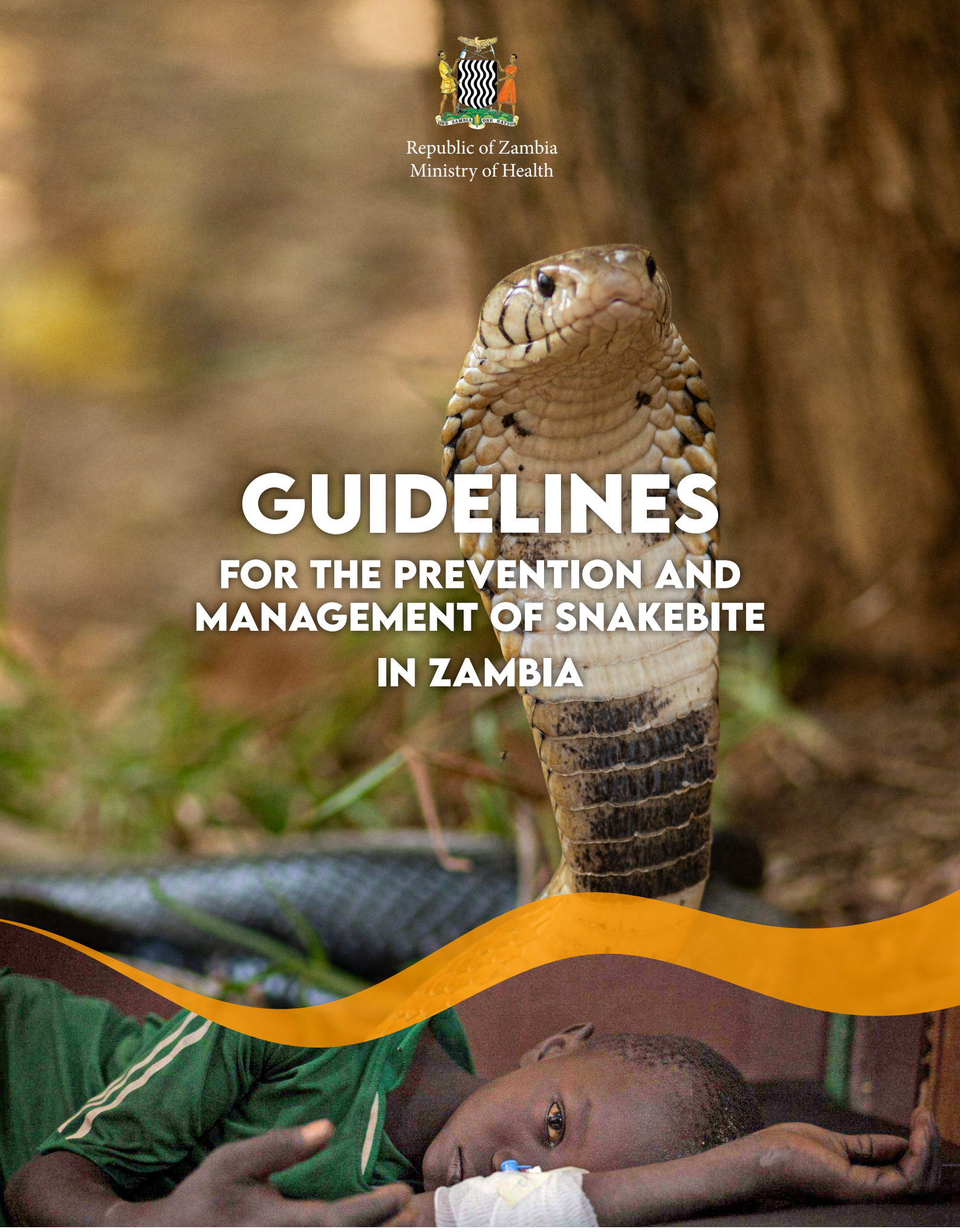
Republic of Zambia
Ministry of Health



GUIDELINES

FOR THE PREVENTION AND MANAGEMENT OF SNAKEBITE IN ZAMBIA

SNAKESAFETY ZAMBIA

TRIDENT FOUNDATION LTD

CONTENTS

FOREWORD

The Ministry of Health is pleased to introduce the **Guidelines for the Prevention of Snake Bites in Zambia**. Snake bites present a significant public health challenge, particularly in rural and remote areas, making it critical to establish standardized prevention and management strategies. This publication marks a key milestone in our commitment to strengthening health services for all Zambians, in line with our national drive toward Universal Health Coverage (UHC).

These guidelines provide healthcare professionals with evidence-based recommendations for both the prevention of snake bites and the effective management of cases. By implementing these guidelines, healthcare facilities can reduce the incidence and severity of snake bites, ultimately saving lives.

The development of these guidelines underscores our dedication to ensuring that every Zambian has access to quality healthcare, including emergency care. This resource is essential for healthcare providers, policymakers, and communities alike.

We strongly recommend that all health facilities across Zambia adopt these guidelines as a standard operating procedure. Together, we can lessen the burden of snake bites and advance the goal of a healthier and productive Zambia.

