

**VENOMOUS SPIDER BITES IN SOUTH AFRICA: EPIDEMIOLOGY AND CLINICAL
FEATURES**

by

Catharina Elizabeth du Plessis

Thesis presented in fulfilment of the requirements for the degree of

Master of Science (Pharmacology)

Division of Clinical Pharmacology

Department of Medicine

Faculty of Medicine and Health Sciences

University of Stellenbosch

Supervisor: Prof Helmuth Reuter

Professor and Head, Division of Clinical Pharmacology, Faculty of Medicine and Health Sciences

April 2019

Declaration

By submitting this thesis electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the sole author thereof (save to the extent explicitly otherwise stated), that reproduction and publication thereof by Stellenbosch University will not infringe any third party rights and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

CE du Plessis

April 2019

Copyright © 2019 University of Stellenbosch

All rights reserved

Summary

Introduction:

Worldwide the number of spider bite calls to poison centres comprises less than 2.5% of calls. Only a small proportion of spiders cause serious envenomation in humans. The known medically important spiders of South Africa include the *Latrodectus* (button), *Cheiracanthium* (sac) and *Loxosceles* (violin) species. The button spiders can cause neurotoxicity called latrodectism while violin and sac spider bites can cause necrotic skin lesions. The clinical syndrome of latrodectism is well defined and an effective antivenom is available. The diagnosis of necrotic arachnidism on the other hand is more difficult, especially if the spider bite is not painful. The necrotic skin lesions are not specific and have a wide differential diagnosis.

Aim:

The main aim of the study was to perform a retrospective assessment of poison centre data regarding spider bites from January 2005 to December 2017 and to develop an algorithm for the diagnosis of spider bites.

Results:

From a total of 83 974 calls, 1917 (2.3%) were related to suspected spider bites. The majority of these calls were from the Western Cape Province. The majority of bites occurred during the warmer months of the year, peaking in January and February. Adults were involved more frequently than children, 1497 versus 420, respectively. In 138 (48.6%) of the 284 reported button spider bites, the spider was positively identified. Of these, 80 (28.1%) patients were treated with antivenom. The most common clinical features were generalised pain (n = 89, 31.3%), muscle pain and cramps (n = 88, 31.0%) and sweating (n = 58, 20.4%). In the cytotoxic spider group only 5 spiders were positively identified. In the majority of calls the spider was not seen or could not be identified (n = 1301, 68%).

Discussion:

The number of spider bite calls to poison centres are low when compared to the total number of calls received. Bites usually involved adults and occurred mostly during the warmer months of the year. There has not been a single death associated with spider bites. In terms of a Poison Information Centre helpline data collection suggested categories for the diagnosis of spider bites include definite, probable and

unlikely. Based on the clinical presentation it is possible to diagnose neurotoxic spider bites caused by button spiders with confidence and advise the use of the antivenom when indicated. A positive response to the antivenom supports the presumed diagnosis. It is more difficult to diagnose cytotoxic spider bites and the majority reported skin lesions are unlikely to be caused by spiders. We have developed a diagnostic algorithm that incorporates the most important clinical features and the distribution of spiders to assist with the diagnosis.

Conclusion:

In the majority of spider bites it is unlikely that serious effects will develop, however the early identification of a spider as well as the recognition of a clinical syndrome associated with certain spider bites, would assure safe and effective treatment. The helpline data is insufficient to fully describe necrotic arachnidism and further prospective studies are warranted.

Opsomming

Inleiding:

Wêreldwyd behels die getal spinnekopbyt-oproepe na gifsentrums minder as 2,5% van die totale oproepe. Slegs 'n klein aantal spinnekoppe veroorsaak ernstige envenomasie by die mens. Die spinnekoppe van Suid-Afrika wat van mediese belang is, sluit die *Latrodectus* (knopie)-, *Cheiracanthium* (sak)- en *Loxosceles* (viool)-spesie in. Die knopiespinnekop kan neurotoksisiteit bekend as latrodektisme veroorsaak, terwyl viool- en sakspinnekopbyte tot nekrotiese velletsels kan lei. Die kliniese sindroom van latrodektisme is goed omskryf en 'n doeltreffende teengif is daarvoor beskikbaar. Die diagnose van nekrotiese arachnidisme daarenteen is egter moeiliker, veral as die spinnekopbyt nie waargeneem is nie. Die nekrotiese velletsels is nie spesifiek nie en het 'n wye differensiële diagnose.

Doel:

Die hoofdoel van die studie was om 'n retrospektiewe assessering van gifsentrumdata, vanaf Januarie 2005 tot Desember 2017, oor spinnekoppe uit te voer en om 'n algoritme vir die diagnose van spinnekopbyte te ontwikkel.

Resultate:

Uit altesaam 83 974 oproepe wat ontvang is, het 1 917 (2,3%) vermoedelik met spinnekopbyte verband gehou. Die meerderheid van hierdie oproepe was van die Wes-Kaap. Die byte het meestal gedurende die warmer maande van die jaar plaasgevind en in Januarie en Februarie 'n hoogtepunt bereik. Volwassenes het meer gereeld deurgeloop as kinders, onderskeidelik 1 497 teenoor 420. In 138 (48,6%) van die 284 aangemelde knopiespinnekopbyte is die spinnekop positief geïdentifiseer. Hiervan is 80 (28,1%) pasiënte met teengif behandel. Die algemeenste kliniese kenmerke was algemene pyn ($n = 89$; 31,3%), spierpyn en krampe ($n = 88$; 31,0%), en sweet ($n = 58$; 20,4%). In die sitotoksiese spinnekopgroep is slegs 5 spinnekoppe positief geïdentifiseer. In die meeste oproepe is die spinnekop nie opgemerk nie of kon dit nie geïdentifiseer word nie ($n = 1\ 301$; 68%).

Bespreking:

Die aantal spinnekopbyt-oproepe na gifsentrums is laag vergeleke met die totale aantal oproepe wat ontvang is. Dit was gewoonlik volwassenes wat gebyt is en dit het meestal gedurende die warm maande van die jaar plaasgevind. Daar was nie 'n enkele sterfte wat met spinnekoppe verband gehou het nie. Die

insameling van data by 'n gifinligtingsentrum het dit laat blyk dat voorgestelde kategorieë vir die diagnose van spinnekopbyte “beslis”, “waarskynlik” en “onwaarskynlik” moet insluit. Op grond van die kliniese presentasie is dit moontlik om neurotoksiese spinnekopbyte wat deur knopiespinnekoppe veroorsaak word, met sekerheid te diagnoseer en die gebruik van die teengif aan te beveel wanneer dit as gewens aangedui word. 'n Positiewe reaksie op die teengif ondersteun die veronderstelde diagnose. Dit is moeiliker om sitotoksiese spinnekopbyte te diagnoseer, en die meerderheid gerapporteerde velletsels is waarskynlik nie deur spinnekoppe veroorsaak nie. Ons het 'n diagnostiese algoritme ontwikkel wat die belangrikste kliniese kenmerke en die verspreiding van spinnekoppe insluit om diagnostisering te vergemaklik.

Gevolgtrekking:

By die meeste spinnekopbyte is dit onwaarskynlik dat ernstige gevolge sal ontwikkel, maar die vroeë identifisering van 'n spinnekop, asook die herkenning van 'n kliniese sindroom wat met sekere spinnekopbyte verband hou, verseker veilige en effektiewe behandeling. Die hulplyndata is onvoldoende om nekrotiese arachnidisme volledig te beskryf en verdere prospektiewe studies is geregverdig.

Dedication

“Hierdie tesis word opgedra aan my ouers. Dankie vir al jou liefde, ondersteuning en aansporing deur die jare. Mamma, jy is n wonderlike voorbeeld vir ons kinders; 89 en nogsteeds aan die gang. Pappa, mis jou baie. Jou teenwoordigheid is nog elke dag met my. Lief julle altyd.”

Acknowledgements

I would like to thank the following individuals for their contribution, input and support without which this study would not have been possible:

Firstly my supervisor, Prof Helmuth Reuter, for his believe in me to make a success of this project. Thank you for your positive attitude and all the words of encouragement. You are a true leader.

To Dr Gerbus Muller, who was the one responsible for my relocation to the poison centre. Thank you for sharing your vast knowledge of toxicology; especially the biological toxins. Because of you the poison centre ladies have a tremendous interest in all biological toxins.

To Dr Joy Veale for all the editing and encouragement, a heartfelt thank you.

To my colleagues, Cherylynn Wium and Carine Marks for giving me the opportunity to complete this project. Thank you for all your positive support.

To the rest of my colleagues from the division of Clinical Pharmacology, thank you for the support and positive attitudes.

A special word of thanks to Lejandra Hanekom and Cherylynn Wium. Thank you for being a friend on top of a colleague.

To everybody that made a contribution to the TPIC and PIHWC throughout the years. There have been many of you, thank you for contributing to my project by collecting data.

To my family, thank you for the encouragement and believe that I can make a success.

To my friends, thank you for your support.

List of abbreviations

Abbreviation	Description
α -latrotoxin	Alpha-latrotoxin
α -LTX	Alpha-LTX
<i>C. africanum</i>	<i>Cheiracanthium africanum</i>
<i>C. furculatum</i>	<i>Cheiracanthium furculatum</i>
<i>C. vansoni</i>	<i>Cheiracanthium vansoni</i>
ED	Emergency department
ICK	Inhibitor cystine knot peptides
LPH	Latrophillin
<i>L. cinctus</i>	<i>Latrodectus cinctus</i>
<i>L. geometricus</i>	<i>Latrodectus geometricus</i>
<i>L. hasselti</i>	<i>Latrodectus hasselti</i>
<i>L. indistinctus</i>	<i>Latrodectus indistinctus</i>
<i>L. karrooensis</i>	<i>Latrodectus karrooensis</i>
<i>L. renivulvatus</i>	<i>Latrodectus renivulvatus</i>
<i>L. rhodesiensis</i>	<i>Latrodectus rhodesiensis</i>
<i>L. bergeri</i>	<i>Loxosceles bergeri</i>
<i>L. parramae</i>	<i>Loxosceles parramae</i>
<i>L. pilosa</i>	<i>Loxosceles pilosa</i>
<i>L. simillima</i>	<i>Loxosceles simillima</i>
<i>L. speluncarum</i>	<i>Loxosceles speluncarum</i>
<i>L. spinulosa</i>	<i>Loxosceles spinulosa</i>
LTXs	Latrotoxins
NRX	Neurexin
PIC	Poison Information Centre
PIHWC	Poison Information Helpline, Western Cape
PTP σ	Protein tyrosine phosphatase σ

RXHPIC	Red Cross War Memorial Children's Hospital Poison Information Centre
TCTP	Translationally controlled tumour protein
TPIC	Tygerberg Poison Information Centre
USA	United States of America

List of figures

- Figure 1.1: Anatomy of the spider
- Figure 1.2: Distribution map of *L. indistinctus*
- Figure 1.3: Distribution map of *L. karrooensis*
- Figure 1.4: Distribution map of *L. renivulvatus*
- Figure 1.5: Distribution map of *L. cinctus*
- Figure 1.6: Distribution map of *L. geometricus*
- Figure 1.7: Distribution map of *L. rhodesiensis*
- Figure 1.8: Distribution map of *C. furculatum*
- Figure 1.9: Distribution map of *L. bergeri*, *L. parramae*, *L. pilosa*, *L. spinulosa*
- Figure 1.10: Mechanisms of action of bite of *Latrodectus* spp
- Figure 1.11: Multiple mechanisms of α -LTX action
- Figure 4.1: Comparison between spider bite calls outside of the Western Cape Province compared to spider bite calls from the Western Cape Province, 2005 - 2017
- Figure 4.2: Seasonal distribution of spider bite calls, 2005 - 2017
- Figure 4.3: Number of spider bite calls per month of the year, 2005 - 2017
- Figure 4.4: Different type of spider bite calls as recorded from Poison centre data, 2005 - 2017
- Figure 4.5: Seasonal distribution of the *Latrodectus* species bites, 2005 - 2017
- Figure 4.6: Distribution map of bites from *Latrodectus* spp illustrating the number of patients positive for *Latrodectus* bites and the number of patients who received antivenom, 2013 – 2017
- Figure 4.7: Distribution map of positively identified and probable cytotoxic spider bites, 2005 - 2017
- Figure 4.8: Annual distribution of unidentified spider bites, 2005 - 2017
- Figure 5.1: Algorithm for suspected spider bites in South Africa

List of tables

- Table 1.1: Conditions that have been or can be misdiagnosed as necrotic arachnidism
- Table 1.2: Clinical features of latrodectism
- Table 1.3: Summary of clinical effects of widow spider bites from different regions of the world
- Table 4.1: Number of spider bite calls relative to total number of calls received, 2005 - 2017
- Table 4.2: Distribution of type of callers for spider bite calls, 2005 – 2017
- Table 4.3: Distribution of spider bite calls as per province, 2005 - 2017
- Table 4.4: Age distribution of calls received regarding spider bites, 2005 – 2017
- Table 4.5: Comparison between males and females per age group in cases where all information was recorded, 2005 - 2017
- Table 4.6: Time after bite and body part affected, 2005 - 2017
- Table 4.7: Number of reported button spider calls per year with advice given per case, 2005 - 2017
- Table 4.8: Time after bite for *Latrodectus* spiders recorded with calls received within an hour of the bite, 2005 - 2017
- Table 4.9: Clinical features reported for suspected cytotoxic spider bites, 2005 - 2017
- Table 4.10: Clinical features reported for unidentified spider bites, 2005 - 2017

List of photos

Photo 1.1: Adult female black button spider

Photo 1.2: Brown button spider with typical orange hourglass on the ventral surface

Photo 1.3: Brown button spider showing geometrical pattern on the dorsal surface

Photo 1.4: Sac spider showing typical black eye regions and mouth parts

Photo 1.5: Violin spider depicting the violin-shaped marking on the cephalothorax

Photo 4.6.1.1 – 4.6.1.2: Case study 4.6.1

Photo 4.6.2.1 – 4.6.2.6: Case study 4.6.2

Photo 4.6.3.1 – 4.6.3.3: Case study 4.6.3

Photo 4.6.4.1 – 4.6.4.5: Case study 4.6.4

Photo 4.6.5.1 – 4.6.5.5: Case study 4.6.5

Appendices

Appendices: Spider bite: Neurotoxic (widow spider) and cytotoxic (sac and violin) spiders (Patient case report form)

Table of contents

Declaration	i
Summary	i
Opsomming	iv
Dedication	vi
Acknowledgements	vii
List of abbreviations	viii
List of figures	x
List of tables	xi
List of photos	xii
Appendix	xiii
Table of contents	xiv
Chapter 1	1
Introduction	1
1.1 Background information	1
1.2 Anatomy of the spider.....	2
1.3 South African spiders.....	3
1.4 Necrotic arachnidism	7
1.5 Latrodectism.....	10
1.6 Antivenom.....	13
1.7 Poison Centres experiences.....	15
1.8 History of South African Poison Centres.....	16
Chapter 2	17
Aims and Objectives	17
Chapter 3	19
3.1 Methods.....	19
3.2 Data collection and analyses	19
3.3 Ethics.....	20
Chapter 4	21
Results	21

4.1 Total spider bites	21
4.2 Neurotoxic spider bites, <i>Latrodectus spp</i>	28
4.3 Cytotoxic spider bites.....	31
4.4 Other spiders	34
4.5 Unidentified spiders	34
4.6 Case studies – ‘suspected’ cytotoxic or unidentified spider bites.....	35
Chapter 5	45
Discussion	45
References	60
Appendices	64

Chapter 1

Introduction

1.1 Background information

According to legend the word spider originates from Greek mythology. Various versions exist, but in one of the stories, Arachne challenged Athena to a weaving competition. When Arachne proved to be the better weaver, Athena transformed her into a spider. The Greek word ‘Arachne’ means ‘spider’, the origin of Arachnida. Spiders belong to the phylum Arthropoda and together with all the eight legged animals such as ticks, mites and scorpions belong to the class of Arachnida. Eleven arachnid orders exist, including the spiders, the second largest order of Arachnida.^{1,2}

For centuries spiders have been the focus of fears and mythologies in many cultures and in book and movies. Spiders are usually depicted as a symbol of malice. The toxic venom of the spider is portrayed as the cause of a slow and dreadful death by whomever was unfortunate to have been bitten. But spiders are also recognized for their ability to produce silk and spin a web and nowadays even words like ‘internet’ and ‘world wide web’ evoke connectivity to a spider web.

Spiders are found in every part of the world except Antarctica.¹ Currently more than 46 000 species of spiders are recorded in the World Spider Catalogue.³ Few of these are considered as medical important and some experts in the field regard only lactordectism (caused by *Latrodectus* spp.) and loxoscelism (caused by the *Loxosceles* spp) as the two clinical syndromes of medical importance⁴, whereas others have shown that bites by the sac spider (*Cheiracanthium* spp.) should be included in the group of medical important spiders.^{5,6,7} Other medically important spiders are limited to certain areas in other countries or continents, e.g. the Australian funnel-web spiders (*Atrax* and *Hadronyche* spp.) and the armed or wandering spider (*Phoneutria* spp) found in Brazil.⁴ The highest number of venomous spiders are found in Latin America.²

Knowledge of the distribution, taxonomy and behaviour of spiders is an important factor to consider when trying to make an accurate diagnosis of spider bite. Although a number of spider species are found in and around houses and come into contact with humans, the majority of these spiders do not bite humans.^{2,8} The databases from Arachnida unit at the Agricultural Research Council (ARC), the National Museum in Bloemfontein and the South African National Survey of Arachnida (SANSA) Virtual Museum showed that a total of 50 spp. of spiders are found inside and outside of houses. Most of these spiders are small and do not come in contact with humans.⁹ Also, the venom of most spiders has very

little or no effect on humans.^{10,11} Several factors influence the action of the venom. Firstly, a spider must be big enough and have fangs sharp enough to penetrate the human skin and inject enough venom to cause toxicity. Usually only a drop of the venom is injected. Secondly, bites near the head are usually of more concern than those on the extremities. Thirdly, the age of the patient can be a factor as children and old people are more at risk of toxic effects. Fourthly, a difference in venom composition is found between the different spider species and, are therefore, some are more venomous than others.^{12,13,14} Multiple lesions or lesions on more than one body part or more than one person in a household presenting with bite marks are usually an indication of an alternative aetiology.¹¹

Research has focused mainly on the isolation of spider toxins for the development of drugs and other pharmacological uses,¹⁵ whereas the information on spider bite effects is based mainly on case studies and reviews of previous publications. Stuber and Nentwig (2016) found that only 22% of 134 medical case studies on spider bites published in 91 journal articles, fulfilled the criteria of a verified spider bite, the majority of which were due to *Loxosceles* and *Latrodectus* species.¹⁶

Although the medical literature suggests that spider bites can have serious health implications, some arachnologists point out that spider bites are mostly harmless and that it may be difficult to establish a correct diagnosis.¹⁶ Currently the literature^{10,17} defines a bite as a definite spider bite only if the following criteria are met: (i) evidence of a bite (a spider must be seen inflicting the bite); (ii) clinical effects associated with a spider bite must be seen during or soon after the bite; (iii) the spider must be collected at the time of the bite and (iv) the identification of the spider must be made by a qualified arachnologist.^{10,17} A prospective study which included 750 definite spider bites showed that pain and discomfort was experienced in all of the cases.¹⁸ A recording of the duration of pain and discomfort is important. The duration of and the increase in pain can assist in distinguishing between different species. Other local effects that can help with the identification of spiders include fang marks, redness and itching. Fang marks can be an indication of the size of the spider. Redness was found in 60 – 80% of all spider bites, whereas swelling is not regarded as a common finding.¹⁷ Circumstances of bites like geographical location, season and activities at the time of the bite can also be a useful tool in determining the type of spider especially where no spider was collected.¹⁷

1.2 Anatomy of the spider

Spiders have four pairs of jointed legs and two main body parts, namely the cephalothorax and the abdomen, Figure 1.1. The chelicerae are situated in front and above the mouthparts and consist of a basal segment and a fang. The venom gland is found inside the basal segment. The venom is released from there through a duct section to the fangs. The silk glands open onto the spinnerets, which are found on the posterior part of the abdomen and are used for the spinning of spider webs. Different body parts are used to identify spider family, genus or species. Different pattern variations are often found on the dorsal surface of the abdomen and cephalothorax. In some genera the colour patterns can help to identify the species^{1,2,12}

