoxicity and all had received antivenom. Anticholinesterases were not administered.

Letters were sent to potential patients inviting them to attend the hospital for a neurological assessment to see how well they had recovered from their snake bite. Control data were obtained from relatives or friends who accompanied the cases to the study clinic and who were willing to participate in the study. By recruiting family members and friends it was expected that cases and controls would be similar in terms of socioeconomic status, nutritional status and geographical residence. Most snake bite victims in Sri Lanka work in rural areas where organophosphate and other agrochemicals are commonly used, and exposure to these compounds is likely to be similar in both groups.

### 2.2. Clinical procedures

On arrival at the study clinic, the study was explained in further detail and participants were asked to give written informed consent. Cases or controls were excluded if they had a history of excessive alcohol intake, leprosy or if they were receiving therapy for tuberculosis (TB) or diabetes mellitus (DM). Baseline demographic details were collected and a random blood sugar was measured. The neurological assessment included a detailed clinical questionnaire relating to possible neurological symptoms noticed by the participant. This was followed by a detailed neurological examination, which was performed by one of two members of the study team (DJB and UKR) to ensure consistency.

Neurophysiological evaluation was done using standard techniques and was carried out by the same investigator (DW), a Consultant neurologist, who was blinded to whether the patient was a case or control. All studies were performed using a Nihon Kohden Neuropack EMG machine (model MEB 5504K; Nihon Kohden, Tokyo, Japan) in an air-conditioned room with the ambient temperature maintained at approximately 22 °C. Patients were seen on one occasion only. The following tests were performed.

#### 2.2.1. Sensory nerve conduction studies of the left ulnar nerve and left sural nerve

The peak amplitude of the sensory action potential (SAP), latency to the peak of the SAP, and sensory conduction velocity using onset latency were measured. Ulnar nerve sensory conduction was assessed using ring electrodes over the fifth digit to stimulate the ulnar nerve orthodromically, with surface recording electrodes placed 12 cm proximally in the wrist. For the sural nerve, surface recording electrodes were placed over the lateral aspect of the ankle posterior to the lateral malleolus, with stimulating electrodes placed 14 cm proximally over the posterior foreleg. Maximal SAPs were recorded using supramaximal stimulation.

#### 2.2.2. Motor nerve conduction studies of the left ulnar nerve and left posterior tibial nerve

The distal latency of the compound motor action potential (CMAP), peak amplitude of the CMAP, motor conduction velocity (MCV) and the minimum F-wave latencies were measured. The posterior tibial nerve was selected for motor studies in the lower limb to minimise the effect of possible compression neuropathy of the common peroneal nerve in this population largely involved with farming and heavy manual work. Motor nerve conduction studies were performed using surface stimulating electrodes placed over the wrist (ulnar nerve) and ankle posterior to the medial malleolus (posterior tibial nerve) and recording electrodes placed over the abductor digiti minimi (ADM) and abductor hallucis (AH), respectively, after supramaximal stimulation. MCVs were recorded by stimulating at two points at a fixed distance apart. Minimum F-wave latencies were recorded as the shortest latencies of 16 supramaximal stimuli of the ulnar and posterior tibial nerves with recording electrodes placed over the over ADM and AH, respectively.

#### 2.2.3. Repetitive nerve stimulation of the left ulnar nerve and left posterior tibial nerve

The percent change in the amplitude of the motor action potential over the ADM for the ulnar nerve and the AH for the posterior tibial nerve were recorded. Nerves were stimulated supramaximally at 3 Hz over the wrist for the UN and the ankle for the PT nerve for a total of five stimuli and the percent change in amplitude after the fourth response compared with the first response was recorded. A decrease of >10% in amplitude after the fourth response was considered abnormal.