Dr. Elijah Muchima, MP

Honorable Minister of Health

PREFACE

Snakebite envenoming remains a critical, yet neglected, global health issue, with the World Health Organization (WHO) recognizing it as a "Highest Priority Neglected Tropical Disease" in 2017. Annually, millions of people suffer from snakebites, particularly in developing regions where healthcare access is limited. In sub-Saharan Africa, the true scale of snakebite cases is vastly underreported, and the socio-economic impact is profound, as it disproportionately affects rural, impoverished communities.

In Zambia, the situation mirrors regional trends, with thousands of cases recorded annually, though many go unreported. Rural areas are most affected, and healthcare facilities are often under-resourced and ill-equipped to manage snakebites effectively. This leads to preventable deaths, disabilities, and economic hardship.

To address this, the Guidelines for the Prevention and Management of Snakebite in Zambia were developed by adapting WHO's guidelines for Africa and incorporating recent advances in snakebite treatment. These guidelines aim to provide a practical framework for improving prevention, diagnosis, and treatment in Zambia, while advocating for the necessary resources and infrastructure to tackle this urgent public health issue.

ACKNOWLEDGMENTS

The Ministry of Health, Zambia, would like to express its sincere gratitude to all individuals and organizations who played a role in the successful development of the Guidelines for the Prevention and Management of Snakebite in Zambia. We are particularly thankful to the Trident Foundation Limited for their generous financial and technical support, which was instrumental in shaping the content and ensuring the evidence-based recommendations presented herein.

Special appreciation is extended to Marcel Van Driel from Snake Safety Zambia for the technical support and providing the imaging included in the guidelines for demonstrative purposes. Your efforts in guiding the stakeholders and ensuring timely completion were invaluable.

Finally, we acknowledge all the technical teams, experts, and partners whose insights and expertise enriched the final product. Your collaboration, dedication, and attention to detail are deeply appreciated.

Dr Kennedy Lishimpi

Permanent Secretary - Technical Services

Ministry of Health

ABBREVIATIONS

aPTT	Activated Partial Thromboplastin
ASV	Adaptive Support Ventilation
AV	Antivenom
BS	Bleeding Syndrome
Fab	Immunoglobine
F(ab')2	
FC	Receptors for antibody fragments
FDP	Fibronogen Degradation Product
FEV1	Forced Expiratory Volume
IgE	immunoglobine
IgG	Immunoglobine G
INR	International Normalisation Ratio
MAHA	Microangiopathies Haemolythic Anaemia
NSAID	Non-steroidal Anti-inflammatory Drugs
PLA2	Phospholipases A_2
PPSS	Painful Progressive Swelling Syndrome
PT	Prothrombin time
PWS	Progressive Weakness Syndrome
SIMV	Synchronised Intermittent Mandatory Ventilation
TMA	Thrombotic Microangiopathy
VICC	Venom-induced Consumptive Coagulopathy
20MWBCT	Twenty Minutes Whole Blood Clotting Test

1. INTRODUCTION

In 2017, The World Health Organisation recognised snakebite as one of the "*Highest Priority Neglected Tropical Diseases*". Its estimation is that annually, five-and-a-half million people get bitten by snakes worldwide (of which up to 2.7 million include envenoming) and that between 81,000 and 138,000 people die, resulting from snakebite. A much higher number than that survive with disabilities (estimated between 243,000 and 414,000), either through maiming and amputations or through neurological disabilities and brain damage. This makes snakebite a socio-economic problem as well as a health issue, especially in the developing world where most (dangerous) snakebite incidents occur and health facilities are usually ill equipped to treat snakebite.

In Sub-Saharan Africa, the number of estimated snakebite incidents that require medical attention are between 435,000 - 480,000. However, the WHO also estimates that in this region, 70% of all snakebite cases go unrecorded. This would mean that the number could be well over a million!

In an article published in the scientific journal Toxicon in 2019, the number of estimated snakebite cases in sub-Saharan Africa is 270,000 per year, with close to 15,000 amputations and 12,300 deaths. Add to this a large number of long-lasting disabilities from neurological disorders and a severe health issue in Africa is identified. Further, victims of snakebite can develop severe anxiety disorders from the suffered trauma. Finally, lost life or disabilities from snakebite often results in loss of income, making snakebite a significant socio-economic problem as well as a medical one.

The numbers show two things: snakebite is a serious health problem *and* there is no reliable, comprehensive data on snakebite cases for sub-Saharan Africa.

It should, finally, be noted that snakebite is predominantly a poverty related problem. The poor, especially in the rural areas, encounter snakes the most and they are furthest from adequate medical service providers. This, while safe and effective health care can significantly reduce the number of casualties and reduce the severity of long-lasting effects from snakebite.

In Zambia, the situation is reflective of that in other African countries. The records of the Ministry of Health show an annual average of 23,000 snakebite, with 36 recorded deaths. If applying the 70% of estimated under-recording (WHO), these numbers could be 76,670 bites and 120 deaths per year. The Ministerial records show no data on disabilities or other life-long afflictions.