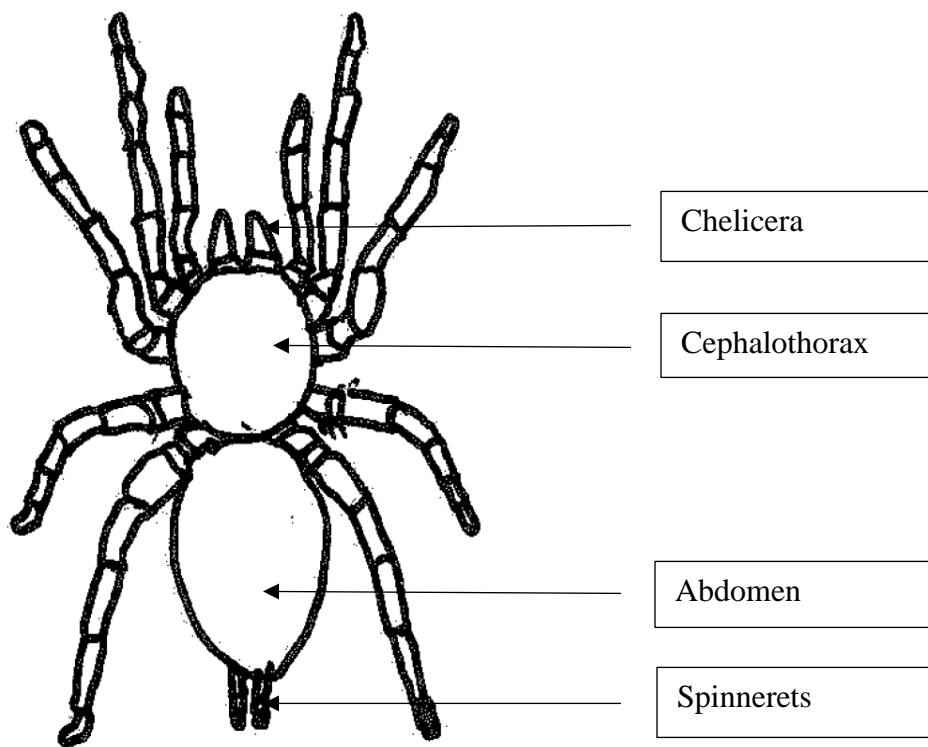


Figure 1.1 Anatomy of the spider (adapted from A Dippenaar-Schoeman)¹²

1.3 South African spiders

In South Africa there are 70 families of spiders represented by 2020 species.¹² The medically important spiders can be divided into two groups, namely cytotoxic and neurotoxic. Although case studies describing other spiders causing neurotoxic bites are also found in the literature,^{19,20} most neurotoxic spiders belong to the genus *Latrodectus* (button or widow spiders). The cytotoxic spiders are represented by two genera, *Cheiracanthium* (sac spiders) and *Loxosceles* (violin or recluse spiders).^{12,21,22}

Two case studies from South Africa reported on other spiders causing neurotoxic effects, namely the *Harpactirella lightfooti* and *Aranues apricus* (orb web spider).^{19,20} The *Harpactirella lightfooti* caused pain, vomiting and signs of shock in two patients. Subsequent experimental studies in mice showed convulsions and death after the bite of a *Harpactirella lightfooti*.¹⁹ A bite by the *Aranues apricus* caused localised pain, swelling and pain in the shoulder and lateral and pectoral muscles of a 21-year old male that was known to be allergic to bee stings. Under arm lymph glands were also affected. Most symptoms resolved within 8 hours.²⁰

Six species of the genus *Latrodectus* are found in South Africa.²³ They are divided into the black button complex and brown button complex. The black button spiders¹³ are the most venomous of the *Latrodectus* species and consist of four species, namely *L. indistinctus*, *L. renivulvatus*, *L. cinctus* and *L. karrooensis*.²³ The female black button spiders are dark brown to pitch-black in colour with no characteristic ventral markings, Photo 1.1. The female black button spiders have dorsal markings that vary from red to yellow orange stripes to red spots above the spinnerets. In older spiders, these become less distinct. The male black button spiders are much smaller in size compared to the female black button spiders.²² The egg sacs of the black button spiders are round and smooth in appearance. They are predominantly a so-called veld species occurring in open, uncultivated country or grassland.²¹ *L. indistinctus* spiders are found along the western coast of South Africa and Namibia.^{12,21} Figures 1.2 to 1.5 show the distribution maps of *L. indistinctus*, *L. renivulvatus*, *L. cinctus* and *L. karrooensis*.²⁴



Photo 1.1 Adult female black button spider, photo courtesy of Johan Marais

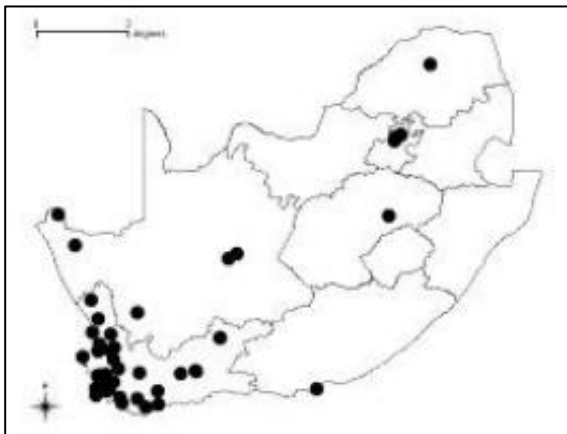


Figure 1.2 Distribution map of *L. indistinctus*²⁴

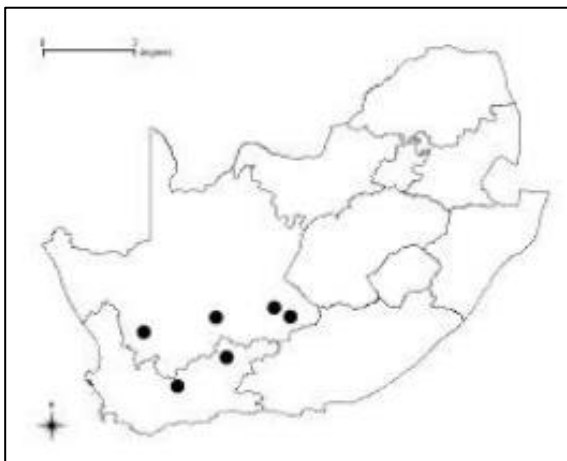


Figure 1.3 Distribution map of *L. karrooensis*²⁴

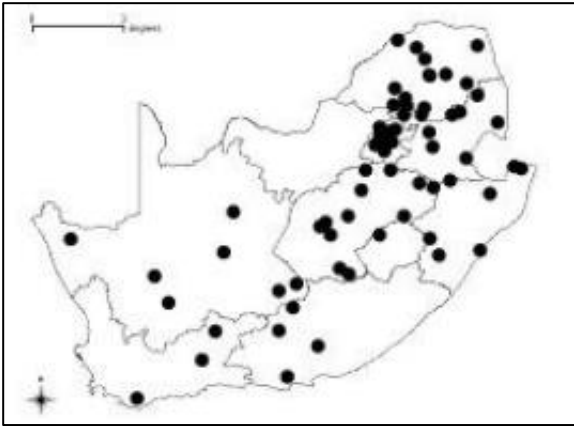


Figure 1.4 Distribution map of *L. renivulvatus*²⁴

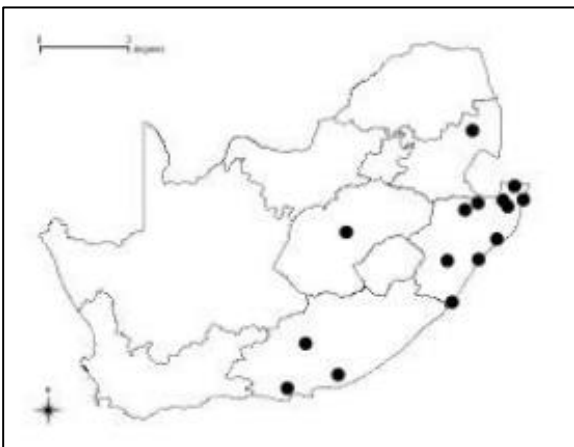


Figure 1.5 Distribution map of *L. cinctus*²⁴

The brown button complex consists of *L. geometricus* and *L. rhodesiensis*. Colours vary from cream to grey to brown and pitch-black. An orange/red hourglass mark, Photo 1.2 is seen on the ventral surface of the abdomen while the dorsal surface show a geometrical pattern in the paler specimens, Photo 1.3. Some of the most venomous species in Europe and America have the same hourglass pattern as the brown button species found in South Africa. The egg sacs of the *L. geometricus* are spiky in appearance while the egg sacs of the *L. rhodesiensis* are larger and woolly in appearance, without the spikes. *L. geometricus* spiders are found throughout South Africa, especially in built-up areas under windowsills and garden furniture.^{12,21} Figure 1.6 and 1.7 show the distribution maps of *L. geometricus* and *L. rhodesiensis*.²⁴



Photo 1.2 Brown button spider with typical orange hourglass on the ventral surface (photo courtesy of Niela du Preez)



Photo 1.3 Brown button spider showing geometrical pattern on the dorsal surface (photo courtesy of Niela du Preez)

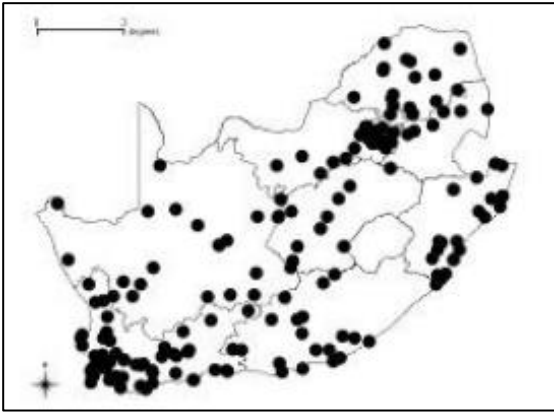


Figure 1.6 Distribution map of *L. geometricus*²⁴

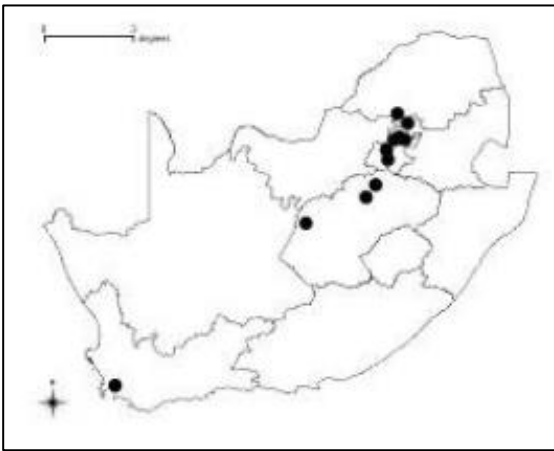


Figure 1.7 Distribution map of *L. rhodesiensis*²⁴

Only female button spiders, which are larger than the males, are able to penetrate the skin of humans due to their larger fangs.²⁵ According to LD₅₀ studies, the venom of *L. indistinctus* is four times more venomous than that of the *L. geometricus*.^{13,21}

Spiders from the genus *Cheiracanthium* (sac spiders) and genus *Loxosceles* (violin spiders) produce cytotoxic venom which affects the tissue around the bite site causing necrotic lesions.^{7,21,22} It is difficult to identify a specific spider species from a bite site since the lesions look similar and most bites occur during night time and patients are usually unaware of being bitten and do not see the spider. Symptoms only present a few hours after the bite.^{12,21}

Nine species of sac spiders are found throughout South Africa of which *C. furculatum*,²⁶ Figure 1.8, *C. vansonii* and *C. africanum* are the most common. *C. furculatum* is often found in houses.^{27,28} Sac spiders

are not web bound, but can be found during the day in their sac-like retreats in the folds of curtains and clothes. Sac spiders are active at night and because of their wandering nature frequently end up in bedding where they may encounter humans.²⁹ *C. furculatum* is the miturgid most frequently found in vineyards and orchards.³⁰ Sac spiders are pale yellow in colour with typical black eye regions and mouthparts, Photo 1.4. Another feature is the arrangement of their legs, two pairs directed forwards and two pairs backwards with the first pair of front legs much longer than the others.^{12,21}

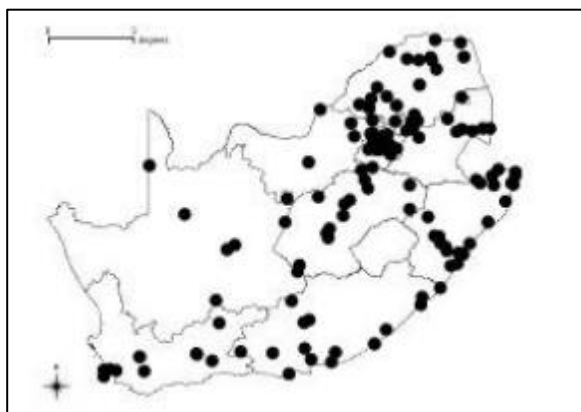


Figure 1.8 Distribution map of *C. furculatum*²⁶



Photo 1.4 Sac spider showing typical black eye region and mouth parts (photo courtesy of P. Webb)

Six species of violin spiders are widely distributed throughout South Africa, namely *L. bergeri*, *L. parramae*, *L. simillima*, *L. pilosa*, *L. speluncarum* and *L. spinulosa*, Figure 1.9.³¹ *L. parramae* has been introduced into houses in the Gauteng area where they are found behind picture frames and in dark

corners or cupboards. They are nocturnal and hunt during night time ending up in beds where they may often encounter humans.^{7,22} Violin spiders are brown to tan in colour with long slender legs. They owe their name to the characteristic violin-shaped marking on the dorsal surface of their cephalothorax, Photo 1.5. Violin spiders are not web bound.^{12,21}

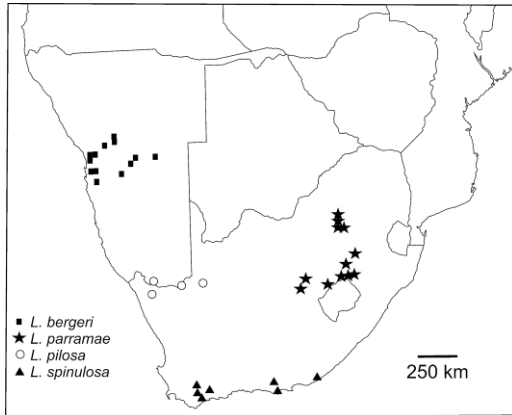


Figure 1.9 Distribution map: *L. bergeri*, *L. parramae*, *L. pilosa* and *L. spinulosa*³¹



Photo 1.5 Violin spider depicting the violin-shaped marking on the chephalothorax (photo courtesy of Ansie Dippenaar)

Both sac spiders and violin spiders are nocturnal and this is the likely reason why most patients are bitten while they are asleep. No antivenom is available for the treatment of cytotoxic spider bites.^{12,21}

A recent report showed cytotoxic effects after the bite of a running spider, *Philodromus* sp. Immediate burning pain was followed by blisters on day 2 and haemorrhagic necrosis was visible within 45 hours post bite.³² Another spider that may be of medical importance is the six-eyed sand spider (genus *Sicarius*), which is found in the arid regions of South Africa. They bury themselves in sand and contact with humans is scarce.¹² Although considered to be cytotoxic by some, there is a lack of substantive clinical data.²¹

1.4 Necrotic arachnidism

Necrotic arachnidism is the clinical syndrome associated with the bite of cytotoxic spiders.²¹ The venom of the *Loxosceles* spiders is a complex mixture of toxins enriched by proteins, glycoproteins and low molecular mass peptides. Several protein classes have been identified including astacin-like metalloprotease, low molecular mass insecticidal peptides, the inhibitor cystine knot peptides (ICK) and phospholipase-D. Other toxins, present in low levels, include hyaluronidase, serine proteases, serine protease inhibitors, venom allergens and translationally controlled tumour protein (TCTP).³³

Although there is uncertainty regarding the mechanism of action of the *Loxosceles* venom, it is believed that a unique enzyme, sphingomyelinase D is responsible for the development of the necrosis. An inflammatory reaction is triggered by the venom, which includes the release of pro-inflammatory cytokines and lipid mediators.³⁴ Phospholipids, such as sphingomyelin and lysoglycerophospholipids are hydrolysed by phospholipase-D at the outer surface of the cell membranes.³⁵ The phospholipids are hydrolysed at a terminal phosphodiester bond to release choline and produce ceramide 1-phosphate. Phospholipase-D, in the presence of Mg^{2+} –cofactor, can also hydrolyse lysophosphatidylcholine.³³ The venom may also cause complement activation, haemolysis of the red blood cells and platelet aggregation. Hyaluronidase has been identified as the ‘spreading factor’ that results in the increase of the size of the lesion.^{4,36}

Systemic toxicity is seen in a small percentage of patients. Haemolytic anaemia is the main feature of systemic toxicity.⁴ Other toxic effects include coagulopathy, renal failure and multiple organ damage. This is however rare, and no cases have been recorded in South Africa.²¹

The bite of the violin spider is most often painless and swelling is not a prominent feature.^{21,22} A red lesion develops 2 hours after the bite, sometimes with a purple centre. Within the next day or two the

bite site may become oedematous and often bullous. Necrosis may take 3 – 7 days to develop. The necrotic tissue detaches after 2 to 3 weeks leaving an ulcer that is slow to heal. Surgical debridement and skin grafts are sometimes necessary.^{21,29,37}

The venom of the *Cheiracanthium punctorium* has a cytolytic effect on the erythrocytes.³⁸ Foradori and colleagues (2005) suggested that the haemolytic agent in *Cheiracanthium mildei* is phospholipase A₂,³⁹ whereas other studies found a two-module polypeptide toxin, CpTx1 to be present, which caused membrane-damaging and cytolytic effects.³⁸

Bites usually occur at night and, therefore, the patient is usually unaware of being bitten. Patients that did witness the bite described it as an initial sharp pain and in some ways comparable to that of a bee or wasp sting.^{5,40,41} Bite marks are sometimes visible. A bull's eye lesion is seen characterised by a surrounding red, swollen and painful area. Necrotic changes occur over the ensuing days and leave an ulcerating wound. Systemic symptoms are rare.⁴²

The diagnosis of necrotic arachnidism is often unconfirmed and based on the clinical picture without evidence of a spider bite.²¹ Studies in California and Arizona, USA have shown that up to 80% of suspected spider bites can be attributed to bites by other arthropods or infection with micro-organisms.⁴³ In a study conducted at an academic emergency department in California, USA almost 90% of reported spider bite cases were subsequently diagnosed as skin and soft tissue infections.⁴⁴ Less than 4% of the so-called spider bites could be clinically confirmed.⁴⁴ A comparative study conducted in Australia and the United States of America (USA) on 20 verified yellow sac spider bites (*Cheiracanthium* spp.) showed no evidence of necrosis.⁴¹ A long list of medical conditions exists that can cause necrotic skin lesions and therefore be mistaken for a cytotoxic spider bite.²¹ If there is no evidence of an actual bite other causes of dermal necrotic lesions should be considered, including *Staphylococcus aureus* and *Streptococcus pyogenes* infections, herpes zoster virus, spirotrichosis, tick and other arthropod bites, cutaneous vasculitis or environmental exposures, Table 1.1.^{10,21}

Table 1.1 Conditions that have been or can be misdiagnosed as necrotic arachnidism (adapted from Vetter & Isbister)¹⁰

<p>Infections</p> <p>Bacterial:</p> <p><i>Staphylococcus</i></p> <p><i>Streptococcus</i></p> <p>Lyme borreliosis</p> <p>Cutaneous anthrax</p> <p>Syphilis</p> <p>Gonococemia</p> <p>Rickettsial disease</p> <p>Tularemia</p> <p>Deep fungal:</p> <p>Sporotrichosis</p> <p>Aspergillosis</p> <p>Cryptococcosis</p> <p>Ecthyma gangrenosum</p> <p><i>Pseudomonas aeruginosa</i></p> <p>Parasitic infection:</p> <p>Leishmaniasis</p> <p>Viral:</p> <p>Herpes simplex</p> <p>Herpes zoster</p> <p>Atypical mycobacterial:</p> <p><i>Mycobacterium ulcerans</i></p> <p><i>Mycobacterium tuberculosis</i></p> <p>Environmental pathogens:</p> <p><i>Chromobacterium violaceum</i></p> <p>Vascular occlusive or venous disease</p> <p>Antiphospholipid-antibody syndrome</p> <p>Livedoid vasculopathy</p> <p>Small-vessel occlusive arterial disease</p> <p>Venous stasis ulcer</p>	<p>Necrotizing vasculitis</p> <p>Leukocytoclastic vasculitis</p> <p>Polyarteritis nodosa</p> <p>Takayasu's arteritis</p> <p>Wegener's granulomatosis</p> <p>Necrotizing vasculitis</p> <p>Leukemia cutis</p> <p>Lymphoma (mycosis fungoides)</p> <p>Primary skin neoplasms:</p> <p>Basal-cell carcinoma</p> <p>Malignant melanoma</p> <p>Squamous-cell carcinoma</p> <p>Topical</p> <p>Chemical burn</p> <p>Thermal burn</p> <p>Poison ivy</p> <p>Poison oak</p> <p>Other conditions</p> <p>Calcific uremic arteriopathy</p> <p>Cryoglobulinemia</p> <p>Diabetic ulcer</p> <p>Langerhans' cell histiocytosis</p> <p>Lymphomatoid papulosis</p> <p>Other arthropod bites</p> <p>Pemphigus vegetans</p> <p>Pyoderma gangrenosum</p> <p>Pressure ulcers (bed sores)</p> <p>Radiotherapy</p> <p>Self-induced injury</p> <p>Septic embolism</p>
---	--

1.5 Latrodectism

Latrodectism is the clinical syndrome associated with the bite of the *Latrodectus* spp. A neurotoxin, alpha-latrotoxin (α -latrotoxin) is responsible for the clinical effects of the button spider's bite. This neurotransmitter binds to the presynaptic nerve terminals resulting in a massive neurotransmitter release of especially acetylcholine and norepinephrine, Figure 1.10.^{13,25,45} At first the bite causes a hyperactive state characterised by a stimulation of the somatic and autonomic nerve endings, followed by a phase of relative paralysis due to the depletion of neurotransmitters. The toxin is unable to cross the blood-brain barrier and therefore the central nervous system is not affected.²¹