A recently published study (Farooq et al, 2022) on the snakebite incidence numbers in a rural Province in Mozambique shows that bite numbers are 352.16 per 100.000 people in the research area, with 45.51 deadly bites. Extrapolating these numbers to Zambia's rural population would mean 36,519 bites per year with 4,719 deadly bites (Van Driel, 2022).

Besides the under-estimation of snakebite and related death numbers, there is no data on the true extend of the negative socio-economic impact. The reasons for under-reported snakebite cases are simple: a snakebite isn't always recognised or registered as such and victims often don't visit or reach a health facility.

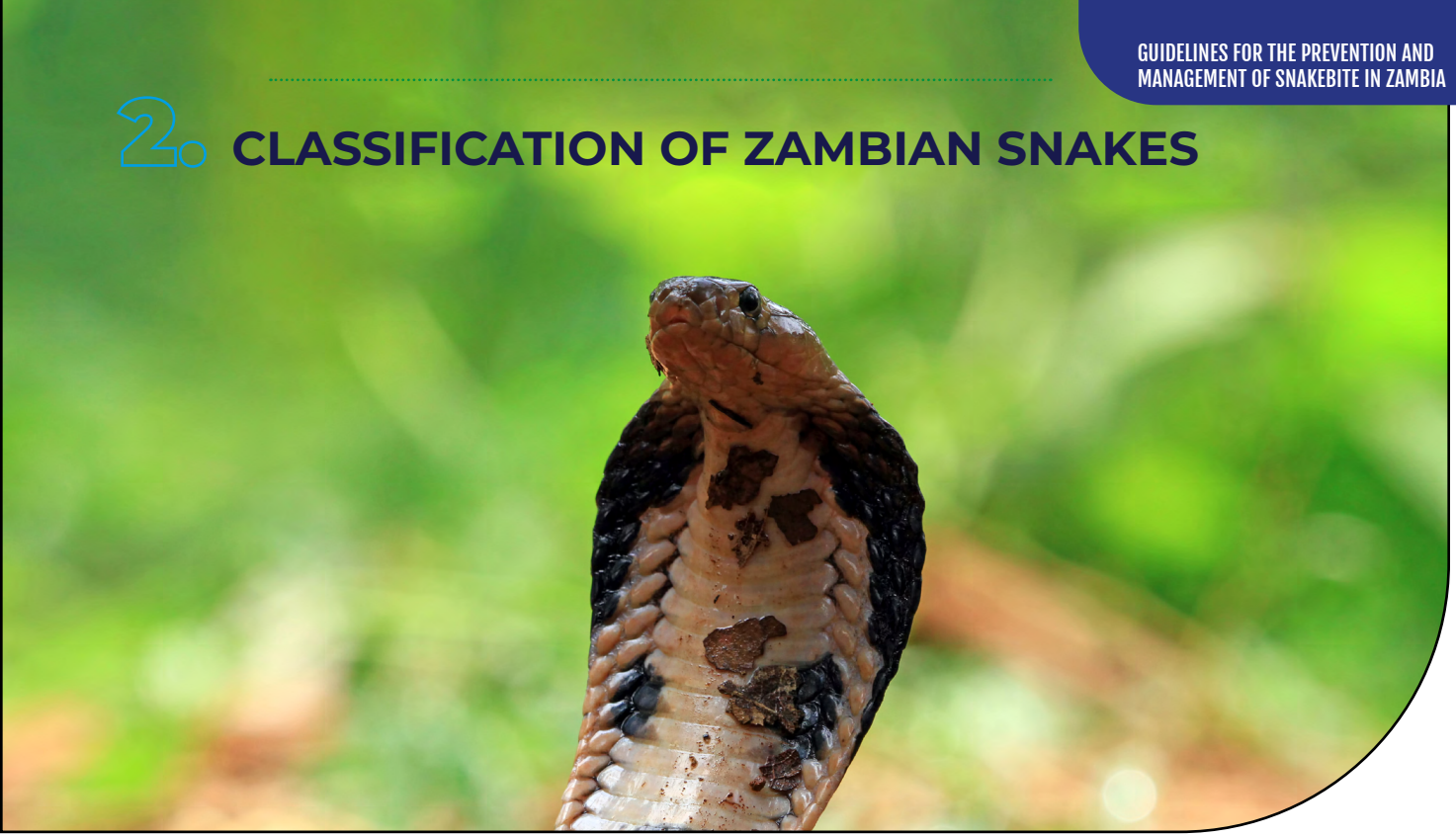
The majority of hospitals, clinics and other health facilities in Zambia are under-equipped, under-staffed and staff are not trained to deal with a snakebite effectively and safely. This situation is worse the closer a health facility is to the remote rural areas, where snakebite incidences are most prolific.

Properly capacitating all of Zambia's numerous health facilities in effective snakebite treatment is costly. It is a long-term strategy of training health staff and providing them with all necessary equipment and medication, which *must* be pursued, but requires significant resource allocations. In addition, communities need to be taught what they can do to prevent snake bite incidences.

To reduce snakebite cases and improve snakebite management, policies need to be put in place. With the development of guidelines for the prevention and management of snakebite in Zambia, a crucial step is made to provide a framework for further strategies which include the development of treatment capacity and the allocation of resources, including antivenom.