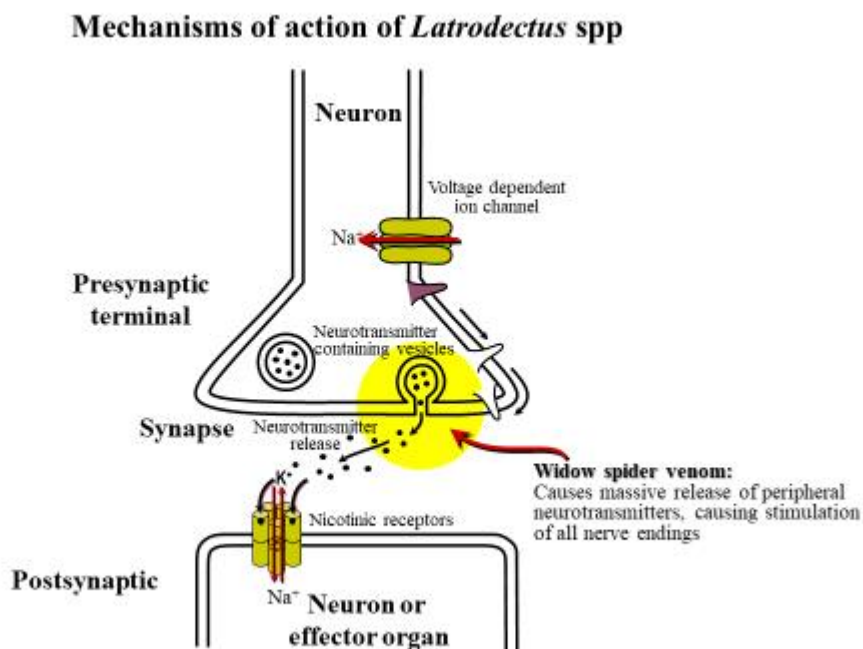


Figure 1.10 Mechanisms of action of bite of *Latrodectus* spp (adapted from Muller *et al*)²¹

Although not yet properly isolated or characterized, it seems that *Latrodectus* venom contains a number of toxins and other biologically active substances. Different techniques, such as ion exchange chromatography and hydrophobic chromatography, have isolated seven different latrotoxins (LTXs) from the venom of the *L. tredecimguttatus*. These LTXs, also known as latroinsectotoxins, are large acidic proteins that are poisonous to insects. Alpha-LTX (α -LTX) is the only component of the venom that is specifically targeted at vertebrates. Two low-molecular-mass proteins, called lactroductins, that

were isolated from black widow spider venom seem to increase the toxicity of LTXs, probably by enhancing their affinity for the membrane targets and causing the α -LTXs to become active.²⁵

It seems that α -LTX is found in all *Latrodectus* species. According to Western blotting analyses there are structural differences in the α -LTX of different *Latrodectus* species.^{13,25} Three classes of α -LTX receptors have been identified, namely neurexin (NRX), latrophillin (LPH) and protein tyrosine phosphatase σ (PTP σ). NRX only binds to α -LTX when extracellular Ca^{2+} is present. LPH and PTP σ can bind to α -LTX even if Ca^{2+} is not present. Of these two, LPH is the key receptor for Ca^{2+} -independent release of neurotransmitters.^{25,45}

Alpha-LTX causes Ca^{2+} influx at the presynaptic membrane and this influx is largely responsible for the effects of α -LTX.²⁵ The α -LTX binds to the receptor leading to its effects through two mechanisms: Ca^{2+} -dependent action and Ca^{2+} -independent action. The Ca^{2+} -dependent action involves the insertion of α -LTX into the plasma membrane as well as pore formation. α -LTX acts as a transmembrane channel that leads to the influx of extracellular calcium through α -LTX's central port resulting in massive exocytosis of neurotransmitters.^{46,47} Receptor-mediated signalling is associated with the Ca^{2+} -independent action. α -LTX binds to the σ LPH causing intracellular calcium release. Both pathways can thus lead to neurotransmitter release. Studies of the structure and function of LTXs guide our understanding of the mechanisms of spider toxin associated neurotransmitter release, Figure 1.11.^{25,46,47}

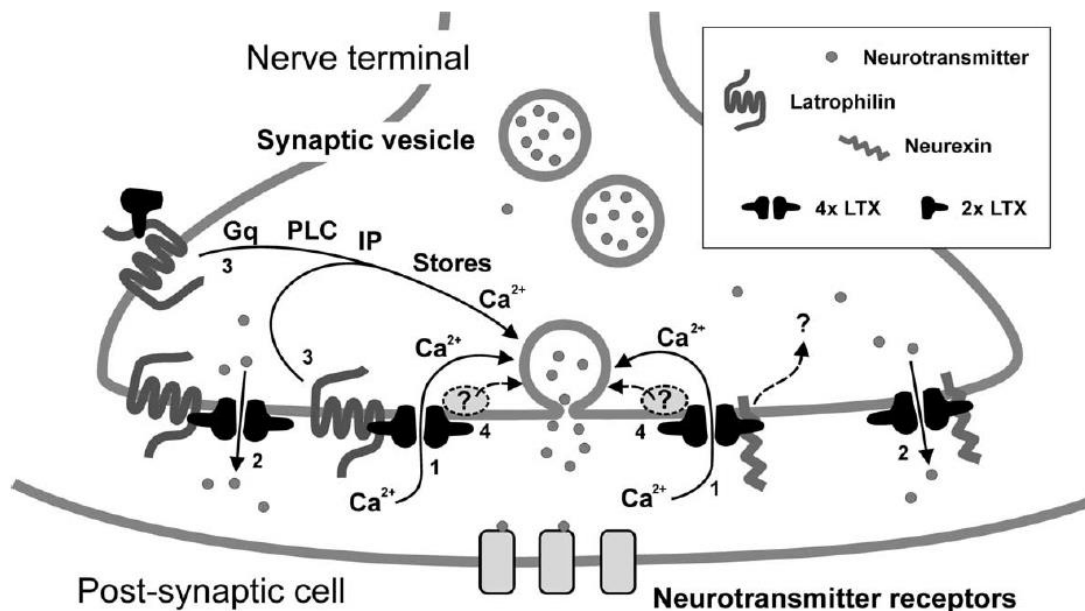


Figure 1.11 Multiple mechanisms of α -LTX action (adapted Ushkaryov *et al*)⁴⁷

The clinical features of latrodectism are described in Table 1.2. In 30% of the cases the bite mark could not be detected. Young children and the elderly are particularly at risk of developing clinical complications.^{21,29,48}

Table 1.2 Clinical features of latrodectism

At time of bite	Burning pain at bite site
5 – 15 min	Pain spread to regional lymph nodes
15 – 60 min	Generalised muscle pain and cramps especially in abdomen, back, chest and thighs are prominent
	Weakness in legs
	Difficulty in walking
	Tightness of the chest – described as difficulty in breathing
	Profuse sweating
	Anxious
	Board-like rigidity of the abdomen
	Raised blood pressure
	Rapid pulse rate
Coarse involuntary movements	

A milder form of envenomation is encountered with brown button spider bites.¹³ A local burning sensation can spread to the area of the regional lymph nodes. Abdominal and general muscular pain and weakness can be seen in a small number of patients. The bite site appears typically as a red spot. The condition usually resolves within 1 – 3 days. Children may develop signs and symptoms of systemic envenomation.²¹

A diagnosis of latrodectism can easily be missed or delayed, because other illnesses can present with similar symptoms. These conditions include scorpionism, acute peritonitis, myocardial infarction, alcohol withdrawal and poisoning by cholinesterase inhibitors.²¹

Diaphoresis is a common and characteristic feature of latrodectism. The pattern thereof may, however, differ between species, Table 1.3.⁴ Pain is another common symptom in bites from most of the *Latrodectus* species worldwide, although the pain pattern seems to differ between the different species. Local and radiating pain is more common in bites from *L. hasselti* from Australia, while the bite from

the *Latrodectus* spp in Africa, America and Europe is more likely to cause back, abdominal and chest pain.¹⁰ In South Africa the definitive treatment is with antivenom²¹ in contrast to most parts of the world where the main focus of treatment is on pain control with analgesics.⁴⁵

Table 1.3. Summary of clinical effects of widow spider bites from different regions of the world (adapted Isbister and Fan)⁴

	<i>Latrodectus indistinctus</i>	<i>Latrodectus geometricus</i>	<i>Latrodectus hasselti</i>	<i>Latrodectus mactans</i>	<i>Latrodectus tredecimguttatus</i>
Number of bites	30	15	68	163	56
Positive identification	20%	67%	100%	72%	-
Localised pain	67%	93%	100%	38%	90%
Radiating pain to the limb	57%	7%	38%	18%	-
Abdominal pain	67%	27%	9%	17%	35%
Chest pain	30%	0%	6%	4%	14%
Back pain	47%	7%	-	56%	45%
Diaphoresis	70%	-	34%	22%	55%

1.6 Antivenom

Specific black button spider antivenom (South African Institute for Medical Research Spider Venom Antiserum SAVP) is available and an effective treatment for latrodectism.²¹ If antivenom is not administered, symptoms can last for up to a week leaving the patient exhausted and dehydrated.^{21,48} A standard dose of 5 – 10 ml of antivenom is recommended for adults and children. A dramatic response to the antivenom has been observed within 30 – 60 minutes after its administration.^{21,48}

The antivenom is produced by fractionating blood from horses immunized with *L. indistinctus* venom.⁴⁹ The mechanism of action of antivenom is not entirely clear. Proposed theories include the blocking of the active site of a toxin or binding to the toxin to prevent interaction with the substrate. The antivenom-venom complex may also prevent distribution of the toxin to the target area. Lastly, it may increase the rate of elimination from the body.⁴⁵

Isbister defines the ‘efficacy’ of antivenom as its ability to bind and neutralise venom-mediated effects, while the ‘effectiveness’ of antivenom is defined as its ability to reverse or prevent envenoming in human patients.⁵⁰ Possible reasons for the failure of the antivenom can be (i) the inability of antibodies to bind

to the toxin; (ii) certain effects of the venom e.g. renal injury which cannot be reversed or (iii) the onset of symptoms that are too rapid.⁵⁰

According to the literature, the advantage of giving antivenom as treatment for latrodectism differs in various parts of the world. In South Africa, the antivenom is highly effective first line treatment, whereas the experience in Australia and the USA has been negative and it has been claimed that the antivenoms administered for scorpions and snakes are more effective than those for spider bites with the exception of funnel-web spiders, where the treatment is also regarded as being highly effective.⁴

In a South African case series of 45 patients, 30 were identified as black button spider bites (*L. indistinctus*) and 15 as brown button spider bites (*L. geometricus*). All but one of the patients bitten by a black button spider were highly symptomatic and received antivenom, which resolved all symptoms and signs within 6 hours in 19 of the patients.⁴⁸ No allergic or adverse reactions were reported.⁴⁸

In the USA the reluctance to give antivenom for latrodectism is largely due to general perception of a high risk for allergic reactions.^{10,51,52} Diaz and Leblanc (2007) suggested that antivenom should only be given in cases where severe systemic toxicity is present, especially for patients with uncontrollable hypertension, seizures or respiratory arrest.⁵¹ A phase 2 trial for a novel F(ab)₂ antivenom investigated the efficacy and safety in patients with moderate to severe pain in spider envenomations.⁵³ The primary outcome investigated the pain decrease at 150 minutes with the secondary outcome being treatment failure as well as time to clinically important decrease in pain. This F(ab)₂ antivenom is a highly purified equine antibody preparation that was expected to be less immunogenic and therefore a safer treatment option than whole antibody products. Although no difference was found in pain reduction at 150 minutes between the antivenom and placebo group, antivenom use did result in significantly better pain relief at 30 minutes. This indicated that antivenom did shorten the course of spider envenomation in *Latrodectus* spp. No serious adverse effects were documented.⁵³

In Australia the concerns of using antivenom in spider bites involved two aspects, firstly the route of administration (intramuscular versus intravenous), and secondly the lack of data about the analgesic efficacy of antivenom for redback spider (*L. hasselti*) bites. Older smaller studies suggested that intravenous administration was more effective than intramuscular injections (pain scores lower after 24 hours), whereas later and larger studies did not show a significant difference in pain resolution when comparing intravenous to intramuscular administration.⁵² A study to compare the serum antivenom concentrations after intravenous and intramuscular administrations of redback spider antivenom showed detectable levels of antivenom 30 minutes after IV administration. At no point were antivenom levels

detected after intramuscular administration suggesting poor absorption and hence a less efficacious route of antivenom administration.⁵⁴

The aim of Isbister and colleagues' comparative study (2014)⁵⁵ was to determine if the use of antivenom was more effective than placebo for treatment of the pain and systemic effects of latrodectism. Study patients were recruited from emergency departments throughout Australia between 2009 and 2013. Inclusion criteria included a definite bite by a redback spider (*L. hasselti*) with either increasing pain or radiating pain and local or regional diaphoresis. All patients received a standard analgesia treatment protocol prior to the study intervention. The analgesia protocol included paracetamol (1g), ibuprofen (800mg) and oxycodone (5mg) respectively. Equine Fab2 antivenom (redback spider antivenom) was administered to the study group and normal saline to the placebo group. Although 34% of the patients that received antivenom did show improvement in pain at 2 hours after treatment, no significant improvement in pain or systemic effects was shown at 4 hours and 24 hours compared to the placebo group. Hypersensitivity reactions were recorded in 4% of study participants.⁵⁵ Based on these findings the benefit of antivenom use was questioned and standard analgesia preferred for the management of redback spider envenomation.⁵⁵

1.7 Poison Centres experiences

Worldwide, the incidence of spider bite calls to Poison Centres comprise less than 1.5% of all calls, and the majority of spider bite cases reported to poison centres were attributed to unidentified spiders and unproven bites.^{52,56}

The 2013 annual report of the New South Wales Poison Centre, the largest poison centre in Australia, showed that 1 249 calls were received regarding spider bites. Although it was only 1.2% of the total number of calls received for that year, it was the seventh most frequent type of call received. The species of spider was not stipulated in the report.⁵⁷ In 2015 the Victorian Poison Information Centre in Australia received 474 spider bite calls which included 130 (27%) redback spider bites (*L. hasselti*), 75 (16%) white-tailed spider bites (*Lampona* spp.) and 269 (57%) unidentified spider bites. The report does not state how the identification of these spiders was made.⁵⁸

The American Association of Poison Control Centres compiles data from all the poison centres in the USA. Their 2015 annual report showed 7 024 enquiries regarding spider bites of which 6 963 were due to single exposures. The following spiders were reported to have caused the bites: 1631 (23%) black

widow (*Latrodectus* spp.), 1185 (17%) brown recluse, 109 (1.5%) other spiders causing necrotic effects at the bite site, 4049 (58%) other spiders and 50 (0.5%) tarantulas. Spider bites comprised less than 1% of the total calls received at the combined poison centres.⁵⁹ Data from the Texas Poison Centre Network, which includes six poison centres in Texas, showed that more than 70% of spider bites were attributed to unidentified spiders. The other bites were attributed to black widow spiders, brown recluse spiders and tarantulas. Almost 80% of the cases reported were not referred to a medical facility. In 24.2% of the cases moderate to severe clinical effects developed.⁵⁶

1.8 History of South African Poison Centres

Over 45 years ago the importance of a Poison Centre to give advice on the treatment of poisoned patients was recognised and this resulted in the first Poison Information Centre (PIC) in South Africa based at Stellenbosch University's Department of Pharmacology in 1970. In 1977 due to an ever increase in calls a toxicology division was started in the Department of Pharmacology at the newly opened Tygerberg Hospital. It was initially called 'The Tygerberg Drug and Poison Information Centre'. Right from the start it operated as a 24/7 service. In 1998 the name was changed to 'Tygerberg Poison Information Centre' (TPIC). This centre did not only support Tygerberg Hospital but many other hospitals throughout southern Africa as well as the general public on poisoning queries. During the years the TPIC built a reputation as a centre with expertise in snake bites, scorpion stings and spider bites. More or less during the same period (1970's) the Red Cross War Memorial Children's Hospital also realised the need for a centre, specifically for poisoning in children. The Red Cross War Memorial Children's Hospital Poison Information Centre (RXHPIC) was established. The RXHPIC realised the need for a poisoning database to assist with identifying poisons and provide relevant treatment guidelines. The result was AfriTox, a database specifically for the South African market.

During 2015 the two Cape Town based poison centres combined their expertise and in June 2015 the Poison Information Helpline of the Western Cape (PIHWC) was established. The PIHWC provides a 24/7 consultant based service to medical professionals and the general public throughout South Africa and neighbouring countries.

A third poison centre is situated in Bloemfontein and is associated with the Free State University. Personnel from the Department of Pharmacology is responsible for poisoning calls, most often from physicians from the Free State.

Chapter 2

Aims and Objectives

The data on South African spiders and their medical effects is limited. The current study will aim to address some of the uncertainties surrounding spider bites and their effects specifically in the South African context. Furthermore, the study will aim to compile an algorithm for the identification of suspected spider bites to ensure more rapid and effective treatment.

Data regarding spider bites were collected from the consultation forms from the TPIC as well as electronic data from AfriTox TeleLog. Data from the consultation forms were for the period January 2005 to May 2015 and the data from AfriTox TeleLog was from June 2015 – December 2017.

Objective 1

To retrospectively compile a detailed assessment of poison centre data regarding spider bites.

Specific aims

- 1.1 To determine the total number of suspected spider bite calls and express these as a proportion of total calls received at the Tygerberg Poison Information Centre (TPIC) as well as the Poison Information Helpline, Western Cape (PIHWC).
- 1.2 To determine if the call data can be used to differentiate between ‘definite’, ‘probable’ and ‘unlikely’ spider bites.
- 1.3 To classify the suspected spider bites as undeterminable, neurotoxic or cytotoxic spider bites.

Objective 2

To prospectively collect specific spider bite cases to determine whether or not the bite was cytotoxic or due to other causes of dermal necrosis.

Specific aim

- 2.1 To identify positive cytotoxic spider bites and describe the clinical progress of these bites.
- 2.2 To identify those suspected spider bites that were later diagnosed as a different skin pathology.
- 2.3 To describe the clinical progress of these bites.
- 2.4 To illustrate these cytotoxic bites with photos received.

Objective 3

To develop a diagnostic algorithm for the diagnosis of spider bites.

Specific aim

To develop an algorithm for the diagnosis of spider bites from the information gathered retrospectively and prospectively regarding the circumstances and clinical effects of spider bites.

Chapter 3

3.1 Methods

The TPIC made use of consultation forms in the past to keep records of calls received, whereas the PIHWC has, since its inception, used an electronic database, AfriTox TeleLog, for the record keeping of all received calls.

All records have been reviewed, including the records of the TPIC for the period 1 January 2005 to 31 May 2015 and the records of the PIHWC from 1 June 2015 to 31 December 2017.

3.2 Data collection and analyses

All cases of suspected 'spider bites' involving humans have been extracted from both data sets, whereas bites involving pets or other animals have been excluded. If more than one call was made relating to the same bite, it has been recorded as one exposure.

Data extraction included the date of call, the caller and patient demographics (age group and sex), duration of time elapsed since suspected bite and whether a spider was seen and/or identified, whether treatment had been received and if the advice had been given to the caller. Other variables included season (month of the year), geographical location, location of bite on body and any local and/or systemic effects observed.

All data were entered into a Microsoft Excel spreadsheet and all documents will be stored on a password protected computer.

In addition to the telephonic data collection a number of calls about suspected cytotoxic spider bites were followed-up by consultants and these have been included as cases studies. With the permission of patients photos were obtained to illustrate the necrotic skin lesions.

This is a descriptive study of data accumulated from consultation forms and an electronic database.

3.3 Ethics

This study was approved by the Health Research Ethics Committee of the University of Stellenbosch (Ref: S17/09/171).

Chapter 4

Results

4.1 Total spider bites

During the period 1 January 2005 to December 2017, 83974 telephonic consultations were dealt with of which 1917 (2.3%) involved reported spider bites (annual mean = 147.5). The percentage of spider bite calls relative to the total number of spider bites seen has remained between 2.2% and 4.9% for the study period from 2005 to 2014, but has dropped to less than 1.8% after the merging of the two poison centres in 2015, Table 4.1.

Table 4.1. Number of spider bite calls relative to total number of calls received, 2005 - 2017

Year	Total number of calls n	Calls related to spider bites n (%)
2005	3287	128 (3.9%)
2006	2965	96 (3.2%)
2007	3077	152 (4.9%)
2008	5097	169 (3.3%)
2009	6101	146 (2.4%)
2010	5988	144 (2.4%)
2011	6260	140 (2.2%)
2012	6596	202 (3.1%)
2013	6661	162 (2.4%)
2014	6228	166 (2.7%)
2015	8366	145 (1.7%)
2016	11186	132 (1.2%)
2017	12163	135 (1.1%)
2005-2017	83974	1917 (2.3%)

The majority of calls were received from the general public (n = 1139; 59.4%); followed by government hospitals (n = 355; 18.5%); general practitioners (n = 219; 11.4%) and private healthcare facilities (n = 204; 10.6%), Table 4.2.