These Guidelines for the Prevention and Management of Snakebite in Zambia were developed by localising the WHO's Guidelines for the prevention and clinical management for Africa, published in 2010. In addition, recent developments and experiences in snakebite management, especially in South Africa (Hardcastle, T.C. et al., 2023, 2 publications under the title "Approach to the diagnosis and management of Snakebite"), have been incorporated in this document as well.

2. CLASSIFICATION OF ZAMBIAN SNAKES



From a medical perspective, the snakes of Zambia can be divided in the following four categories:

Table 1: Zambian snake categories

Category 1	Snakes that bite frequently and are associated with serious or life-threatening envenoming
Category 2	Snakes that bite frequently but rarely cause serious of life-threatening envenoming
Category 3	Snakes that bite rarely but are capable of causing severe or life-threatening envenoming
Category 4	Non-venomous snakes that can deliver a harmful bite

There are three more categories which won't be considered in these guidelines:

- Snakes that are venomous and could cause bodily harm (but no human fatality) but are not recorded to be implicated in snakebites.
- Snakes that are mildly venomous and cause no harm to humans.
- Non-venomous snakes that are too small to inflict a bite that requires medical attention.

These three categories together account for 86 of the 102 currently known Zambian snake species.

2.1. CATEGORY 1

Snakes that frequently bite humans and are associated with serious or life-threatening envenoming.

2.1.1. Puff Adder – Bitis arietans

Length:

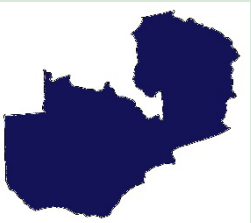
Average: 70-100 cm.

Maximum 120 cm

Description:

This is a relatively short, but large, heavy-bodied snake. Its colour tone can vary from very dark to light, with distinctive white, black-edged V-markings along the dorsum, becoming annular rings around the tail. The belly is pale with dark spots. It inflates its body and hisses loudly, expelling the air when threatened.

Clinical Toxinology: Potently cytotoxic. Severe local pain and extensive swelling, blistering and necrosis. Compartment syndrome may feature in extreme cases. Hypovolaemic shock. Blood coagulation abnormalities



2.1.2. Black-necked Spitting Cobra – Naja nigricollis

Length:

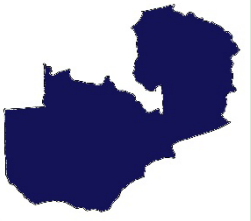
Average 100-150 cm.

Maximum 200 cm

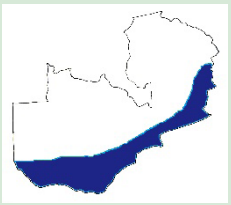
Description:

Dorsal may vary from light grey, greyish brown to black. Diagnostic is the broad, black band on the throat. They spread a broad hood in threat display. Can spit venom as well as bite.

Clinical Toxinology: Potently cytotoxic with potential heamotoxicity. Spits and bites. Severe local pain, swelling, tissue necrosis. Eye envenoming



2.1.3. Mozambique Spitting Cobra – Naja mossambica

Length: Average 80-130 cm. Maximum 150 cm.	
Description: Brown with black interstitial skin (fish net-like effect/ black skin between the scales). Pale throat with black bars and patches. Black edges on pale cheek-scales. Spreads a broad hood in threat display. Can spit venom as well as bite.	
Clinical Toxinology: Potently cytotoxic with potential mild neurotoxicity. Spits and bites. Severe local pain, swelling, tissue necrosis. Eye envenoming	

2.1.4. Black Mamba – Dendroaspis polylepis

Length: Average: 200-300 cm. Maximum 400 cm.	
Description: Long, slender, swift snake. Olive brown to greyish brown. No markings. May have slashed barring or spots or both towards the tail. Relatively small head. May rear up and spread a narrow hood. Opens mouth in threat display besides narrow 'hooding'.	
Clinical Toxinology: Potently neurotoxic	

2.2. CATEGORY 2

Snakes that bite frequently but rarely cause serious or life-threatening envenoming.

2.2.1. Rhombic Night Adder – Causus rhombeatus

Length:

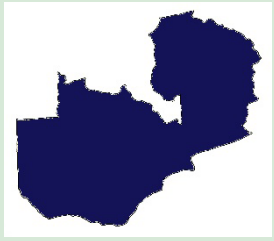
Average 40-60 cm

maximum 90 cm.

Description: Thickish body with dark brown to greenish brown with faint, rhomboid marks along the dorsal and a faint V-mark on top of the head. Hisses and coils up in defensive pose. Can have very faint markings.

Clinical Toxinology:

Cytotoxic, leads to pain and swelling. Swelling in small children can be extensive and potentially life-threatening. No blisters, necrosis.



2.2.2. Snouted Night Adder – Causus defilippii

Length:

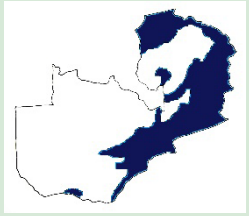
Average 20-35 cm. Maximum 42 cm.