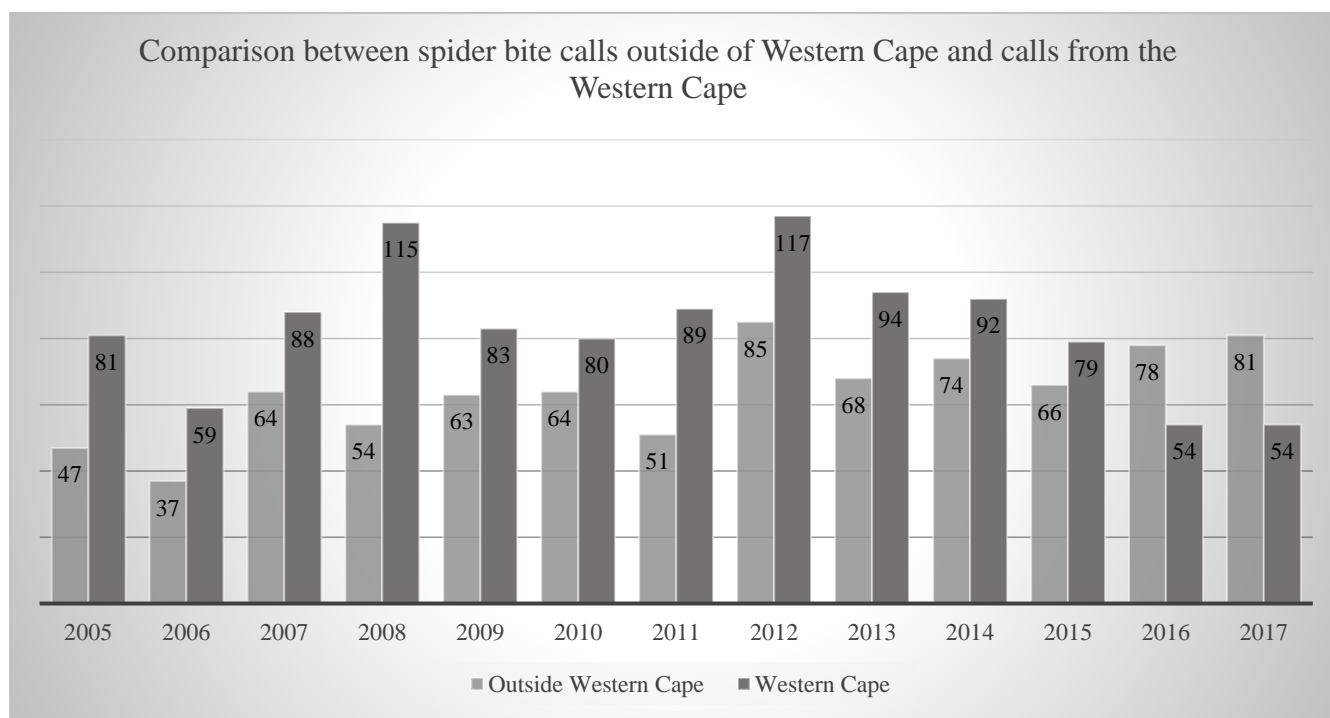
Table 4.2 Distribution of type of callers for spider bite calls, 2005 – 2017

Year	GP	Private Hospital	Public	State Hospital	Total Calls
2005	31 24.2%	9 7.0%	64 50.0%	24 18.8%	128
2006	16 16.7%	6 6.3%	52 54.2%	22 22.9%	152
2007	30 19.7%	15 9.9%	75 49.3%	32 21.1%	152
2008	24 14.2%	11 6.5%	96 56.8%	38 22.5%	169
2009	18 12.3%	20 13.7%	85 58.2%	23 15.8%	146
2010	17 11.8%	8 5.6%	97 67.4%	22 2.3%	144
2011	15 10.7%	18 12.9%	91 65.0%	16 11.4%	140
2012	14 6.9%	18 8.9%	145 71.8%	25 12.4%	202
2013	17 10.5%	25 15.4%	87 53.7%	33 20.4%	162
2014	15 9.0%	22 13.3%	104 62.7%	25 15.1%	166
2015	7 4.8%	21 14.5%	82 56.6%	35 24.1%	145
2016	11 8.3%	10 7.6%	80 60.6%	31 23.5%	132
2017	4 3.0%	21 15.6%	81 60.0%	29 21.5%	135
Total	219 11.4%	204 10.6%	1139 59.4%	355 18.5%	1917

More than 50% of the spider bite calls originated from the Western Cape (n = 1085; 56.6%), followed by Gauteng (n = 410; 21.4%) and KwaZulu-Natal (n = 118; 6.2%), Table 4.3. After 2015 the proportion of spider bite calls from outside the Western Cape has increased substantially and for the study period 2016 and 2017 there have been more calls from outside the Western Cape than from the Western Cape, Figure 4.1.

Table 4.3 Distribution of spider bite calls as per province, 2005 - 2017

Province	Number of calls per province, n (%)
Eastern Cape	67 (3.3%)
Free State	32 (1.7%)
Gauteng	410 (21.4%)
KwaZulu-Natal	118 (6.2%)
Limpopo	22 (1.2%)
Mpumalanga	49 (2.6%)
Northern Cape	30 (1.6%)
North West	35 (1.8%)
Other (calls outside of South Africa)	18 (0.9%)
Unknown province	51 (2.7%)
Western Cape	1085 (56.6%)
Total	1917 (100%)

**Figure 4.1 Comparison between spider bite calls outside of the Western Cape Province compared to spider bite calls from the Western Cape Province, 2005 - 2017**

The majority of spider bites in the study period 2005 – 2017 occurred during the warmer months of the year: 503 (26.2%) consultations during spring (September to November), 575 (30.0%) consultations during summer (December to February), 514 (26.8%) consultations during autumn (March to May) and 325 (17.0%) consultations during winter (June to August), Figure 4.2. January and February were the months during which the majority of calls were received, $n = 208$ (10.9%), Figure 4.3.

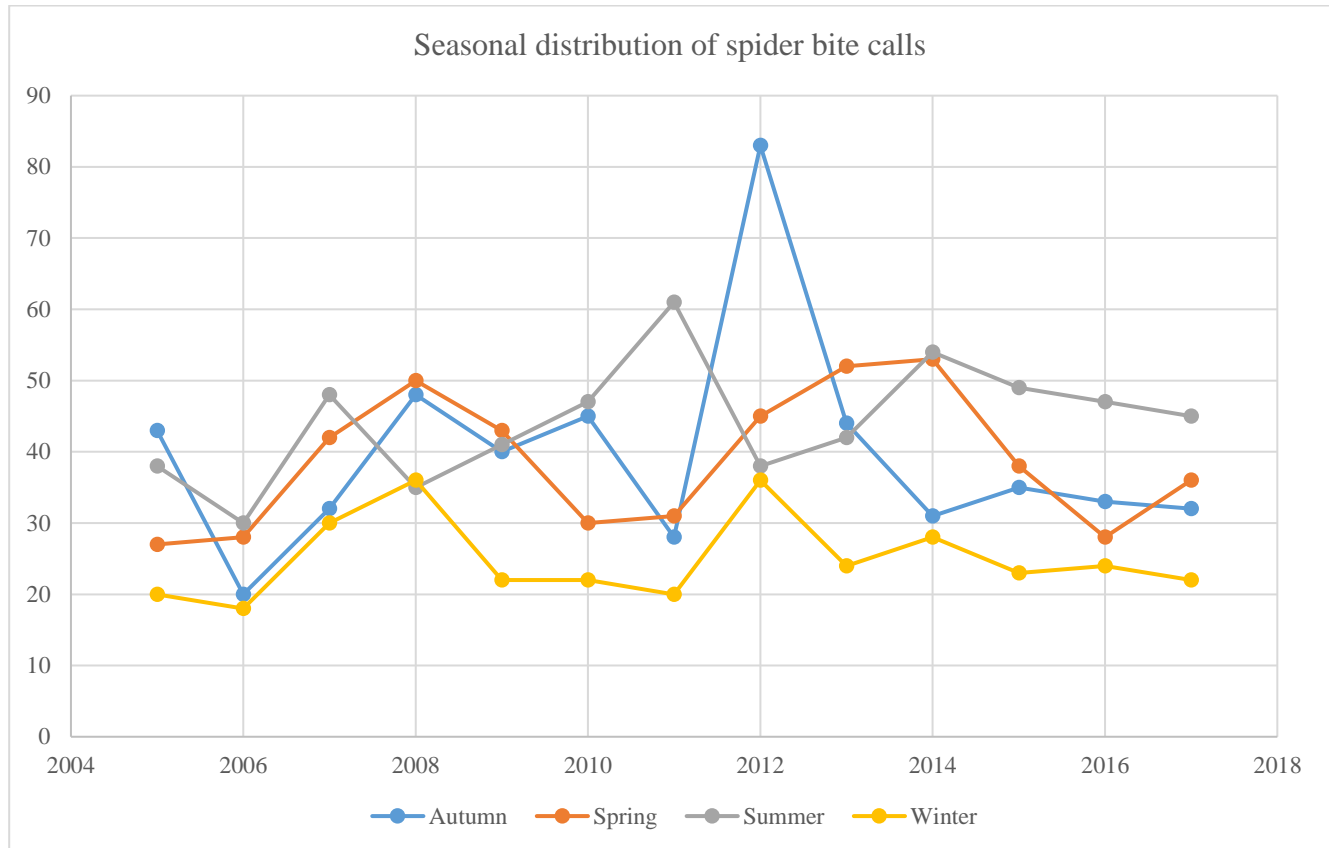


Figure 4.2 Seasonal distribution of spider bite calls, 2005 - 2017

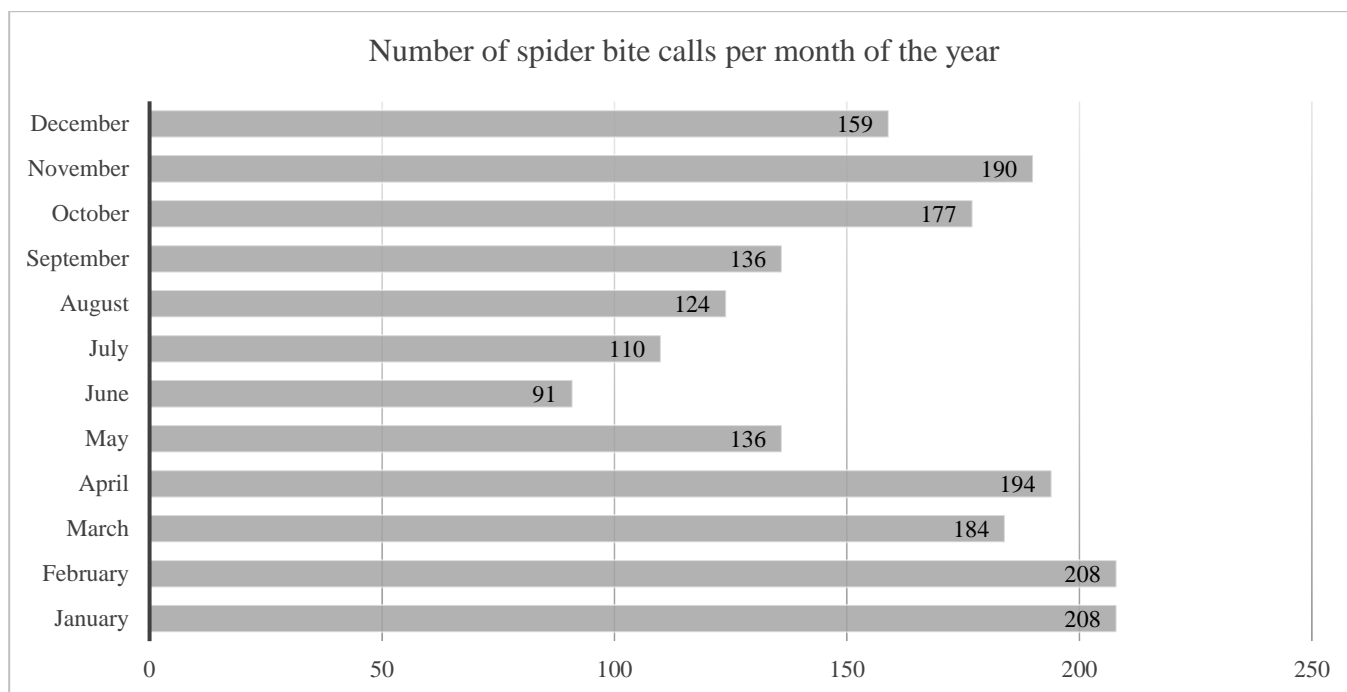


Figure 4.3 Number of spider bite calls per month of the year, 2005 - 2017

Most patients were older than 20 years of age ($n = 1497$; 78.1%) followed by those in the 1 – 5 year age group ($n = 128$; 6.7%), 6 – 13 year age group ($n = 116$; 6.1%), 14 -19 year age group ($n = 100$, 5.2%) and the <1 year group ($n = 17$; 0.9%), Table 4.4. In 59 (3.1%) cases the age was not recorded. Bites were recorded in 974 (50.8%) female patients, compared to 878 (45.8%) male patients. The sex were not recorded in 65 (3.4%) cases. In the cases where all information was recorded (sex and age) the male: female ratio was 47:53, Table 4.5.

Table 4.4 Age distribution of calls received regarding spider bites, 2005 – 2017

Year	<1yr (%)	1 - 5y (%)	6 - 13y (%)	14 - 19y (%)	20 - 99y (%)	Total
2005	1 (0.8%)	6 (5.0%)	10 (8.3%)	2 (1.7%)	102 (84.3%)	121
2006	0 (0%)	2 (2.6%)	3 (3.9%)	3 (3.9%)	70 (89.7%)	78
2007	0 (0%)	16 (10.7%)	7 (4.7%)	9 (6.0%)	118 (78.7%)	150
2008	1 (0.6%)	10 (6.3%)	13 (8.2%)	8 (5.0%)	127 (79.9%)	159
2009	1 (0.7%)	9 (6.3%)	15 (10.6%)	5 (3.5%)	112 (78.9%)	142
2010	1 (0.7%)	7 (5.2%)	3 (2.2%)	8 (5.9%)	117 (86.0%)	136
2011	2 (1.5%)	4 (2.9%)	8 (5.8%)	11 (8.0%)	112 (81.8%)	137
2012	1 (0.5%)	12 (6.0%)	11 (5.5%)	12 (6.1%)	165 (82.1%)	201
2013	2 (1.2%)	12 (7.5%)	7 (4.4%)	12 (7.5%)	128 (79.5%)	161
2014	1 (0.6%)	10 (6.1%)	14 (8.5%)	9 (5.5%)	131 (79.4%)	165
2015	2 (1.4%)	11 (7.8%)	6 (4.2%)	9 (6.3%)	114 (80.3%)	142
2016	2 (1.5%)	10 (7.6%)	5 (3.8%)	6 (4.6%)	108 (82.4%)	131
2017	3 (2.2%)	19 (14.1%)	14 (10.4%)	6 (4.4%)	93 (68.9%)	135
Total	17 (0.9%)	128 (6.9%)	116 (6.2%)	100 (5.4%)	1497 (80.6%)	1858

Table 4.5 Comparison between males and females per age group in cases where all information was recorded, 2005 - 2017

Age group	Sex		Total
	Male	Female	
20 - 99y	658	798	1456
% as per age group	45.2%	54.8%	
% of total gender	77.3%	82.9%	
14 - 19y	53	44	97
% as per age group	54.6%	45.4%	
% of total gender	6.2%	4.6%	
6 - 13y	70	44	114
% as per age group	61.4%	38.6%	
% of total gender	8.2%	4.6%	
1 - 5y	62	62	124
% as per age group	50.0%	50.0%	
% of total gender	7.3%	6.4%	
<1yr	8	15	23
% as per age group	34.8%	65.2%	
% of total gender	0.9%	1.6%	
Total	851	963	1814
	46,9%	53,1%	

During the study period, 1917 spider bites were recorded and included 284 (14.8%) bites by black or brown button spiders (neurotoxic bites), 241 (12.6%) bites allegedly by sac spider or violin spider (cytotoxic bites), and 91 (4.7%) bites by other spiders including baboon and rain spiders. The majority of callers (n = 1301; 68%) were not able to identify the spider (unidentified spiders) as shown in Figure 4.4.

A definite spider bite was reported for 616 (32.1%) of the consultations. Only 217 (11.3%) bites met the criteria of a definite bite, namely the development of a compatible clinical presentation and/or the identification of the implicated spider by a spider expert. The majority of these identified spiders (n = 138; 63.6%) belonged to the *Latrodectus* group (button spiders).

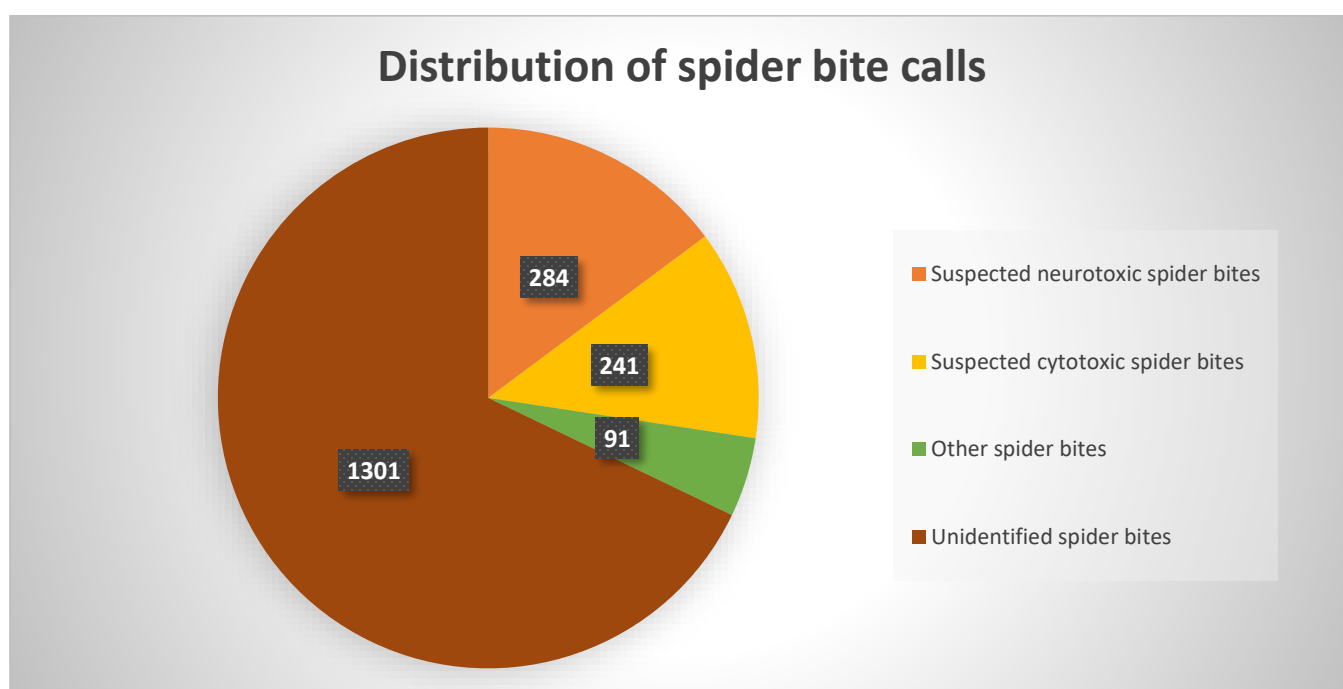


Figure 4.4 Different type of spider bite calls as recorded from Poison centre data, 2005 - 2017

Overall, swelling (n = 481; 26.8%), local pain (n = 400; 22.3%) and redness (n = 384; 21.4%) were the clinical features most often reported. The time after the bite was recorded in 1363 consultations (71.1%) and the affected part of the body was recorded in 1087 consultations (56.7%), Table 4.6. Most bites occurred on the legs and feet (n = 416; 38.3%) followed by bites on arms and hands (n = 379; 34.9%). Fewer bites were seen on the trunk (n = 158; 14.5%) and the head region (n = 134; 12.3%).

Table 4.6 Time after bite and body part affected, 2005 - 2017

Year	Total number of spiders	Time after bite recorded	Body part affected recorded
2005	128	59 46.1%	63 49.2%
2006	96	45 46.9%	52 54.2%
2007	152	76 50.0%	85 55.9%
2008	169	96 56.8%	96 56.8%
2009	146	106 72.6%	99 67.8%
2010	144	126 87.5%	94 65.3%
2011	140	104 74.3%	80 57.1%
2012	202	144 71.3%	100 49.5%
2013	162	133 82.1%	87 53.7%
2014	166	127 76.5%	81 48.8%
2015	145	116 80.0%	77 53.1%
2016	132	114 86.4%	89 67.4%
2017	135	117 86.7%	84 62.2%
Total	1917	1363 71.1%	1087 56.7%

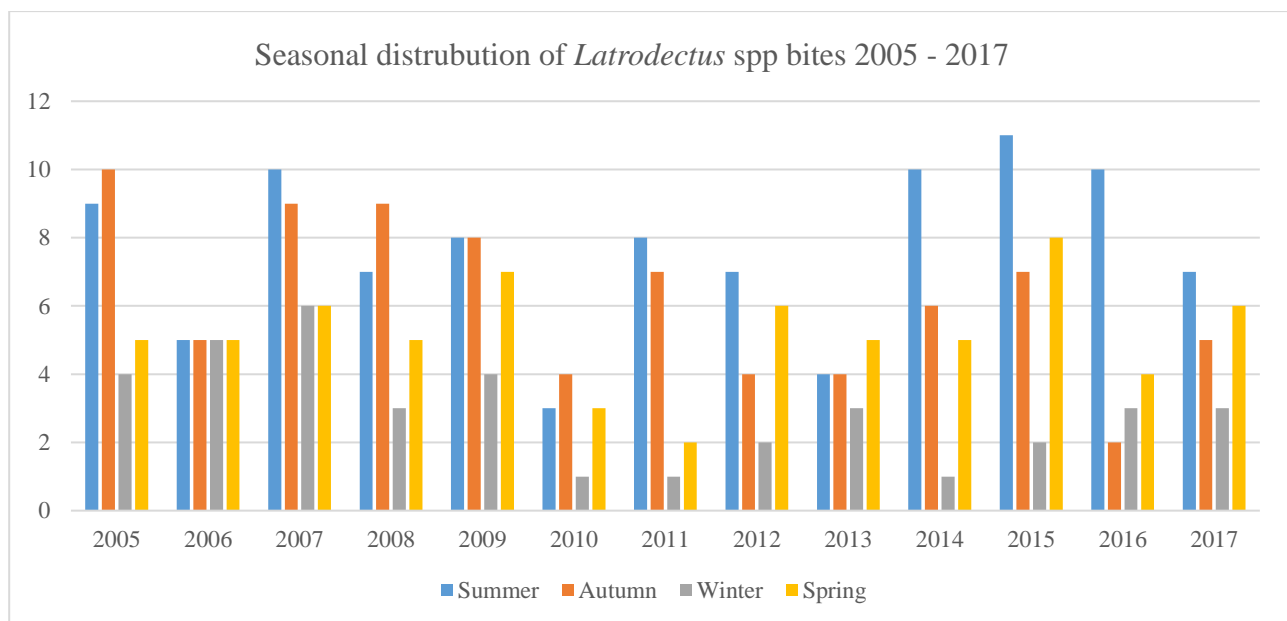
4.2 Neurotoxic spider bites, *Latrodectus spp*

Of the 284 reported button spider bites, 138 (48.6%) were positively identified by either the clinical picture of envenomation or photo/description of the spider. In 80 of the 284 consultations (28.1%) administration of antivenom was advised. Seven patients had already received antivenom at the time of the consultation, one of these received antivenom prior to symptoms developing. Observation was advised in 177 (62.3%) consultations and 27 (9.5%) patients were referred to hospital for medical evaluation, Table 4.7.

Table 4.7 Number of reported button spider calls per year with advice given per case, 2005 - 2017

Year	Reported <i>Latrodectus</i> bites	Positively identified	Antivenom advised	Antivenom already administered at time of call	Observation advised	Referred to hospital
2005	28	13	9	1	19	0
2006	20	9	8	0	10	2
2007	31	13	6	3	22	3
2008	24	8	3	0	16	5
2009	27	8	5	1	19	3
2010	11	7	5	0	4	2
2011	18	12	7	0	9	2
2012	19	10	1	0	16	2
2013	16	10	7	1	8	1
2014	22	14	9	0	10	3
2015	28	21	11	1	15	2
2016	19	9	6	0	13	0
2017	21	4	3	0	16	2
Total	284	138	80	7	177	27

In the *Latrodectus* group, most of the bites occurred during the warmer months of the year: 99 (34.9%) during summer (December to February), 80 (28.6%) during autumn (March to May) and 67 (23.6%) during spring (September to November) and 12 (4.2%) during winter (June to August), Figure 4.5.

**Figure 4.5 Seasonal distribution of the *Latrodectus* spp bites, 2005 - 2017**

Generalised pain (n = 89; 31.3%), muscle pain and cramps (n = 88; 31.0%), and sweating (n = 58; 20.4%) were the symptoms and signs most often recorded with the *Latrodectus* spp bites. Other clinical features included anxiety (n = 33; 11.6%), tender regional lymph nodes (n = 27; 9.5%), raised blood pressure (n = 14; 4.9%), difficulty in walking (n = 13; 4.6%) and increase in heart rate (n = 12; 4.2%).

The duration of time between the occurrence of the bite and the telephonic consultation was recorded in 185 (65.1%) consultations, and only 37 (13.0%) calls were received within an hour of the bite, Table 4.8. The part of the body where the bite occurred was recorded in 153 (53.9%) consultations and most bites were on the arms and hands (n = 66; 43.1%) followed by the legs and feet (n = 46; 30.1%).

Table 4.8 Time after bite for *Latrodectus* spp. recorded with calls received within an hour of the bite, 2005 - 2017

Year	<i>Latrodectus</i> spp	Time after bite	Calls received within an hour
2005	28	11	1
2006	20	6	1
2007	31	14	3
2008	24	9	2
2009	27	19	7
2010	11	10	0
2011	18	14	1
2012	19	14	2
2013	16	12	2
2014	22	16	2
2015	28	22	4
2016	19	19	3
2017	21	19	9
Total	284	185	37

To illustrate the geographical areas in which the button spiders can be of concern, towns and cities were specifically looked at for the last five years of the study. The period was chosen because it included the time when Afritox TeleLog was used as electronic database for PIHWC. Prompt fields encouraged better record keeping. Between January 2013 and December 2017, 106 possible *Latrodectus* spp bites were recorded. Of these, 58 (54.7%) were positively identified as *Latrodectus* spp bites and in 38 (35.8%) patients administration of antivenom was advised. The geographical location (town/city) was available

for these cases. Figure 4.6 is a distribution map of patients who received antivenom.¹² The largest concentration of ‘definite’ *Latrodectus* bites were reported from the area where *L. indistinctus* is found.

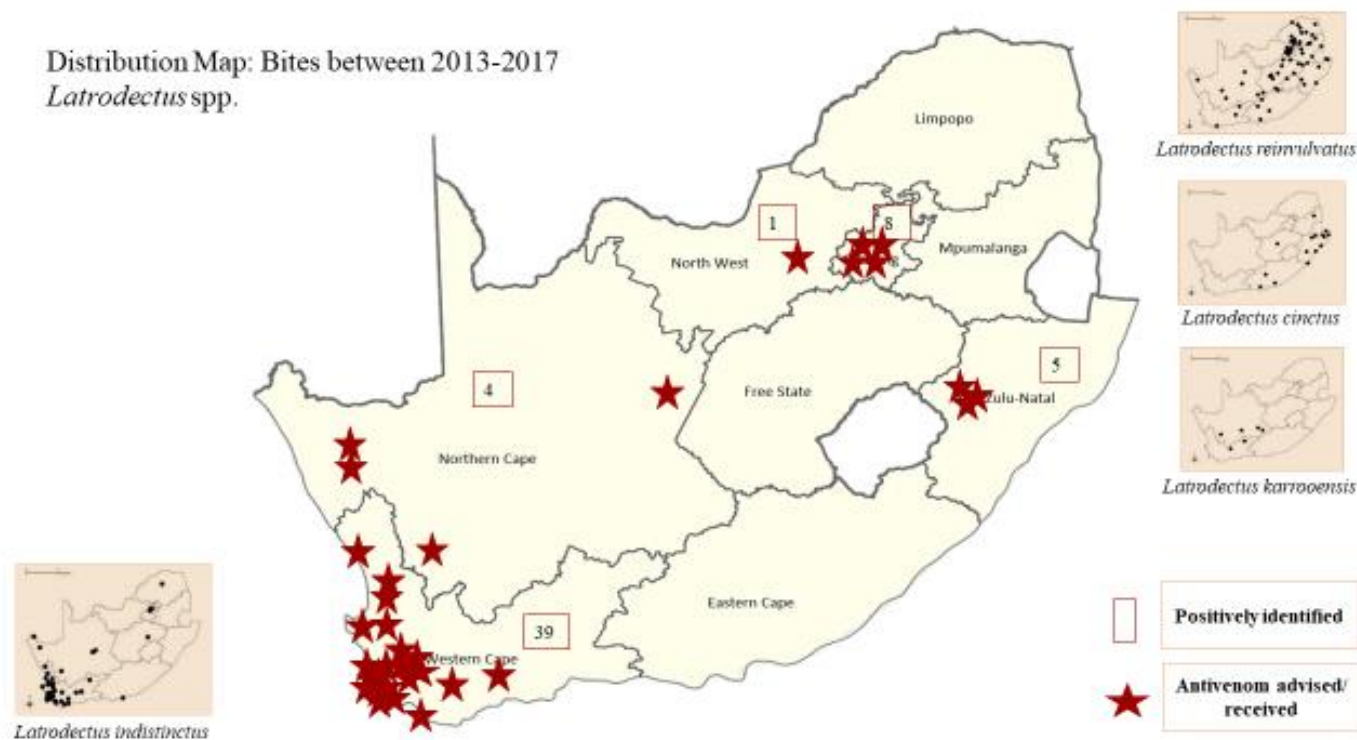


Figure 4.6 Distribution map of bites from *Latrodectus* spp illustrating the number of patients positive for *Latrodectus* bites and the number of patients who received antivenom, 2013 - 2017

4.3 Cytotoxic spider bites

During the study period, 242 (12.6%) possible cytotoxic spider bites were reported with only 5 (2.1%) spiders positively identified in this group, namely two sac spiders, two violin spiders and one six eyed sand spider, Figure 4.7.

If taking known endemic areas of cytotoxic spiders and clinical features associated with cytotoxic bites, like necrotic lesions as a classification factor for probable cytotoxic bites, another 27 (11.2%) suspected cytotoxic bites could be classified as probable cytotoxic bites, Figure 4.7.¹² The largest group, 211 (86.8%) of the suspected spider bites could not be confirmed as definite or probable cytotoxic bites and should be classified as unlikely spider bites.

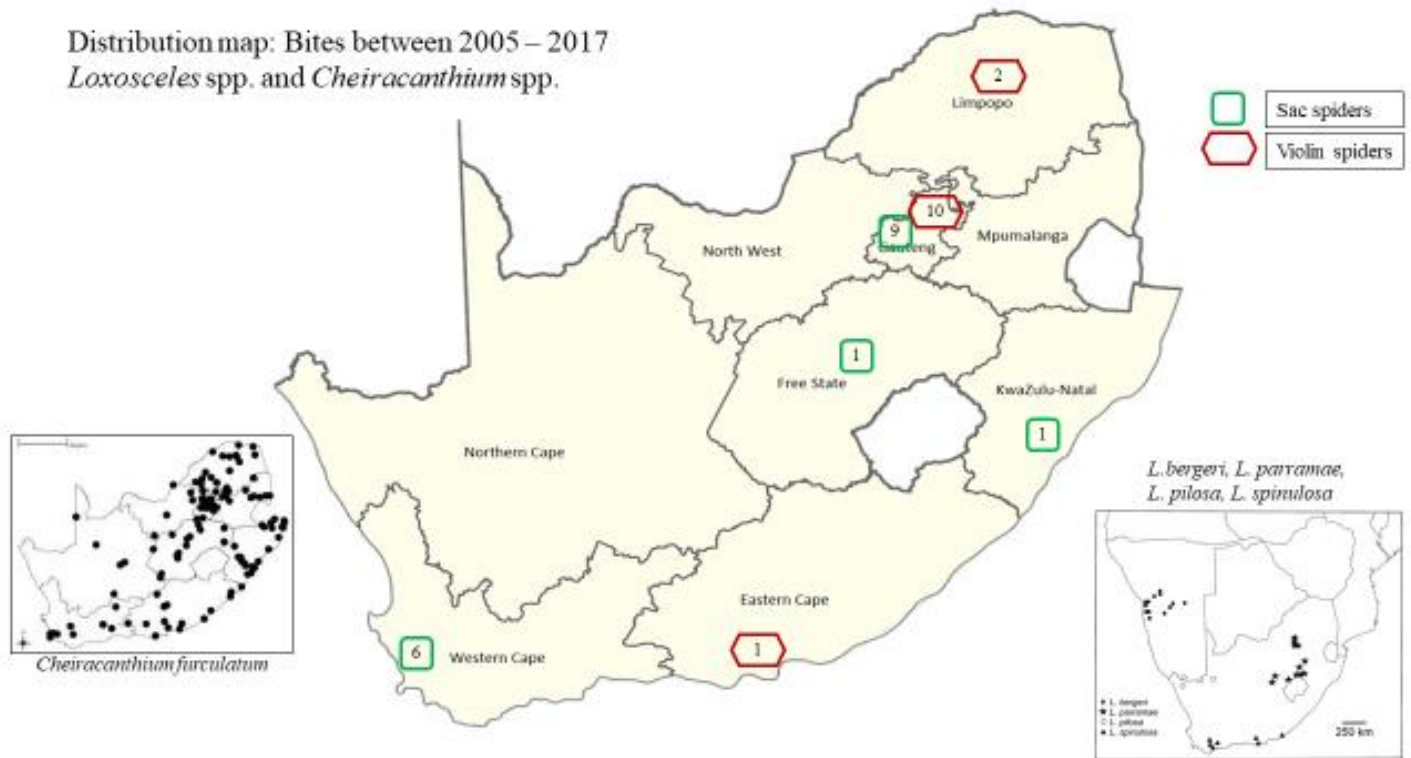


Figure 4.7: Distribution map of positively identified and probable cytotoxic spider bites, 2005 – 2017

Swelling (n = 54; 22.4%), redness (n = 41; 17.0%) and pain (n = 38; 15.8%) were the clinical features reported most commonly in the cytotoxic spider bite group. A necrotic skin lesion was described in 37 (15.4%) cases and suspected skin infection in 49 (20.3%) consultations. Blisters were reported 28 times (11.6%) as shown in Table 4.9.

Table 4.9 Clinical features reported for suspected cytotoxic spider bites, 2005 - 2017

Year	Cytotoxic bites	Local pain	Local swelling	Local redness	Infection	Itchy	Blisters	Fever	Ulcer	Necrotic area
2005	29	2	6	4	6	0	0	0	5	3
2006	10	1	2	2	1	0	1	0	0	0
2007	23	1	7	3	4	0	2	1	1	3
2008	20	4	2	5	4	1	2	1	3	3
2009	16	2	2	3	3	0	1	0	0	3
2010	19	1	7	0	1	0	1	1	2	3
2011	16	4	3	5	3	2	1	1	1	5
2012	22	4	4	3	4	1	3	3	4	6
2013	10	4	3	2	3	1	2	3	1	1
2014	22	1	2	3	3	0	3	1	1	0
2015	21	6	7	4	3	0	2	2	2	2
2016	15	2	4	4	7	0	4	2	2	4
2017	18	6	5	3	7	2	6	2	2	4
Total	241	38	54	41	49	7	28	17	24	37

The duration of time that had elapsed between the suspected bite and the telephone call was recorded in 185 (76.8%) consultations and the affected part of the body in 113 (46.9%) consultations. The majority of bites affected the legs and the feet (n = 61; 54.0%).

Because the nature of the skin lesion was not always clear 116 (47.9%) callers were referred to a medical facility for evaluation and 58 (24.1%) patients had already been to a medical facility or were admitted to a medical facility at the time of their call. In 27 (11.2%) consultations there were few or no symptoms at the time of the call, and callers were advised to clean the wound and contact a medical facility if symptoms should develop or worsen. A total of 96 (39.8%) of the patients in the cytotoxic spider bite group were treated with antibiotics and 17 (7.1%) patients had already undergone a surgical procedure like skin grafts at the time of their call.

4.4 Other spiders

Ninety (4.7%) bites were caused by other spiders, including 29 (31.9%) baboon spider (family Theraphosidae) and 29 (31.9%) rain spider bites (family Sparassidae, *Palystes* spp.) (n = 29; 31.9%). The affected part of the body was recorded in 48 (53.3%) of these consultations and more than half of the bites were on the hands (n = 25; 51.0%). Most patients were advised to clean the wound and seek medical attention if necessary (n = 74; 81.3%). Swelling (n = 18; 19.8%) and pain (n = 17; 18.7%) were the most common symptoms. The time between the suspected bite and telephonic consultation was recorded in 53 (58%) consultations and more than half of these (n = 34; 64.2%) were within the first hour after the bite. Three wolf spider bites (Family Lycosidae) were recorded during the study period.

4.5 Unidentified spiders

A total of 1301 (68%) consultations were recorded as unidentified spider bites, Figure 4.8. In most cases the patients were referred to a medical facility (n = 523; 40.2%). A total of 237 (18.2%) patients were on treatment with an antibiotic at the time of the call and were referred back to their medical facility for follow-up; 390 (30.0%) patients were advised to disinfect the wound and seek medical attention if an infection was suspected. Surgical procedures like skin grafts had already been performed at the time of the call in 18 (1.4%) patients.

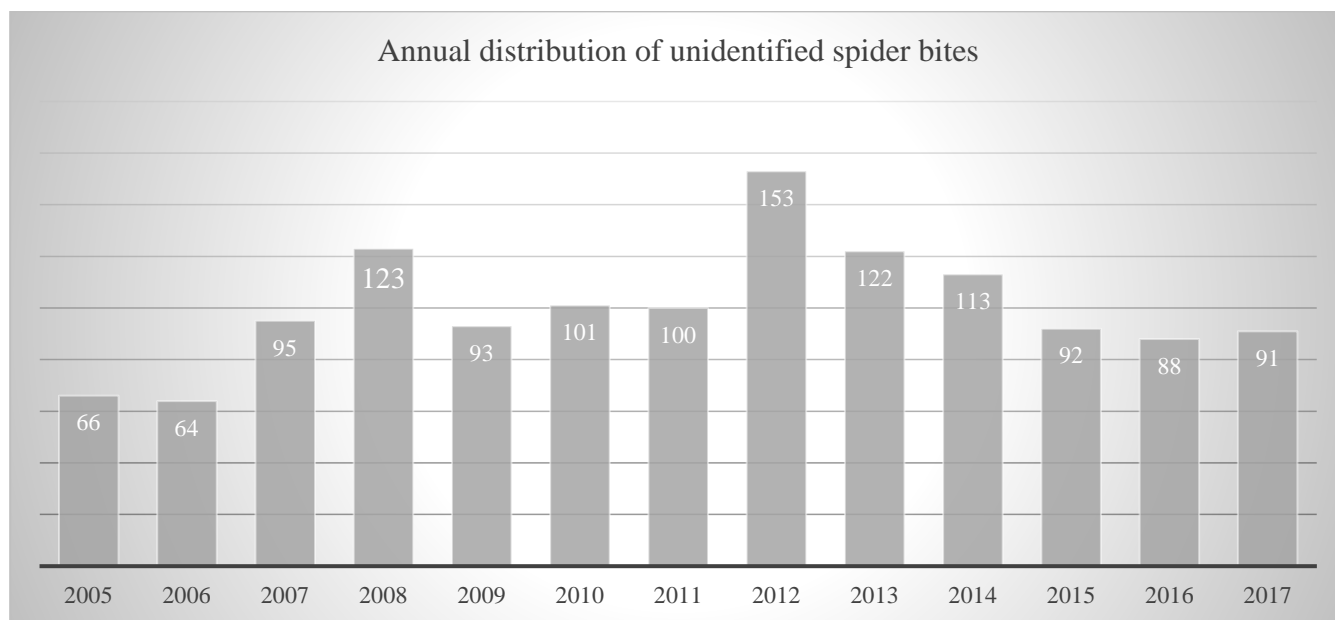


Figure 4.8 Annual distribution of unidentified spider bites, 2005 - 2017

As with the cytotoxic spider bites, swelling (n = 409; 31.4%), redness (n = 335; 25.8%) and pain (n = 256; 19.7%) were the symptoms most often recorded. Other features included blisters (n = 151; 11.6%), necrotic wound (n = 123; 9.5%) or a skin infection (n = 176; 13.5%), Table 4.10.

Table 4.10 Clinical features reported for unidentified spider bites, 2005 - 2017

Year	Suspected bites	Local pain	Local swelling	Local redness	Infection	Itchy	Blisters	Fever	Ulcer	Necrotic area
2005	66	9	13	12	11	1	5	2	8	3
2006	64	6	14	19	12	2	7	2	4	3
2007	95	13	24	27	10	2	9	2	9	7
2008	123	17	32	30	14	3	12	2	7	17
2009	93	12	20	28	6	3	7	4	6	6
2010	101	17	33	21	12	6	12	5	2	5
2011	100	41	79	46	31	14	25	9	7	16
2012	153	23	40	22	9	8	19	11	3	22
2013	122	23	33	35	11	6	15	11	6	8
2014	113	25	40	26	11	7	11	6	0	7
2015	92	20	25	20	14	2	12	8	3	11
2016	88	26	27	25	18	6	8	5	1	10
2017	91	24	29	24	17	5	9	10	3	8
Total	1301	256	409	335	176	65	151	77	59	123

The affected part of the body was recorded in 772 (59.3%) consultations with most bites on the legs and feet (n = 296, 22.8%)

4.6 Case studies – ‘suspected’ cytotoxic or unidentified spider bites

In the current study five patients were studied prospectively after reporting skin lesions initially thought to be due to cytotoxic spider bites. These five patients were scrutinised in more detail and a number of relevant tests were performed to elicit the most likely cause of their necrotic lesion. These cases were all followed over a period of time to determine the progression of the lesions. All consultations and follow-up communications were captured on patient case report forms: ‘Spider bite in Southern Africa: Neurotoxic (widow spider) and cytotoxic (sac and violin) spiders’, Appendices.

Case 4.6.1

A 23-year old female KwaZulu-Natal contacted the investigator through a Facebook group, The Spider Club of Southern Africa, on the same day as the bite occurred, Photo 4.6.1.1. She reported that she was bitten by a spider on her left arm while getting dressed. The spider was inside the sleeve of the top she was putting on. She felt a burning sensation and hit at the painful area with her hand. A spider fell out of the sleeve and was subsequently identified by a qualified arachnologist as a sac spider.

The pain was felt exclusively at the site of the bite and redness could be seen around the bite site which also felt itchy. One day later the area around the bite site was described as swollen and hard, Photo 4.6.1.2. Pain and itchiness was still present. The patient's parent took her to the doctor out of concern that the lesion might worsen. Antibiotics were prescribed by the physician. The patient was contacted 4 days later for a progress report. It was reported that the bite site was no longer visible and that the swelling and redness had subsided. This course of events is compatible with a sac spider bite and sac spiders occur in KwaZulu-Natal.



Photo 4.6.1.1



Photo 4.6.1.2

Case 4.6.2

The mother of a 22-year old female from Johannesburg contacted the investigator at the TPIC. According to the mother the patient was allegedly bitten by a spider on the left cheek near the eye, Photo 4.6.2.1. Apparently this was the fourth time she had allegedly been bitten by a spider. The suspected bite site was accompanied by redness and periorbital swelling. She was seen by her general practitioner, who made the diagnosis of spider bite and prescribed the antibiotic ciprofloxacin (Ciprobay[®] XR, 1000 mg per os once daily) as well as oral methylprednisolone (Medrol[®], 4 mg per os twice daily). At the time of the fourth suspected bite, a dead spider was found in the patient's bed room and a photograph was sent for identification. The photo was of poor quality, but a qualified arachnologist nevertheless identified the spider as either a wolf spider or a flat-bellied ground spider (Gnaphosidae), both of these are not known to cause necrotic skin lesions.