Description:

Thickish body with clear black rhomboid markings with white edges on a light to dark brown background. Has a clear dark V-mark on the head. Hisses and coils up in defensive pose.

Clinical Toxinology:

Cytotoxic, leads to pain and swelling. No blisters, necrosis.



2.2.3. Stiletto Snake – Atractaspis bibronii & A. congica

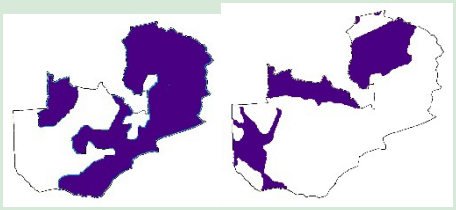
Length:

Average 30-35 cm. Maximum 70 cm.

Description:

Slender, tubelike body. Black or dark brown dorsal colour and cream or black/dark brown ventral. Arches neck in defensive pose when threatened. Both species look similar.

Clinical Toxinology: Cytotoxic, leads to pain and swelling. Swelling in small children can be extensive and potentially life-threatening. Necrosis can occur. Mismanagement can lead to amputation of (part of) digit. Sarafotoxins may lead to cardiovascular effects.



A. Bibronii A. congica

2.2.4. Garter snakes – Elapsoidea spp.

Length:

Average 40-70 cm.

Maximum 75 cm.

Juvenile

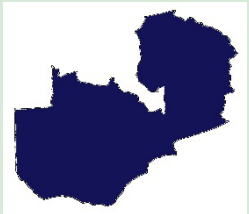
sub-adult

Description:

Small snake with slender body. Juveniles are banded black and white. Adults are completely black or dark brown.

Clinical Toxinology:

Local pain and rapid swelling. Lymphangitis. Mild neurotoxic effects including fainting observed.



2.3. CATEGORY 3

Snakes that bite rarely but can cause severe or life-threatening envenoming

2.3.1. Boomslang – Dispholidus typus spp.

Length:

Average 120-150 cm.

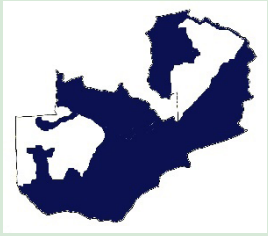
Maximum 210 cm.

Description:

Adults are green or brown. Juveniles brown grey on dorsal and light grey with dark spots on ventral. Juveniles have an emerald-green eye. May inflate neck in threat display. Arboreal snakes.

Clinical Toxinology:

Most potently venomous snake in Africa. Potently haemotoxic. Venom contains enzymes which activate prothrombin and factor X, leading to a consumptive coagulopathy, severe hypo-fibrinogenaemia and fatal bleeding if untreated



2.3.2. Twig Snake – Thelotornis capensis spp.

Length:

Average 100-150 cm.

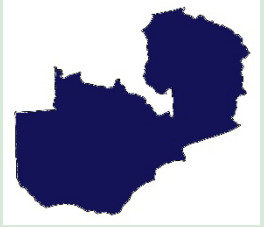
Maximum 170 cm.

Description:

Long, elegant and agile thin snake with a light grey body. Long thin head with white sides. May inflate neck in threat display. Arboreal snakes.

Clinical Toxinology:

Potently haemotoxic. Venom contains enzymes which activate prothrombin and factor X, leading to a consumptive coagulopathy, severe hypo-fibrinogenaemia and fatal bleeding if untreated



2.3.3. Forest Cobra – Naja subfulva

Length:

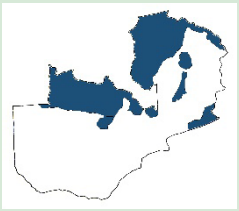
Average 140-220 cm.

Maximum 280 cm.

Description:

Largest cobra in Africa. Dorsal colour is light brown on the head, gradually changing to darker brown on the body to black on the tail. Clear black lines on light cheeks. Body is very glossy. May display a hood when threatened. A non-spitting cobra.

Clinical Toxinology: Potently neurotoxic and cytotoxic



2.3.4. Snouted Cobra – Naja annulifera

Length:

Average 130-180.

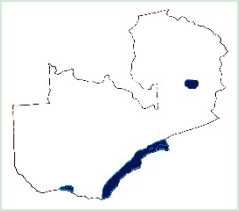
Maximum 250.

Description:

Dorsal can be a variety of brown colours and even a yellow and brown banded phase is known. Robust cobra that may display a hood when threatened. A non-spitting cobra.

Clinical Toxinology:

Potently neurotoxic and cytotoxic



2.3.5. Anchieta's Cobra – Naja anchietae

Length:

Average 130-180 cm.

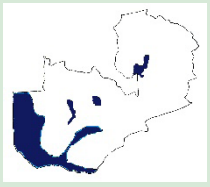
Maximum 230.

Description:

Dorsal can be a variety of brown colours and even a yellow and brown banded phase is known. Robust cobra that may display a hood when threatened. Told apart from the Snouted Cobra by the larger neck scales which have a metallic sheen to them. A non-spitting cobra.

Clinical Toxinology:

Potently neurotoxic and cytotoxic



2.3.6. Gaboon Adder – Bitis gabonica

Length:

Average: 80-140 cm.