On the following day she was taken to a private hospital and she required a drainage procedure of an abscess that had formed. Photo 4.6.2.2 shows the lesion one month after the hospital procedure. On follow-up two months later it was reported that the wound had healed, but had left a scar.

Seven months after the surgical drainage procedure the 22-year old female patient developed a similar skin lesion as previously experienced, this time involving her buttock and under her arm. The affected areas were very painful. She was seen by her physician who diagnosed her with bacterial folliculitis and prescribed the antibiotic Augmentin. On telephonic follow-up a month later the wound had healed and patient was doing well.

This case demonstrates that bacterial skin infections may be confused with necrotic spider bites. The repetitive episodes, the identification of a spider that does not cause necrotic lesions, the response to surgical drainage and antibiotic therapy are all clues that this was these suspected spider bites were not caused by spiders.

Five months later the husband of the original caller experienced a similar episode involving his leg. The 70-year old husband reportedly had two severe bites on the calf of his left leg which they assumed to have happened the previous week. He developed a painful red swollen lesion. His physician prescribed amoxicillin (Macropen[®] 1000 mg, per os 3 times per day). The wife thought that his lesions were due to bites by a violin spider. The wife, however, also mentioned that he suffered from varicose eczema and that he had experienced a flare-up 2 weeks prior to the incident and that his doctor had treated this with clarithromycin (Klacid[®]). Photos 4.6.2.3 – 4.6.2.6 show the progression of the lesions.



Photo 4.6.2.1



Photo 4.6.2.2



Photo 4.6.2.3



Photo 4.6.2.4



Photo 4.6.2.5



Photo 4.6.2.6

Case 4.6.3

A 74-year old gentleman contacted the PIHWC regarding a suspected spider bite. He reported that he had been bitten by a spider on his left leg 5 months prior to contacting the PIHWC, Photo 4.6.3.1. Itchiness was the only symptom experienced. This lasted for a few days, but subsided without problems. Two months later a red area developed at the same site of the suspected bite. Blisters developed with little ulcers forming around the affected area. It was painful and the patient went to his general practitioner, who suspected a bacterial infection and prescribed an antibiotic cream. He advised the patients to keep the area covered with a bandage. It is unclear whether the general practitioner agreed with the patient's spider bite suspicion. It was at this point in time that the patient contacted the PIHWC and because it did not sound like a spider bite and the diagnosis of a bacterial infection seemed uncertain, the patient was referred back to his physician for re-evaluation. It transpired that the patient had been diagnosed with a haematological cancer, polycythaemia vera in 2004. His haematologist had changed his medication for the polycythaemia approximately two weeks before the skin lesions had started and the physician subsequently diagnosed an adverse reaction to his new medication (interferon injections) rather than a spider bite, photos 4.6.3.2 and 4.6.3.3.



Photo 4.6.3.1



Photo 4.6.3.2

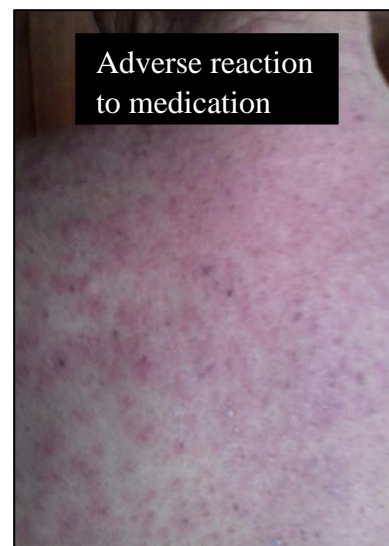


Photo 4.6.3.3

Case 4.6.4

A doctor from the emergency department contacted the researcher regarding a suspected spider bite. The referring doctor was aware of the research on suspected spider bites as he had attended a toxicology symposium presented by the TPIC a month prior to the incident.

A 45-year old gentleman presented to Karl Bremer hospital with the history of a suspected spider bite on his right ankle two days prior to presentation. Although no spider had been seen the patient was convinced that his lesion must have been caused by a spider bite. The affected area of skin was itchy, the leg was red and swollen from the ankle to the thigh. No specific bite site could be seen. The attending physician diagnosed cellulitis and prescribed Augmentin[®] and an analgesic. On day 6 the patient was still in hospital on intravenous antibiotics. He complained about severe pain. On day 14 the patient was still experiencing pain and what he described as 'water' leaking from the infected area. At week 6 the patient reported that the leg was healing. Photos 4.6.4.1 – 4.6.4.5 show the progression of the lesion.

Cellulitis is a bacterial infection involving the inner layers of the skin. It specifically affects the dermis and subcutaneous fat. Signs and symptoms include an area of redness which characteristically increases in size over a few days. The borders of the area of redness are generally not sharp and the skin may be swollen. The area of infection is usually painful. Necrotic spider bites cause local necrosis rather than a larger area of erythema.



Photo 4.6.4.1



Photo 4.6.4.2



Photo 4.6.4.3



Photo 4.6.4.4



Photo 4.6.4.5

Case 4.6.5

The concerned daughter of a 70- year old gentleman called the PIHWC. According to the daughter her father woke up at 02h00 in the morning with a burning pain over his right ankle. This event happened 4 weeks prior to the call, Photo 4.6.5.1. Over the next few days several blisters formed in the painful area. He went to his general practitioner, who did a number of special investigations, including a blood culture. After the tests the doctor allegedly stated that all tests, and specifically the culture result had confirmed his clinical impression of a violin spider bite and that antibiotics were needed to treat this. The patient was impressed by the doctor's thoroughness and diagnostics skills and did not query the nonsensical statements concerning diagnosis of spider bite by culture and need for antibiotics for a nonbacterial affliction.

The practitioner was not contacted for clarification. The patient had by then completed four courses of antibiotics. The family was concerned that the affected area was deteriorating rather than improving. During the telephonic call it was established that the patient had a long history of cigarette smoking and it was thought wise for him to get a second opinion from a medical specialist. A dermatologist diagnosed an atypical ulcer and was of the opinion that a spider bite was extremely unlikely. He referred the patient to vascular surgery for further evaluation. The attending surgeon made a diagnosis of peripheral vascular disease and an ischemic ulcer. Subsequently, the patient underwent a below knee amputation. Photos 4.6.5.2 – 4.6.5.5 show the progression of the lesions.



Photo 4.6.5.1



Photo 4.6.5.2



Photo 4.6.5.3



Photo 4.6.5.4



Photo 4.6.5.5

Chapter 5

Discussion

Spider bites constitute a small proportion of the PIC telephonic consultations. During the 13-year study period 1917 consultations regarding spider bites were recorded, which equates to 2.3% of the total number of calls received. This correlates well with data from poison centres worldwide where the proportion of spider bite calls relative to the total number is usually less than 1.5%.⁵⁶⁻⁵⁹

We did not see an increase in the number of spider bite calls received after the merger of the two PICs to form the PIHWC in 2015. There was however, a significant increase in total calls received during 2016 and 2017. This interesting finding of not seeing an increase in spider bite calls can probably be explained by the historically different strengths of the two PICs. Firstly, the RXHPIC dealt more with exposures in children than adults.⁶⁰ Previous studies showed that spider bites occur more frequently in adults than in children and this probably resulted in more calls received at TPIC, which dealt preferentially with calls in adults.^{18,56,61} Secondly, the TPIC was renowned for its expertise in biological toxins and specifically Dr Gerbus Muller, who is nationally recognised as the expert on biological toxins including spider bites.

A significant increase in the number of spider bite calls to the TPIC was seen during 2012 due to an article titled 'Klein gog, Groot gif' / 'Eaten away by poison', by Carol Coetzee. The article appeared in the 'Huisgenoot' and its sister magazine 'You' on 12 April 2012. Both these magazines are read by a substantial proportion of the population. The claim was that the lady living in Paarl was bitten by a violin spider and nearly lost her arm because of the bite. The article contained several unverified facts e.g. the treating doctor diagnosed the skin lesion as that of a violin spider bite. Skin lesion was treated with anti-inflammatory drugs, pain tablets and high doses of antihistamines. The patient complained of a high fever and pus running from the affected areas. The end result was an operation to remove the large area that was contaminated by poison. The contact number of the TPIC was mentioned in the article as contact number for people concerned about spider bites. The number was used without permission of the TPIC and could have given the perception that we agreed with what was said in the article. This article led to the publication of 18 further articles in newspapers like 'Die Burger', 'Cape Argus', 'Beeld' and 'Volksblad' over the next three or four months. In August 2012 another article was published in the 'Times Live' claiming the death of a 53-year old woman due to the bite of a sac spider, under the title: 'Spider bite kills Western Cape businesswomen'. The ensuing media frenzy led to many concerned patients thinking they could have been bitten by a spider and subsequently resulted in an increase in the

number of calls received regarding suspected spider bites. This increase in calls is clearly reflected by a change in the seasonal pattern for 2012 with a significant increase seen from April (autumn) throughout the winter months into spring as depicted in Figure 4.2. The number of unidentified spiders was also higher in 2012, 75.7% in 2012 compared to the average of 68% for the entire study. The observed increase in calls demonstrates the remarkable influence that the media can have, not only on the distribution of facts (or misinformation), but also on public reaction and on poison centre calls.⁶² The reaction of the public to the articles emphasised the important role that a poison centre can play in not only giving advice on the effect of spider bites, but also to educate the public that most spiders are not venomous and that they are rarely of concern to humans.

More than 50% of all the spider bite calls (1085 calls) were received from callers in the Western Cape. This was probably due to the fact that both centres are located in the Western Cape. As mentioned before, the presence of well-recognised spider bite expertise at the TPIC by health care professionals in the Western Cape could also have had an influence on most calls being received from the Western Cape. An interesting observation was the change in the distribution of the total number of spider bite calls during the study period. Prior to 2015 the number of calls from provinces outside of the Western Cape was less than the calls received from the Western Cape itself. During 2016 and 2017, the first two full years that the combined PIHWC was in operation, the number of spider bite calls from the provinces outside of the Western Cape showed a disproportionate increase compared to the number of calls from the Western Cape. The reason for this is probably the fact that most spider bite calls from the Western Cape had previously preferentially been made to the TPIC before the merger, whereas callers from other provinces might have been less aware of the TPIC spider bite expertise. Secondly, it is possible that the ongoing drought that was experienced in the Western Cape in 2016 and 2017 could have had an influence on the number of spiders and consequently spider bites. Thirdly, the 24-hour telephone number of the PIHWC was made available on many household products and insecticides in 2016 and 2017. This might have led to other provinces becoming aware of the existence of the PIHWC and caused an increase in the number of calls from other provinces. It will be interesting to see if this trend will continue.

Several findings in this current study support previous reports stated the following: (i) the majority of spider bites occur during the warmer months of the year, (ii) adults are affected more often than children, (iii) suspected spider bites occur more commonly in female than male patients or that females are more likely to call about suspected bites, and (iv) the majority of spider bites occur on the extremities.^{17,18,56,61} In South Africa the warmer months of the year are between September and May (spring to autumn). In

this current study the highest proportion of spider bites were recorded in January and February (mid-summer), normally the warmest months of the year.

Almost 60% of the spider bite calls were received from the general public compared to about 40% from health care providers. This shows how well the helpline has been advertised and that the expertise of the helpline consultants is regarded highly. It may also show a lack of trust in health care providers concerning suspected spider bites or the ignorance from the public wanting to believe that their condition was caused by a spider bite rather than another disease.

Based on multiple telephonic consultations it has been noted that a part of the general public can confidently identify button spiders, but that there is uncertainty and confusion regarding many other spiders. Callers would regularly be quite adamant that their skin lesion was caused either by a sac or a violin spider, even if these spiders were unlikely to occur in the geographical region from where the call was made. Patients were often concerned about the slow healing of their wounds and were looking for confirmation that they had received appropriate therapy. Previous articles alluded to the fact that humans attribute many skin lesions to spider bites and that might explain the concern and confusion among the public regarding spider bites.^{10,44}

By applying criteria like the development of a compatible clinical presentation and/or the identification of the implicated spider by a spider expert, only 11.3% of the suspected spider bite cases would have been identified as a definite bite, which is substantially less than the international trend of about 40% positively identified bites.^{56,58,59,63} It is, however an international trend that most spider bite cases are attributed to unknown spiders ($\geq 60\%$). The low number of positively identified spider bites may in part be due to the fact that many suspected bites are not caused by spiders and can be attributed to either a bite from another arthropod or a skin lesion with another aetiology.

Neurotoxic spider bites

In South Africa, most neurotoxic spider bites are due to black or brown button spiders. The clinical features are worse in the case of the black button spiders and include generalised muscle pain and cramps, chest pain, abdominal pain and rigidity, profuse sweating, anxiousness, raised blood pressure, rapid heart rate and difficulty in walking, constituting the clinical syndrome of latrodectism.^{2,4,22,29,48,64}

Almost 50% of the 284 recorded neurotoxic bites were positively identified. Identification was either made by a reliable and recognisable description of the spider, a definite photo identification, the clinical

presentation of the person or a good response to antivenom resulting in reversal of spider bite related neurotoxic symptoms. Both black and brown button spiders were included in the neurotoxic spider bites group. Almost a third (28.1%) of the neurotoxic bites required the administration of antivenom. Although it is not impossible that the antivenom may exert some placebo effect, the effect of the antivenom is highly impressive in positively identified cases. Based on extensive observation Muller et al⁶⁵ has postulated that a positive response to the antivenom in a person suffering from latrodectism can be used as a diagnostic tool for neurotoxic spider bites. By applying this postulate 31% of the neurotoxic bites could be regarded as definite button spider bites.⁶⁵ The other 18% of patients were either bitten by a brown button spiders or not enough venom was injected to cause toxicity. The other 50% of suspected neurotoxic bites were possibly misidentified by the caller, because there was uncertainty about the type of spider, the caller phoned from an area where button spiders are uncommon and there were no symptoms suggestive of latrodectism.

Bites from button spiders mostly occurred in the warmer months of the year, similar as what we see in literature.^{2,10}

Although *Latrodectus* bites usually become symptomatic within one hour after the bite,^{2,21,29} only 13% of neurotoxic spider bite calls were received within that short time frame. There are several explanations for this delay: (i) the time was recorded in only 65% of the calls, (ii) time spent to get to hospital for most patients, (iii) overcommitted hospital services or (iv) a combination of these. The same factors may have played a role in the delay of administering the antivenom. Only 30 of the 80 patients (37.5%) received antivenom within 12 hours of the bite. The longest delay was one week, but that happened because the symptoms were not originally recognised as those of latrodectism. Other reasons for the delay in administration of antivenom include patient being unaware of being bitten by a spider or symptoms not recognised as those of button spider envenomation resulting in misdiagnosis of another disease state. It is well known that latrodectism can mimic other disease states for example myocardial infarction (chest pain and sweating), acute abdomen (pain and abdominal muscle rigidity), alcohol withdrawal (sweating and tremor) and scorpionism. Muller and colleagues has witnessed and described several cases of misdiagnosis before he made the correct diagnosis of latrodectism.^{21,48,65}

The distribution map of spider bites recorded from 2013 to 2017 clearly shows the area in which button spider bites occur most frequently. Although sparsely populated, the area along the western coast of South Africa contributed the largest proportion of neurotoxic bites by the *Latrodectus* spp. corresponding with previously published distribution maps of *L. indistinctus*.^{21,24} Physicians and staff at medical

emergency facilities should be made aware of the possibility of *Latrodectus* bites and patients with possible neurotoxic bites should be observed for symptoms associated with latrodectism. The need for spider specific antivenom should be emphasized in medical facilities in this area. An algorithm for the diagnosis of neurotoxic spider bites should be made available to medical facilities in this area. A correct diagnosis can help to decrease the misdiagnosis of neurotoxic spider bites, as well as shorten the delay in treatment thus ensuring more rapid and effective treatment for the patient.

Cytotoxic spider bites

Swelling, redness and pain were the most common features of cytotoxic bites which is in keeping with previously published data.^{4,21} Although these are features of early necrotic arachnidism, they are non-specific and can be seen in a broad spectrum of other illnesses.^{11,66} Because spider bites are seldom witnessed and the non-specificity of the clinical features, it would be helpful to consider a new classification for the grading of aetiological certainty of cytotoxic spider bites.

There is little clinical or epidemiological data available on the bites of cytotoxic spiders found in South Africa. Poison centre data indicate that such bites are rare and therefore necrotic lesions caused by spider bites are probably rare. It is possible that patients may develop minor lesions that do not require medical attention and heal without complications and these cases are not captured in any medical publications.

Only 2.1% of bites recorded in the cytotoxic spider bite group were witnessed and positively identified. These included two sac spiders (*Cheiracanthium* spp.), two violin spiders (*Loxosceles* spp.) and one six-eyed sand spider. Although mostly found outside of houses, two species, *C. furculatum* and *L. parramae* have been introduced into households.^{12,29} Besides these five definite cases a further 26 reported cytotoxic bites were considered to be probable, based on the clinical description, the lack of an alternative diagnosis and the affected callers resided within endemic areas of sac spiders or violin spiders.¹² The distribution map of the cytotoxic spiders showed the low number of identified and probable cytotoxic spider bites. The low number of witnessed bites might be explained by the fact that both sac and violin spiders are nocturnal spiders. The assumption is that most patients were bitten while asleep and therefore did not witness the bite or were not able to collect the specimen.^{12,29}

Of the recorded cytotoxic bites 87.2% could not be positively diagnosed as spider bites. Reasons for this included spider bites being reported outside of endemic areas, the clinical picture being more compatible with another illness or incompatible with that of a spider bite.

Only one patient, who was bitten by a positively identified sac spider, experienced pain at the bite site, describing it as a burning sensation. Pain similar to a bee sting (or worse) following a sac spider bite has previously been described in the literature.^{5,41} Necrosis was not seen in the two recorded sac spider bite patients, but both calls were received within an hour of the bite and as there was no follow-up, it is not known if any further clinical signs developed. Necrosis has previously been described in sac spider bites, but this data was later queried by studies done in America and Australia.⁴¹

In the current study only one violin spider bite was recorded. Within the first 11 hours after the bite, the patient had not experienced pain or any other symptoms. This is in keeping with the literature, which suggested that pain is only seen later in the course of the violin spider bite when skin changes occur and necrosis develops.^{4,35} The second recorded violin spider bite (*Loxosceles* spp) occurred while the patient was working in the USA. The progression of the wound was similar to what is described in literature and ended in a necrotic wound.^{4,36} Antibiotics were prescribed and debridement executed before the lesion healed.

Systemic symptoms have not been noted with the *Loxosceles* spp found in South Africa.²¹ Newlands and Atkinson reasoned that it was due to South African violin spiders being smaller and less toxic than the *Loxosceles* spp found in the Americas and that the dose administered during a bite is therefore considerably lower.²² According to Vetter most patients bitten by the *Loxosceles* spp. will heal without need for medical intervention and that two-thirds of those that do develop necrosis will heal without further complications, leaving only a small number of patients with a long healing process and possible scar forming.⁶⁷

Bites by the *Sicarius* are not common and only one bite was positively identified during this study. The bite resulted in cytotoxic effects, which is in keeping with studies in rabbits, which showed necrotic effects.⁶⁸

Other spider bites

In the current study three other types of spiders were positively identified as causes of bites, namely baboon spiders, rain spiders and wolf spiders. We recorded 29 bites by baboon spiders (Family Theraphosidae) and 29 bites by rain spiders (Family Sparassidae, genus *Palystes*). These are large spiders that can inflict painful bites.²¹ Baboon spiders are known to be quite aggressive.²¹ The calls reporting the bites of these spiders were usually received within an hour of the bite, indicating that the caller actually

saw the bite and was concerned about possible risk of complications. The majority of these bites were on the hands and occurred while the caller was handling or relocating the implicated spiders. The family Theraphosidae includes the baboon spiders from Africa as well as the tarantulas found in the Americas. According to the literature the urticating hairs of the tarantulas can cause ophthalmologic injuries as well as contact skin reactions, but systemic reactions are not seen.^{2,10} No systemic effects have been reported in the case of the South African baboon or rain spider bites.^{21,69}

In our study the three confirmed cases of wolf spider bites (Family Lycosidae) resulted in pain, redness and swelling without the development of necrotic lesions which is in keeping with a report by Isbister and White.¹⁷ By contrast, earlier reports had speculated that bites from the wolf spiders can cause necrotic lesions, but to our knowledge these cases have not been verified.¹⁰

Unidentified spiders

Sixty-eight percent of suspected spider bites were recorded in the unidentified spider bite group. This is similar to what is experienced in poison centres in other parts of the world. Reports from other poison centres show the number of unidentified spider bites are usually about 60% of calls received regarding spider bites.^{56,58}

The high number of unidentified spider bite calls might be explained by Suchard's study.⁴⁴ He found that 70% of patients reporting a spider bite, never felt a bite or sting and that 'other spider' was a common answer to what they thought bit them. According to Russel and Gertsch, 80% of patients are rather bitten by another arthropod or the skin lesion is due to another disease state.⁴³

Swelling, redness and pain was the symptoms most often recorded with these unidentified spider bites, similar as was seen with the possible cytotoxic bites as well as the other spider bite group. This might indicate that these symptoms although seen with spider bites are not an indications of spider bites only. Therefore an alternative diagnosis should be also be considered.

Several other causes for skin lesions have been suggested. Skin and soft tissue infections have been found to often be the cause of skin lesions rather than a 'spider bite'. *Staphylococcus aureus* is a common cause of skin and soft tissue infections and is a likely option in skin infections.⁴⁴ It has been well documented that a range of other causes besides bacterial infections could be the reason for the skin lesions.^{10,21,51} These include fungal infections, viral causes, vascular ulcers, malignant carcinoma and diabetic ulcers. The concern is that more deadly diseases can be missed when an incorrect diagnosis of spider bite is

entertained. This can lead to a delay in a correct diagnosis, a prolonged period to recovery and be of serious consequences to the patients' health. A Swiss study showed a delay in patients seeking medical attention with unverified spider bites compared to verified bites. Patients in the unverified group suffered more severe symptoms in that redness and swelling were more prominent, pain was experienced for a longer period of time and these patients took longer to recover. This might indicate that these bites were probably caused by the bite of another arthropod or the result of another disease.⁷⁰ Although this was a very small study, it is still an interesting observations and demonstrates the importance of establishing a definitive diagnosis rather than a presumptive diagnosis of spider bite.

The approach to the diagnosis of a necrotic ulcer of unknown aetiology should include one or more of the following: (i) establishing if a bite has been witnessed, (ii) undertaking a thorough clinical evaluation considering the duration and time of progression of the wound, as well as various aetiologies including infections, malignant processes, underlying diseases like diabetes, rheumatological diseases and hypercoagulability states, (iii) investigations including skin biopsy, bacterial and fungal cultures and other laboratory tests, (iv) treatment including wound management, and (v) follow-up and monitoring.⁷¹ The approach needs to be relevant to the specific presentation, practically possible and financially affordable. The most important part should be the clinical history and examination. Wound care is very important irrespective of the aetiology and the importance of regular follow-up should be emphasized to the patient.

Case studies

Spiders play a unique role in human society. They do not only involve fields such as medicine and arachnology, but also psychology, mythology and journalism.⁶² During the Middle Ages it was believed that spiders were responsible for devastating illnesses and epidemics such as the Great Plague.⁷² Several articles in the literature allude to the fact that there are several causes for dermal necrosis beside cytotoxic spider bites.^{11,21,51}

The only confirmed spider bite in this case series was by a sac spider described in case 4.6.1. The burning sensation experienced in case 4.6.1 is in contrast to what previous literature on South African sac spider bites suggests, but in agreement with the international literature where the bite is described as painful and similar to a bee sting.^{5,10,11,41} Unlike a previous study by Newlands *et al*⁴², our patient did not develop any necrosis in the area of the bite and this is in keeping with previous reports which stated that necrosis

is not seen with the bite of sac spiders.^{5,41,70} Using a rabbit model, Foradori *et al* were unable to produce necrotic lesions from the *Cheiracanthium* venom gland homogenate.³⁹

Cases 4.6.2 to 4.6.5 confirm the many misattributions to spider bites as the cause of necrotic skin lesions. Cellulitis, folliculitis, reaction to medications and atypical ulcers are just some of the medical conditions that can be misdiagnosed as necrotic arachnidism.^{11,21}

Although a spider was found in case 4.6.2, no bite by a spider was witnessed in any of the cases besides case 4.6.1. Not only was the patient in case 4.6.2 affected more than once, another member of the household was also showing similar symptoms. The literature suggests that re-occurring bites and bites to more than one family member is an indication that the lesion is probably not due to a spider bite and other causes should be considered. In our case an alternative diagnosis was made of bacterial folliculitis.^{4,36,67}

It is an interesting phenomenon that patients often refer to undiagnosed skin lesions as spider bites and at times insist on diagnosis even after receiving a medical opinion suggesting an alternative diagnosis as demonstrated by the majority of our case studies. In spite of a definitive alternative diagnosis and very little evidence in favour of a spider bite the majority of the five patients preferred the spider bite diagnosis and could not be convinced completely that they were not victims of an arachnid attack. This phenomenon is not new and has often been observed and described in literature.¹¹ Many authors suggest that it is probably due to the fear of spiders. Spiders are known for their preying nature, which is extended to humans. For humans it is easier to blame the spider for their cause of illness than a potentially worse scenario.^{11,44,67} Vetter and colleagues put it as: ‘patients find it oddly comforting to blame a familiar external aetiology of perceived danger and have difficulty accepting endogenous disease states for their afflictions.’¹¹ During the last couple of decades different spiders have been blamed for various skin ulcers, the so-called modern day myth.⁷³ An example is the perception that ‘daddy long-legs’ spiders are the most poisonous spiders in the world. In addition, there is a widespread belief that many different spiders can cause necrosis, even if there is absolutely no clinical evidence.⁷³

It has also been suggested that humans like to have an easily understandable name or term for the cause of their illness. So ‘spider bite’ has become a simple and short way to describe certain skin lesions of unknown origin. Spider bite is clearly much simpler than, for example, ‘leukocytoclastic vasculitis due to ANCA-positive microscopic polyangiitis’. Suchard⁴⁴ pointed out that the term ‘spider bite’ is not only used as a collective name for a bite by arachnids, but may also include bites by other arthropods. Spiders

are commonly found and easily recognizable and it easier to blame something that can be seen as a cause of the illness compared to a bacteria or fungal organism that cannot be seen.⁶⁷

Healthcare professionals also contribute to the inappropriate diagnosis and misperceptions concerning spider bites.^{44,66,73} Patients put their faith in their physicians. Our case 4.6.5 is a typical example of this, where the patient was told that tests confirmed his condition as that of a violin spider bite. This reflects very poorly on the physician, who failed to generate an adequate differential diagnosis. Suchard explains it as follows: ‘the primary purpose in diagnosing a “spider bite” seems to be simply to provide a tangible and remotely plausible label for and otherwise unexplained condition.’⁴⁴ It is uncertain what tests were performed, but no test for the confirmation of spider bite exist commercially, either in South Africa or other parts of the world.^{74,75} There might have been a reluctance in requesting too many tests due to cost restraints, but Vetter suggests that this type of behaviour might be due to a lack in training or physicians not actively pursuing the cause of the necrosis. The physician might have fallen into the trap of accepting the belief that many skin lesions are caused by spider bites without any real evidence.⁶⁷

Possible explanations for the misdiagnosis of spider bites

A lack of understanding or the will to establish a definitive diagnosis might explain the misdiagnosis of spider bites by medical practitioners. Some of the explanations include:

1. Physicians do not know much about spiders and are generally not able to identify spiders.
2. Physicians are not adequately trained to diagnose spider bites and cannot recognise the clinical picture of latrodectism or cytotoxic spider bites.
3. Articles appearing in medical journals regarding spider bites, mostly rely on circumstantial evidence with no real proof of an actual bite by a spider. These inaccurate articles may get cited repeatedly until the source of the information becomes obscured and false information is accepted as scientifically sound.⁴¹

Suggested categories for the diagnosis of spider bites

In 2006 Vetter and Furbee suggested that poison centre data were not reliable with regards to the recording of spider bite calls. They pointed out that data for spider bites are rather an interpretation of the callers report than a precise analysis.⁷⁶ Our study has demonstrated that the recording of spider bite calls is largely inaccurate and that the data collected is difficult to interpret with regards to ‘real diagnosis’ and consequently not very helpful to understand the epidemiology and clinical features of cytotoxic spider bites. In terms of data collection we would like to propose the following classification process:

- (i) Start with differentiating between neurotoxic spider bites and cytotoxic spider bites based on clinical picture and / or identification of spider;
- (ii) In the neurotoxic group try to differentiate between black and brown button spiders
- (iii) In case of cytotoxic bites these should be further classified into ‘definite bite’, ‘probable bite’, or ‘unlikely bite’ categories.

The category ‘Definite bites’ should include the following:

- (i) Bite witnessed,
- (ii) Spider identified or presumed spider needs to be endemic to the area,
- (iii) Patients experiencing symptoms that are compatible with the type of spider that bit them.

The category ‘Probable bites’ should include the following:

- (i) A spider found or seen in the vicinity of where the patient was bitten,
- (ii) Suspected (or reported) spider should be endemic to the area where the bite occurred, and
- (iii) The lesions should be typical of the type of spider that allegedly bit the patient.

The category ‘Unlikely bites’ should include the following:

- (i) No spider was seen and alleged bite occurred outside the endemic area for the suspected spider,
- (ii) Clinical picture and time course atypical of any spider bite, or
- (iii) Alternative more likely diagnosis.

Using these categories as a tool to making a diagnosis of a spider bite and for capturing ‘spider bite calls’ on a PIC help line it is of utmost importance to consider whether an alleged spider is endemic to the area where the suspected ‘spider bite’ occurred. If a spider is not known to be found in a certain area, other diagnosis should rather be taken in consideration. It would thus be of value to make spider distribution

maps more readily available and ensure that these would be updated on a regular basis. It is also important to train doctors to improve their knowledge about spiders and the clinical syndromes caused by spider bites, either necrotic arachnidism or latrodectism.

Unique circumstances or locations are often characteristic of a specific spider family or genus. The bites of a specific species or family usually cause characteristic clinical effects.¹⁷ This collective information is vital in the assessment of the patient, establishing the correct diagnosis and deciding on the most appropriate treatment options for the bitten patient.

Diagnostic algorithm

A diagnostic algorithm (decision tree) can assist with spider identification based on the circumstances of the bite and the initial clinical effects. Following identification, decisions on diagnosis and management of spider bites causing severe envenomation can be made more rapidly and effectively. Early identification will direct health care resources to the more severe cases.⁷⁷

According to a study of 371 confirmed spider bites in Australia, there is an association between the type of spider, the circumstances of the bite and the clinical effects of the bite. Useful information about seasonal and geographical differences can be learned by gathering data. A study in tropical Australia show seasonal differences as well as differences in species of spiders involved.⁷⁸ Unique circumstances or locations are often characteristic of a specific spider family or genus. The bites of a specific species or family usually cause characteristic clinical effects.¹⁷

Diagnostic algorithms are used to improve outcomes and to institute more effective and safe treatment options as well as optimising hospital resources.⁷⁷ In a poison information centre the use of an algorithm can help to reduce the number of patients seeking medical attention at a medical facility. In an emergency department setting, an algorithm can help to identify which patients need observation and treatment. An algorithm can also aid physicians in the diagnosis and treatment of spider bites.⁷⁷

We would like to suggest a diagnostic algorithm for spider bites in South Africa as demonstrated in Figure 5.1.

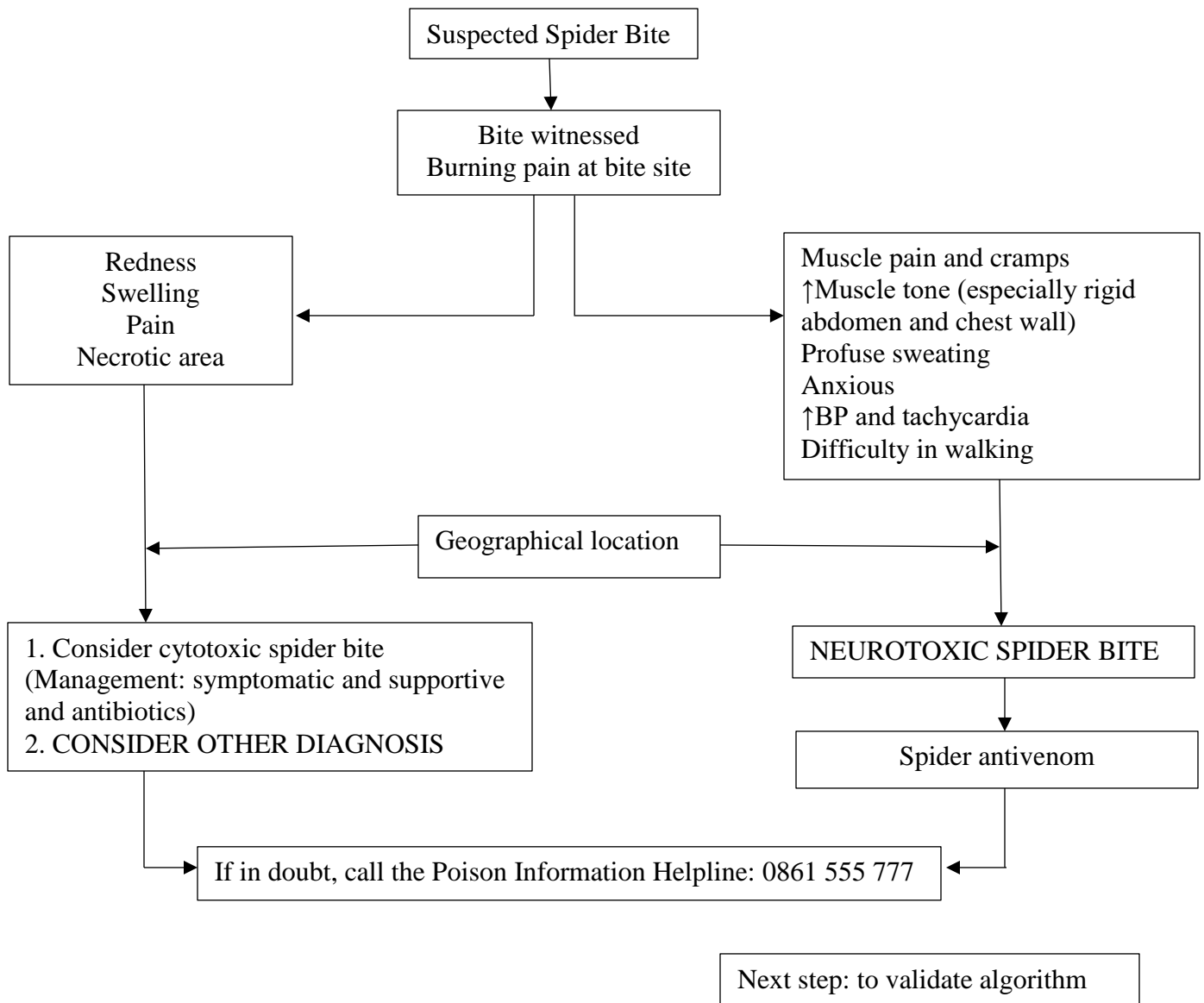


Figure 5.1 Suggested algorithm for suspected spider bites in South Africa

Suggestions for the future

As with other phobias, these will not vanish and there will always be a fear of spiders and they will be blamed for different illnesses or diseases. It is, therefore of importance to gain better understanding of spider bites by prospectively collecting data and to disseminate this information thereby dispelling misinformation regarding spider bites. Prospective data can strengthen and expand the proposed algorithm from this study. Distinguishing features like seasonal variations should be added to the algorithm for this can help with early identification.

The algorithm for suspected spider bites should be introduced into emergency departments for early identification and diagnosis of spider bites. The second step would be to validate the algorithm against symptoms experienced by patients to see if it is effective, practical and useful.

Development and progression of skin lesions should be monitored to differentiate between a wound caused by the bite of cytotoxic spiders and skin lesions caused by other aetiologies. Cases of probable cytotoxic bites should be followed-up over a period of time and the data should be prospectively collected for analysis. We suggest a standardised case report form for spider bites in South Africa (see Appendices) that will support the diagnostic process and at the same time serve as a data collecting tool. We believe that it will assist especially with regards to the accurate diagnosis of necrotic skin lesions and thereby result in more accurate statistics of necrotic arachnidism. Although the course of neurotoxic spider bite effects is fairly well established in the South African context, the claim from other parts of the world is that antivenom is not the most effective treatment option.⁴ Cases in which antivenom was administered should be followed to firstly establish the efficacy of the antivenom and secondly to monitor and establish the frequency of adverse effects and anaphylactic reactions.

Limitations of the study

This is a retrospective study that used data from a database and consultation forms. The recorded data is at times incomplete and lacking accuracy. For this study incomplete cases were not excluded, instead, the specific missing variable was indicated as unknown.

Spider bites were recorded as they were reported by the caller according opinion on what type of spider was involved. This will invariably have resulted in some erroneous and inaccurate data concerning the diagnosis of specific spider bites.

Since the TPIC and PIHWC are located and well known in the Western Cape, it is very likely that the higher proportion of calls from the Western Cape does not necessarily mean that there is a higher frequency of spider bites in the province compared to the other eight provinces and it would be unwise to interpret the call data as a true reflection of the real distribution and the incidence of spider bites in the rest of South Africa. Poison centres are only utilized for information by healthcare professionals and the general public and are not in any way set up to do epidemiological research on spider bites.

Conclusion

Although many spider species exist and is often found in and around houses, only a few are of medical importance and it is unlikely that the majority of suspected spider bites will cause severe effects. The clinical features of the button spiders are well described. Physicians should be able to recognise the clinical syndrome of latrodectism. In South Africa the antivenom against button spiders is effective and when indicated it should be administered without delay.

The suggested diagnostic categories as well as the algorithm for suspected spider bites should be taken into consideration when making the diagnosis of a spider bite.

The PIHWC, being a well-known unit for biological toxins continues to play an important role in providing reliable information to both medical professionals and the public; firstly to reassure the patient and secondly to prevent the over-use of medical facilities. A poison centre also plays an important role in gathering information on suspected spider bites and should be involved in a prospective study on the usefulness of the case report forms for spider bites in South Africa.

Browning noted more than 100 years ago: 'Not infrequently a person discovers a local inflammation which cannot be accounted for in a satisfactory manner, and will say the utmost confidence that it is a 'spider bite', when closer questioning will develop the fact that he does not know what caused the condition, but because it has the appearance of a sting or bite and it is not known what else it could have been, believes it is a spider bite'.⁷⁹

References

1. Filmer MR. Filmer's Spiders, An Identification Guide for Southern Africa. Second edi. Struik Nature; 1991.
2. Rahmani F, Mahdi S, Khojasteh B, Bakhtavar HE, Rahmani F, Nia KS, et al. Poisonous Spiders: Bites, Symptoms, and Treatment; an Educational Review. *Emergency* [Internet]. 2014;2(2):54–8. Available from: www.jemerg.com
3. World Spider Catalog. World Spider Catalog Version 18.0. online at <http://wsc.nmbe.ch>. 2017.
4. Isbister GK, Fan HW. Spider bite. *Lancet*. 2011;378(9808):2039–47.
5. Varl T, Grenc D, Kostanjšek R, Brvar M. Yellow sac spider (*Cheiracanthium punctorium*) bites in Slovenia: case series and review. *Wien Klin Wochenschr*. 2017;129(17–18):630–3.
6. Emtsov V, Ostapenko Y, Larionov S. Unusual cases of the spider *Cheiracanthium punctorium* biting in Volgograd Region, Russia. *Toxicon*. 2012;60(2):228–9.
7. Newlands G, Atkinson P. Behavioural and epidemiological considerations pertaining to necrotic araneism in southern Africa. *South African Med J*. 1990;77:92–5.
8. Jocqué R, Baert L, Smedt P De, Bosselaers J, Souffreau J, Henrard A, et al. An Introductory Study of House Spiders (Araneae) in Belgium. *Arachnology*. 2016;17(3):129–36.
9. Dippenaar-Schoeman A, Lotz L. Spiders in and around the house. *SANSA news*. 2017;5.
10. Vetter RS, Isbister GK. Medical Aspects of Spider Bites. *Annu Rev Entomol* [Internet]. 2008;53(1):409–29. Available from: <http://www.annualreviews.org/doi/10.1146/annurev.ento.53.103106.093503>
11. Vetter RS, Swanson DL. Approach to the patient with a suspected spider bite: an overview [Internet]. UpToDate. 2017. Available from: <https://www.uptodate.com/contents/search>
12. Dippenaar-Schoeman A. Field Guide to the Spiders of South Africa. LAPA Publishers; 2014. 14-23 p.
13. Muller G, Koch H, Kriegler A, Van der Walt B, Van Jaarsveld P. The relative toxicity and polypeptide composition of the venom of two South African widow spider species: *Latrodectus indistinctus* and *Latrodectus geometricus*. *S Afr J Sci*. 1989;85:44–6.
14. Muller G, Kriegler A, Van Zyl J, Van der Walt B, Dippenaar-Schoeman A, Van Jaarsveld P. Comparison of the toxicity, neurotransmitter releasing potency and polypeptide composition of the venoms from *Steatoda foravae*, *Latrodectus indistinctus* and *L. geometricus* (Araneae: Theridiidae). *S Afr J Sci*. 1992;88:113–6.
15. Saez NJ, Senff S, Jensen JE, Er SY, Herzig V, Rash LD, et al. Spider-venom peptides as therapeutics. *Toxins (Basel)*. 2010;2(12):2851–71.
16. Stuber M, Nentwig W. How informative are case studies of spider bites in the medical literature? *Toxicon*. 2016;114:40–4.
17. Isbister GK, White J. Clinical consequences of spider bites: Recent advances in our understanding. *Toxicon*. 2004;43(5):477–92.