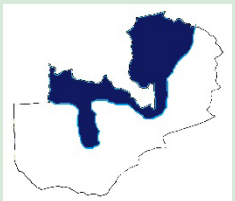
Maximum: 180 cm

Description:

This is a large, heavy-bodied snake. Its colour tone can vary from dark to light, with distinctive, geometrical patterns, including clear white rectangles along the dorsal ridge. The belly is pale with dark spots. It inflates its body and hisses loudly expelling the air when threatened. This adder has the largest fangs (max. 5 cm) of any snake in the world.

Clinical Toxinology:

Same as Puff Adder. Cardiovascular and haemostatic abnormalities may be prominent.



2.4. CATEGORY 4:

Non-venomous snakes that can deliver a harmful bite

2.4.1. Southern African Python – Python natalensis

Length:

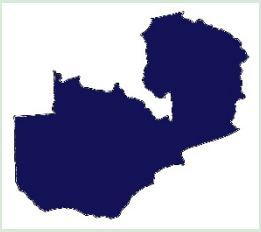
Average 230-400 cm.

Maximum 550 cm.

Description:

Very large, heavy, slow-moving snake. The largest snake in southern Africa. Light brown base colour on the dorsal, with dark markings and blotches.

Clinical relevance: bites from this snake species are treated as normal laceration wounds. In case of a bite of a large sized python, where teeth have penetrated deeply, one of the main blood vessels may be punctured, leading to a catastrophic bleed. In first aid, this requires the application of a broad tourniquet, to be loosened every 1.5 hours to avoid the effects of lack of perfusion and acidosis.



3. PREVENTION OF SNAKEBITE

3.1. Introduction

Snakes have adapted to a wide range of habitats and prey species. All snakes are predatory carnivores. None are vegetarians although some (the Egg Eaters, *Dasypeltis spp*) specialise in eating eggs. Since snakes are preyed upon by other animals, they are secretive and have evolved many survival strategies. Snakes are not apical predators. By understanding something about snake habits, simple precautions can be adopted to reduce encounters and subsequent bites. Some truths apply to all snakes: they prefer not to confront large animals (such as humans); thus, it is best to give them the chance to slither away. Some species are mainly nocturnal while others are diurnal or both. Many snakes are non-venomous, some are mildly venomous and only a few are highly venomous.

Snakes are necessary to maintain a healthy balance in nature; they shouldn't be killed unnecessarily. It is important that everyone learns which dangerous snakes occur in their local community or area.

3.2. Preventive measures in and around the house:

3.2.1. Prevention from entering a house

Snakes may enter a house in search of shelter or food (rodents, insect eaters).

- Do not keep livestock, especially chickens, in the house as some snakes may come to hunt them.
- Store food in rodent-proof containers.
- Keep the house very clean, so as not to attract rodents or insects (which in turn attract lizards and frogs). Snakes may follow these animals into the house.
- Raise beds above floor level and use an insecticide-impregnated mosquito net, completely tucked in under the mattress. This guards against centipedes, spiders, scorpions and snakes as well as mosquitos and many ectoparasites (bed bugs, fleas, lice, etc).

- Create physical barriers to prevent snakes from entering. Ensure well-closing doors and windows. Do not have tree branches reaching within a meter from the house. Consider window fly screens and screen doors with a good seal.
- Consider that security lighting will attract insects, then frogs and lizards and then snakes.

NB: snake repellents are not effective.

3.2.2. Avoid hiding places

In the (farm)yard, compound or garden, try not to provide hiding spaces for snakes.

- Clear heaps of rubbish, building materials, heaps of branches and other refuse from near the house.
- Keep grass short or ground clear around your house and clear underneath low bushes so that snakes can't hide close to the house.
- Keep your granary, water sources, reservoirs and ponds away from the house.

3.3. Preventive measures in fields and bush

- Use a torch/light and wear proper, closed shoes when walking outside at night.
- Listen to wild and domestic animals (especially birds); they may warn of a snake nearby. Some animals have distinct calls/behaviours or may harass a snake.
- In the bush or countryside, firewood collection in the dark is dangerous.
- Watch where you walk. Step on instead of over obstacles.
- Do not put your hands in dark holes, nests or other hiding places where snakes may be resting.
- Be careful when handling dead or seemingly dead snakes. Some snakes play dead (spitting cobras for example). The fang of a dead snake may accidentally pierce the skin and envenomation can thus take place.
- Many snakebites happen during field work. Snakes mostly come out in the warm months and especially after heavy rains (many snakes are flushed out of burrows).
- Drivers or cyclist shouldn't intentionally run over a snake. The snake may not be dead and may lie injured (which causes it unnecessary suffering) and may cause a threat to other road users. The snake may also end up trapped under the vehicle and crawl out once the vehicle is stopped in a compound or garage.

4 SNAKE VENOMS

4.1. Introduction

The primary function of snake venom is to immobilise and kill its prey (as well as help in digestion). Some snakes have developed tools to utilise their venom in defence (spitting cobras). Spitting cobras bite and spit the same venom.

Snake venoms are complex mixtures of numerous toxins and non-toxic components. More than 90% of the dry weight is protein. The most important venom components that lead to significant clinical effects after a bite are enzymes and polypeptide toxins.

The amount of venom injected during a snakebite depends on various factors: species and size of the snake, mechanical efficiency of the bite, duration of the bite, whether one or two fangs penetrated and whether there were repeat bites. Not all bites by venomous snakes lead to venom injection or envenoming. In an average of 50% of occasions, no venom is injected; this is referred to as a “dry bite” as opposed to a “wet bite”. Even after several bites or after eating prey, snakes do not exhaust their venom supply and they remain just as venomous.

Within the same species, larger snakes also tend to inject more venom than smaller ones, but the venom of the latter may be richer in some very dangerous components. Bites by small snakes should therefore not be neglected but should receive the same attention as those by larger snakes.

4.2. Snake venom composition

The most important venom components that cause serious clinical effects are pro-coagulant enzymes, cytolytic or necrolysing toxins, haemolytic and myolytic phospholipases A2, pre- and post-synaptic neurotoxins and haemorrhagins.

Snake venoms vary in their composition from species to species but even within a single species:

- throughout the geographical distribution of that species at different seasons of the year

- as the snake ages (ontogenic)

This composition variety contributes to the enormous and fascinating clinical diversity of snakebite.

4.2.1. Pro-coagulant enzymes

These are found mainly in vipers and dangerous colubrids. They activate different steps of the blood-clotting cascade, typically factors Xa, V and VII. Ultimately, this leads to the formation of fibrin fibres in the blood. Most of the fibrin is broken down by the body's fibrinolytic system. This process depletes the body's own levels of clotting factors and eventually the blood no longer clots. This is called Venom Induced *Consumption Coagulopathy* (VICC). They cause a fibrinogenaemia. Other similar findings may be Thrombotic Microangiopathy (TMA) or Microangiopathies haemolytic anaemia (MAHA).

Haemostatic disturbances are an important feature of envenoming by vipers and dangerous venomous colubrids (Boomslang and Twig Snake). Snake venom can cause bleeding in a number of different ways. Venom procoagulants can activate intravascular coagulation and produce consumptive coagulation leading to incoagulable blood. For example, procoagulants in the venom of colubrids activate prothrombin and in Bitis arietans (Puff Adder) venom has a direct thrombin-like action on fibrinogen.

4.2.2. Cytolytic or necrolysing toxins

These are digestive hydrolases (proteolytic enzymes and phospholipases) and peptides that may destroy cell membranes and tissues and therefore increase the permeability of the vascular endothelium. This leads to local swelling, blistering and oedema.

4.2.3. Haemolytic and myolytic phospolipases A2

These damage cell membranes, endothelium, skeletal muscle nerves and red blood cells. Phospholipases A2 are the most widespread and extensively studied of all venom enzymes. Under experimental conditions, they damage mitochondria, red blood cells, leucocytes, platelets, peripheral nerve endings, skeletal muscle, vascular endothelium and other membranes. They produce presynaptic neurotoxic activity, opiate-like sedative effects and the auto-pharmacological release of histamine.

4.2.4. Pre-synaptic neurotoxins

These are mainly found in Black Mamba venom.

The presynaptic component of the venom, known as Dendrotoxins (DTX) is unique to the genus Dendroaspis. These toxins show homology with Kinutz-type protease inhibitors and exert their pharmacological action by interacting with voltage-dependent potassium channels. As a consequence of its interaction, Dendrotoxins potentiate the effect of the neurotransmitter acetylcholine by facilitating the release of a chemical at the presynaptic nerve terminal, thus provoking an excitatory effect. In turn, a flooding of the synaptic gap with acetylcholine occurs.

4.2.5. Post-synaptic neurotoxins

Post-synaptic neurotoxins are found in non-spitting cobras and in the Black Mamba. They are polypeptides that compete with acetylcholine for binding at neuromuscular junction receptors and lead to curare-like paralysis. This impedes signalling from the nerve endings to the muscles.

4.2.6. Haemorrhagins

Spontaneous systemic bleeding is attributed to haemorrhagins which damage the vascular endothelium. These are zinc metallo-endopeptipases (reprolysins), some of which have disintegrin-like cysteine-rich and lectin domains. The combination of incoagulable blood and thrombocytopenia and vessel wall damage results in massive bleeding.

4.2.7. Biogenic amines

Biogenic amines such as histamine and serotonin (5-hydroxytryptamine) are found particularly in viper venoms. They may contribute to the local pain and permeability changes at the site of the snakebite.

4.3. Classification clinical patterns of snakebite envenoming

Very broadly, the venom components described in chapter 4.2 can lead to four main types of envenoming, three of which are relevant to Zambia.

4.3.1. Cytotoxic envenoming

This is characterised by intense pain and progressive swelling with blood-stained tissue leaking from the bite wound, can cause hypovolemic shock, blistering and bruising. The victim will complain of severe pain at the bite site and throughout the affected limb with painful and tender enlargement of lymph glands draining the bite site. Irreversible death of tissue may occur (necrosis/gangrene).