18. Isbister GK, Gray MR. A prospective study of 750 definite spider bites, with expert spider identification. *QJM*. 2002;95:723–31.
19. Finlayson M. *Harpactirella lightfooti* as a cause of spider bite in the union. *South African Med J*. 1939;13(24):808–9.
20. Haddad C. Symptoms of the bite of an Orb-web spider *Araneus apricus* (Araneae: Araneidae). *SAMJ*. 2002;92(7):528–9.
21. Muller GJ, Wium CA, Marks CJ, du Plessis CE, Veale DJH. Spider bite in southern Africa: diagnosis and management. *Contin Med Educ*. 2012;30(10):382–91.
22. Newlands G, Atkinson P. Review of southern African spiders of medical importance, with notes on the signs and symptoms of envenomation. *South African Med J*. 1988;73:235–9.
23. Lotz LN. Revision of the genus *Latrodectus* (Araneae: Theridiidae) in Africa. *Navorsing van die Nas Museum*. 1994;10(1):27–56.
24. Dippenaar-Schoeman A, Haddad C, Foord S, Lyle R, Lotz L, Helberg L, et al. First Atlas of the Spiders of South Africa [Internet]. 2010. Available from: <http://www.arc.agric.za/arc-ppri/Documents/5.SPIDERATLASFAMILIESSPAZOR.pdf>
25. Yan S, Wang X. Recent advances in research on widow spider venoms and toxins. *Toxins (Basel)*. 2015;7(12):5055–67.
26. Dippenaar-Schoeman A, Haddad C, Foord S, Lyle R, Lotz L, Helberg L, et al. First atlas of the Spiders of South Africa [Internet]. 2010. Available from: <http://www.arc.agric.za/arc-ppri/Documents/3.SPIDERATLASFAMILIESMICPHY.pdf>
27. Lotz LN. The Genus *Cheiracanthium* (Araneae : Miturgidae) in the Afrotropical Region . 1 Revision of Known species. *Navorsing Van Die Nas Museum Bloemfontein*. 2007;23:1–76.
28. Lotz L. The genus *Cheiracanthium* (Araneae: Miturgidae) in the Afrotropical region. 2. Description of new species. *Navorsing van die Nas Museum Bloemfontein*. 2007;23:145–84.
29. Snyman C, Larsen N. Spider bite and its treatment in southern Africa. *Occup Heal SA [Internet]*. 2005;11(2):22–6. Available from: <http://www.occhealth.co.za/?/issue/155>
30. Bosselaers J. An alien in the grapes : a potentially aggressive African spider imported into Belgium . *Nieuwsbr Belg Arachnol Ver*. 2013;28:22–8.
31. Lotz LN. An update on the spider genus *Loxosceles* (Araneae: Sicariidae) in the Afrotropical region, with description of seven new species. *Zootaxa*. 2017;4341(4):475–94.
32. Coetzee M, Dippenaar-Schoeman A, Frean J, Hunt R. First report of clinical presentation of a bite by a running spider, *Philodromus* sp. (Araneae: Philodromidae), with recommendations for spider bite management. *SAMJ*. 2017;107(7):576–7.
33. Gremski LH, Trevisan-Silva D, Ferrer VP, Matsubara FH, Meissner GO, Wille ACM, et al. Recent advances in the understanding of brown spider venoms: From the biology of spiders to the molecular mechanisms of toxins. *Toxicon*. 2014;83:91–120.
34. Barbaro KC, Lira MS, Araújo CA, Pareja-Santos A, Távora BCLF, Prezotto-Neto JP, et al. Inflammatory mediators generated at the site of inoculation of *Loxosceles gaucho* spider venom. *Toxicon*. 2010;56(6):972–9.

35. Nentwig W, Pantini P, Vetter RS. Distribution and medical aspects of *Loxosceles rufescens*, one of the most invasive spiders of the world (Araneae: Sicariidae). *Toxicon*. 2017;132:19–28.
36. Swanson DL, Vetter RS. Loxoscelism. *Clin Dermatol*. 2006;24(3):213–21.
37. Newlands G, Isaacson C, Martindale C. Loxoscelism in the Transvaal, South Africa. *Trans R Soc Trop Med Hyg*. 1982;76(5):610–5.
38. Vassilevski AA, Fedorova IM, Maleeva EE, Korolkova Y V., Efimova SS, Samsonova O V., et al. Novel class of spider toxin: Active principle from the yellow sac spider *Cheiracanthium punctorium* venom is a unique two-domain polypeptide. *J Biol Chem*. 2010;285(42):32293–302.
39. Foradori MJ, Smith SC, Smith E, Wells RE. Survey for potentially necrotizing spider venoms, with special emphasis on *Cheiracanthium mildei*. *Comp Biochem Physiol - C Toxicol Pharmacol*. 2005;141(1):32–9.
40. Papini R. Documented bites by a yellow sac spider (*Cheiracanthium punctorium*) in Italy: a case report. *J Venom Anim Toxins Incl Trop Dis* [Internet]. 2012;18(3):349–54. Available from: http://www.scielo.br/scielo.php?script=sci_arttext&pid=S1678-91992012000300014&lng=en&nrm=iso&tlng=en
41. Vetter RS, Isbister GK, Bush SP, Boutin LJ. Verified bites by yellow sac spiders (genus *Cheiracanthium*) in the United States and Australia: Where is the necrosis? *Am J Trop Med Hyg*. 2006;74(6):1043–8.
42. Newlands G, Martindale C, Berson S, Rippey J. Cutaneous Necrosis Caused by the Bite of *Chiracanthium* Spiders. *South African Med J*. 1980;57:171–3.
43. Russell FE, Gertsch WJ. Letter to the editor. *Toxicon*. 1983;21(3):337–9.
44. Suchard JR. “Spider bite” lesions are usually diagnosed as skin and soft-tissue infections. *J Emerg Med*. 2011;41:473–81.
45. Ryan N, Buckley N, Graudins A. Treatments for Latrodectism—A Systematic Review on Their Clinical Effectiveness. *Toxins (Basel)* [Internet]. 2017;9(4):148. Available from: <http://www.mdpi.com/2072-6651/9/4/148>
46. Garb JE, Hayashi CY. Molecular evolution of α -latrotoxin, the exceptionally potent vertebrate neurotoxin in black widow spider venom. *Mol Biol Evol*. 2013;30(5):999–1014.
47. Ushkaryov YA, Volynski KE, Ashton AC. The multiple actions of black widow spider toxins and their selective use in neurosecretion studies. *Toxicon*. 2004;43:527–42.
48. Muller G. Black and brown widow spider bites in South Africa. A series of 45 cases. *SAMJ*. 1993;83:399–405.
49. SAIMR Spider Antivenom Package Insert. 2004.
50. Isbister GK. Antivenom efficacy or effectiveness: The Australian experience. *Toxicology*. 2010;268(3):148–54.
51. Diaz JH, Leblanc KE. Common spider bites. *Am Fam Physician*. 2007;75(6):869–73.
52. Braitberg G, Segal L. Spider bites: Assessment and management. *Aust Fam Physician*. 2009;38(11):862–7.

53. Dart RC, Bogdan G, Heard K, Bartelson BB, Garcia-Ubbelohde W, Bush S, et al. A randomized, double-blind, placebo-controlled trial of a highly purified equine F(ab)₂ antibody black widow spider antivenom. *Ann Emerg Med*. 2013;61(4):458–67.
54. Isbister GK, O’Leary M, Miller M, Brown SGA, Ramasamy S, James R, et al. A comparison of serum antivenom concentrations after intravenous and intramuscular administration of redback (widow) spider antivenom. *Br J Clin Pharmacol*. 2008;65(1):139–43.
55. Isbister GK, Page CB, Buckley NA, Fatovich DM, Pascu O, MacDonald SPJ, et al. Randomized controlled trial of intravenous antivenom versus placebo for latrodectism: The second redback antivenom evaluation (RAVE-II) study. *Ann Emerg Med* [Internet]. 2014;64(6):620–8. Available from: <http://dx.doi.org/10.1016/j.annemergmed.2014.06.006>
56. Forrester MB, Stanley SK. Epidemiology of spider bites in Texas, 1998-2002. *Public Health*. 2004;118(7):506–7.
57. New South Wales Poisons Information Centre. 2013 annual report (Internet). Available from: https://www.poisonsinfo.nsw.gov.au/site/files/ul/data_text12/4918535-NSWPIC_Annual_Report_2013.pdf [Internet]. 2013. Available from: https://www.poisonsinfo.nsw.gov.au/site/files/ul/data_text12/4918535-NSWPIC_Annual_Report_2013.pdf
58. V ICTORIAN P OISONS I NFORMATION C ENTRE ANNUAL REPORT 2016 Victorian Poisons Information Centre [Internet]. 2016. p. 1–34. Available from: http://www.austin.org.au/Assets/Files/VPIC_Annual_Report_2016.pdf
59. Mowry JB, Spyker DA, Brooks DE, Zimmerman A, Schauben JL. 2015 Annual Report of the American Association of Poison Control Centers’ National Poison Data System (NPDS): 33rd Annual Report. *Clin Toxicol* [Internet]. 2016;54(10):924–1109. Available from: <https://www.tandfonline.com/doi/full/10.1080/15563650.2016.1245421>
60. Mohamed F, Eley B, Roberts JC, Balme KH, Curling L, Stephen C. A 4-year analysis of calls answered by the staff at Red Cross War Memorial Children’s Hospital (RCWMCH) Poisons Information Centre (PIC) in South Africa. *Clin Toxicol*. 2016;54(4):457.
61. Cesaretli Y, Ozkan O. A clinical and epidemiological study on spider bites in Turkey. *Asian Pac J Trop Med*. 2011;4(2):159–62.
62. Du Plessis CE, van Hoving DJ, Wium CA. Pattern of spider bites and the influence of media reports of spider bites on calls received at the Tygerberg Poison Information Centre, South Africa. *Toxicol Int*. 2016;23(2):164–9.
63. Bentur Y, Lurie Y, Cahana A, Kovler N, Bloom-Krasik A, Gurevych B, et al. Poisoning in Israel: Annual report of the Israel poison information center, 2012. *Isr Med Assoc J*. 2014;16:686–92.
64. Clark RF, Wethern-Kestner S, Vance M V., Gerkin R. Clinical presentation and treatment of black widow spider envenomation: A review of 163 cases. *Ann Emerg Med*. 1992;21(7):782–7.
65. Muller G, Marks C, du Plessis C, Wium C. The efficacy and safety of the South African black widow spider antivenom. In: *First Conference of Biomedical and Natural Sciences and Therapeutics*. 2018. p. 124.
66. Benoit R, Suchard JR. *Necrotic Skin Lesions: Spider Bite-or Something Else?* Consultant.

2006;46(12):1386–94.

67. Vetter RS. Spiders of the genus *Loxosceles* (Araneae, Sicariidae): a review of biological, medical and psychological aspects regarding envenomations. *J Arachnol.* 2008;36:150–63.
68. Van Aswegen G, Van Rooyen JM, Van Der Nest DG, Veldman FJ, De Villiers TH, Oberholzer G. Venom of a six-eyed crab spider, *Sicarius testaceus* (Purcell, 1908), causes necrotic and haemorrhagic lesions in the rabbit. *Toxicon.* 1997;35(7):1149–52.
69. Newlands G, Martindale C. Wandering spider bite - much ado about nothing. *SAMJ.* 1981;60:142–3.
70. Gnädinger M, Nentwig W, Fuchs J, Ceschi A. Swiss prospective study on spider bites. *Swiss Med Wkly.* 2013;143:1–12.
71. Isbister GK, White J, Currie BJ, Bush SP, Vetter RS, Warrell DA. Spider bites: Addressing mythology and poor evidence. *Am J Trop Med Hyg.* 2005;72(4):361–7.
72. Davey GCL. The “Disgusting” Spider: The Role of Disease and Illness in the Perpetuation of Fear of Spiders. *Soc Anim.* 1994 Jan 1;2(1):17–25.
73. Isbister GK. Necrotic arachnidism: the mythology of a modern plague. *Lancet* [Internet]. 2004;364(9433):549–53. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/15302201>
74. Sulaj Z, Vyshka G, Gashi A. Analysis of cases caused by acute spider bite. *J Acute Dis* [Internet]. 2015;4(3):255–8. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S2221618915000414>
75. Nentwig W, Gnädinger M, Fuchs J, Ceschi A. A two year study of verified spider bites in Switzerland and a review of the European spider bite literature. *Toxicon.* 2013;73:104–10.
76. Vetter RS, Furbee RB. Caveats in interpreting poison control centre data in spider bite epidemiology studies. *Public Health.* 2006;120:179–81.
77. Isbister GK, Sibbritt D. Developing a decision tree algorithm for the diagnosis of suspected spider bites. *Emerg Med Australas EMA* [Internet]. 2004;16(2):161–6. Available from: <http://ezproxy.library.uvic.ca/login?url=http://search.ebscohost.com/login.aspx?direct=true&db=mnh&AN=15239733&site=ehost-live&scope=site>
78. Isbister GK. Data collection in clinical toxinology: Debunking myths and developing diagnostic algorithms. *J Toxicol - Clin Toxicol.* 2002;40(3):231–7.
79. Browning CC. Original investigations of spider bites in Southern California. *South Calif Pr.* 1901;16:291–300.

Appendices

SPIDER BITE: Neurotoxic (widow spider) and cytotoxic (e.g. sac and violin) spiders - Patient case report form

Please fill in available and applicable data and send to: email: toxicology@sun.ac.za; fax: +27219389860 or post: Tygerberg Poison Information Centre, Division of Clinical Pharmacology, PO Box 241, Cape Town, 8000.

CASE REPORTED BY			
Name:		Date:	
Phone numbers:	Cell:	Landline:	

PATIENT INFORMATION							
Name:		Age:		Gender		Tel	
Name of Hospital/Medical facility:							
Phone No.		Patient Hospital No.:					

SPIDERBITE INCIDENT	
Date & Time:	
Geographical location:	
Spider identified?: <input type="checkbox"/> YES <input type="checkbox"/> NO	Name of spider: Identified by: Specimen available? <input type="checkbox"/> YES <input type="checkbox"/> NO

Photos of the spider: <input type="checkbox"/> YES <input type="checkbox"/> NO	Please attach if available
--	----------------------------

CLINICAL FEATURES (SYMPTOMS AND SIGNS)

(More data may be entered under “additional comments” below to reflect the progression/resolution of the clinical condition).

LOCAL CLINICAL FEATURES		DATE	TIME
Restrictive local bandages applied/in situ	<input type="checkbox"/> YES <input type="checkbox"/> NO	Subcutaneous bleeding (ecchymosis):	<input type="checkbox"/> LOCAL <input type="checkbox"/> EXTENDING BEYOND BITE SITE
Tourniquet applied	<input type="checkbox"/> YES <input type="checkbox"/> NO	Local bleeding/oozing	<input type="checkbox"/> YES <input type="checkbox"/> NO
Bite site Part of body:	<input type="checkbox"/> VISIBLE <input type="checkbox"/> NOT VISIBLE	Ulceration Time to develop in days	<input type="checkbox"/> YES <input type="checkbox"/> NO
Pain	<input type="checkbox"/> YES <input type="checkbox"/> NO	Necrosis Time to develop in days	<input type="checkbox"/> YES <input type="checkbox"/> NO
Swelling Rapidly Spreading: Extent of swelling:	<input type="checkbox"/> ABSENT <input type="checkbox"/> MILD <input type="checkbox"/> MODERATE <input type="checkbox"/> SEVERE <input type="checkbox"/> YES <input type="checkbox"/> NO	Secondary infection and spreading cellulitis Time to develop in days	<input type="checkbox"/> YES <input type="checkbox"/> NO
Redness / Inflammatory reaction around the bite site	<input type="checkbox"/> YES <input type="checkbox"/> NO	Slow to heal over weeks Total time the ulceration and necrotic lesion is present	<input type="checkbox"/> YES <input type="checkbox"/> NO
Blisters	<input type="checkbox"/> YES <input type="checkbox"/> NO <input type="checkbox"/> CLEAR <input type="checkbox"/> BLOOD FILLED	Pain and swelling of regional lymph nodes	<input type="checkbox"/> YES <input type="checkbox"/> NO

Photos of the bite region: <input type="checkbox"/> YES <input type="checkbox"/> NO	Please attach if available, with dates when the pictures were taken
---	---

SYSTEMIC CLINICAL FEATURES, ESPECIALLY APPLICABLE TO NEUROTOXIC SPIDER BITES			
DATE		TIME	
General			
Nausea	<input type="checkbox"/> YES <input type="checkbox"/> NO	Headache	<input type="checkbox"/> YES <input type="checkbox"/> NO
Vomiting	<input type="checkbox"/> YES <input type="checkbox"/> NO	Temperature	
Blood pressure		Pulse rate	
Specific			
Pain and cramps:		Hyperactive stretch reflexes	<input type="checkbox"/> YES <input type="checkbox"/> NO
Abdomen	<input type="checkbox"/> YES <input type="checkbox"/> NO	Muscle fasciculation	<input type="checkbox"/> YES <input type="checkbox"/> NO
Upper legs	<input type="checkbox"/> YES <input type="checkbox"/> NO	Tremor	<input type="checkbox"/> YES <input type="checkbox"/> NO
Chest	<input type="checkbox"/> YES <input type="checkbox"/> NO	Trembling	<input type="checkbox"/> YES <input type="checkbox"/> NO
Girdle muscles	<input type="checkbox"/> YES <input type="checkbox"/> NO	Involuntary movements	<input type="checkbox"/> YES <input type="checkbox"/> NO
Abdominal rigidity	<input type="checkbox"/> YES <input type="checkbox"/> NO	Difficulty in speech	<input type="checkbox"/> YES <input type="checkbox"/> NO
General weakness	<input type="checkbox"/> YES <input type="checkbox"/> NO	Absent gag reflex	<input type="checkbox"/> YES <input type="checkbox"/> NO
Ataxia (incoordination / unsteadiness / wide based gait)	<input type="checkbox"/> YES <input type="checkbox"/> NO	Difficulty in swallowing	<input type="checkbox"/> YES <input type="checkbox"/> NO
General paraesthesiae (pins and needles)	<input type="checkbox"/> YES <input type="checkbox"/> NO	Droopy eyelids	<input type="checkbox"/> YES <input type="checkbox"/> NO
Hyperaesthesia/hyperalgesia (supersensitive skin)	<input type="checkbox"/> YES <input type="checkbox"/> NO	Visual disturbances	<input type="checkbox"/> YES <input type="checkbox"/> NO
Sweating	<input type="checkbox"/> YES <input type="checkbox"/> NO	Increased salivation	<input type="checkbox"/> YES <input type="checkbox"/> NO
Hyperactivity (in children)	<input type="checkbox"/> YES <input type="checkbox"/> NO	Upper respiratory secretions	<input type="checkbox"/> YES <input type="checkbox"/> NO
Abnormal behaviour (in children)	<input type="checkbox"/> YES <input type="checkbox"/> NO	Urinary retention	<input type="checkbox"/> YES <input type="checkbox"/> NO
Restlessness	<input type="checkbox"/> YES <input type="checkbox"/> NO	Penile erection (priapism)	<input type="checkbox"/> YES <input type="checkbox"/> NO
Agitation	<input type="checkbox"/> YES <input type="checkbox"/> NO	Airway obstruction	<input type="checkbox"/> YES <input type="checkbox"/> NO
Anxiety	<input type="checkbox"/> YES <input type="checkbox"/> NO	Difficulty in breathing	<input type="checkbox"/> YES <input type="checkbox"/> NO
Increased muscle tone	<input type="checkbox"/> YES <input type="checkbox"/> NO		

SPECIAL INVESTIGATIONS (where applicable and available) - initial and follow-up			
DATE		TIME	
Urinalysis			
Multistix (or similar “dipstix”) done	<input type="checkbox"/> YES <input type="checkbox"/> NO	Specify:	
Myoglobinuria	<input type="checkbox"/> YES <input type="checkbox"/> NO		
Blood and components:		DATE	
TIME			
Haemoglobin (Hb)	<i>g/dL</i>	Total Creatine Kinase (CK)	<i>IU/L</i>
White blood cell count	<i>X10⁹/L</i>	pH	
Erythrocyte sedimentation rate (ESR)		PCO ₂	<i>kPa</i>
		PO ₂	<i>kPa</i>
Urea	<i>mmol/L</i>	Act. bicarb	<i>mmol/L</i>
Electrolytes		Stand bicarb	<i>mmol/L</i>
Sodium	<i>mmol/L</i>	Base excess	<i>mmol/L</i>
Potassium	<i>mmol/L</i>	Base deficit	<i>mmol/L</i>
Chloride	<i>mmol/L</i>	O ₂ saturation	<i>%</i>
Total CO ₂	<i>mmol/L</i>		
Microbiological cultures and sensitivities of necrotic ulcers (cytotoxic bite)			
DATE		TIME	
Consult laboratory prior to collecting specimens so that appropriate material and transport conditions are used for unusual bacteria (e.g. Mycobacteria) fungi and yeasts (e.g. <i>S. schenkii</i>)			
Results:			
Chest radiography	<input type="checkbox"/> YES <input type="checkbox"/> NO	Date:	
	Results:		
Serological tests for rickettsial infection	<input type="checkbox"/> YES <input type="checkbox"/> NO	Date:	
	Results:		
Auto-immune profile and inflammatory response screenings, eg.	<input type="checkbox"/> YES <input type="checkbox"/> NO	Date:	
Antinuclear antibodies (ANA), antineutrophilic cytoplasmic antibodies (ANCA) and complement levels	Results:		
Histology: Biopsy of the edge of skin lesion(s)	<input type="checkbox"/> YES <input type="checkbox"/> NO	Date:	
	Results:		

TREATMENT		DATE	TIME
Local traditional healing treatments given/applied	<input type="checkbox"/> YES <input type="checkbox"/> NO Type:	Respiratory support/assisted ventilation Total time of respiratory support:	<input type="checkbox"/> YES <input type="checkbox"/> NO
Local bandages	<input type="checkbox"/> YES <input type="checkbox"/> NO		
Tourniquet applied	<input type="checkbox"/> YES <input type="checkbox"/> NO	Black widow spider anti-venom given: Dose Route Effectiveness Approximate time to reach peak effect Adverse reactions Allergic: Anaphylaxis: Treatment: Response to adverse reaction treatment:	<input type="checkbox"/> YES <input type="checkbox"/> NO
Pain medication	<input type="checkbox"/> YES <input type="checkbox"/> NO Type:		
Intravenous fluids	<input type="checkbox"/> YES <input type="checkbox"/> NO Specify:		
Antibiotics given	<input type="checkbox"/> YES <input type="checkbox"/> NO Specify:		
Local surgical interventions, e.g. removal of dead, damaged or infected material (debridement)	<input type="checkbox"/> YES <input type="checkbox"/> NO		
Skin graft	<input type="checkbox"/> YES <input type="checkbox"/> NO		
ADDITIONAL COMMENTS TO REFLECT PROGRESSION / EVOLUTION / RESOLUTION / OUTCOME OF THE CLINICAL CONDITION			