Species that cause this type of envenoming: Puff Adders, Gaboon Adder, Black-necked Spitting Cobra, Mozambique Spitting Cobra, Stiletto Snake, Night Adders and Garter Snakes. The absence of bullae or necrosis may indicate a Night Adder or Garter Snake bite.

4.3.2. Neurotoxic envenoming

This is characterised by mild or absent swelling, progressive descending paralysis starting with droopy eyelids (ptosis) and paralysis of eye movements causing double vision. There may be painful and tender enlargement of lymph glands draining the bite site. The patient may vomit, the saliva may become profuse and stringy and eventually there may be difficulties with swallowing and breathing. Unilateral findings of neurological deficits may indicate non-spitting Cobra as neurotoxic PLA2 affects neurology centrally rather than peripherally.

Species that cause this type of envenoming are Black Mamba and the non-spitting Cobras (Snouted Cobra, Anchieta's Cobra, Forest Cobra).

4.3.3. Haemotoxic envenoming

This is characterised by bleeding from the gums, gastro-intestinal tract, genito-urinary tract and partly and recently healed wounds as well as other mucous membranes or cannulation/venepuncture sites.

Species that cause this type of envenoming: Boomslang, Twig Snake, Puff Adder, Gaboon Adder, Black-necked Spitting Cobra. Note with Black-necked Spitting Cobras they cause a haemolysis as opposed to a fibrinogenaemia.

4.3.4. Myotoxic envenoming

This is characterised by negligible local swelling, increasing generalised muscle pain and tenderness (myalgia) associated with features of neurotoxic envenoming and progressive descending paralysis, culminating in paralysis of breathing. The snake

in Africa involved is the Yellow-bellied Sea Snake (Hydrophis platurus) which doesn't occur in Zambia. Myotoxic envenoming is therefore not further considered in these guidelines.

4.3.5. Mixed types of envenoming

The following mixed types of envenoming may occur.

- Mix of cytotoxic and haemotoxic envenoming occurs in Puff Adders, Gaboon Adders and Black-necked Spitting Cobras.
- Mix of Neurotoxic and cytotoxic envenoming occurs in non-spitting Cobras, Stiletto Snakes and Garter Snakes.
- The Gaboon Adder has a mix of cytotoxic, haemotoxic and neurotoxic venom.

5. CLINICAL FEATURES OF ENVENOMING

5.1. Introduction

Bites by venomous snakes, even the deadliest ones, do not always cause envenoming. The proportion of dry bites ranges from more than 50% in the case of Night Adders to less than 10% in Bitis spp. In someone bitten by a snake, symptoms and signs may result from the effects or complications of any or all of the following: fear, incorrect treatment (first aid, medical or traditional) and type of envenoming.

5.2. Local signs and symptoms in the bitten part

There is immediate pain. Local bruising and persistent bleeding from the fang punctures suggest a haemostatic disturbance (adder and certain colubrid bites). Swelling usually begins within 12-20 minutes. It may become extensive after adder and spitting cobra bites, involving the entire limb, adjacent areas of the trunk and the whole body in children. Regional lymph nodes draining the bitten part may become enlarged, painful and tender on palpation within 30-60 minutes.

Blisters, blood or fluid filled bullae may appear, at first near the fang marks and within 12-24 hours. Demarcated pigmentation or depigmentation and anaesthesia and a distinctive smell of putrefaction are signs of necrosis. This progresses to frank necrosis with spontaneous sloughing of dead tissue or the need for debridement. Eschar may form.

5.3. Generalised (systemic) symptoms and signs

5.3.1. Bleeding and clotting disorders (Adders, some colubrid species)

There is bleeding from the wounds, the fang punctures and venepunctures sites because the blood is defibrinogenated and will not clot and platelet function is impaired. Venom haemorrhagins cause spontaneous systemic bleeding from gingival sulci and nose, haematemesis, rectal bleeding, melaena, haemoptysis, haematuria, retroperitoneal, extra-pleural or intracranial haemorrhage and, in pregnant women, ante-partum haemorrhage.

5.3.2. Shock (hypotension)

There is blurred vision, dizziness, syncope and collapse, sometimes occurring very soon after the bite. These symptoms may be transient, recurrent, persistent, progressive, delayed and life-threatening.

5.3.3. Neurotoxic symptoms

Transient paraesthesia of the tongue and lips, abnormalities in taste or smell, heaviness of the eye lids, increased salivation or a dry mouth, nausea and vomiting are followed by progressive, descending paralysis: bilateral ptosis, pupillary abnormalities, external and internal ophthalmoplegia, paralysis of the facial muscles, jaw, tongue, neck flexors (causing "broken neck" sign) and other muscles innervated by the cranial nerves, dysphonia, difficulty in swallowing secretions and finally respiratory and generalised flaccid paralysis.

Black Mamba bite envenoming causes paraesthesia, sweating, gooseflesh, salivation, viscous respiratory secretions, diarrhoea, fasciculations and other involuntary muscle spasms and rapidly progressive paralysis.

Unilateral findings of neurological deficits may indicate non-spitting Cobra as neurotoxic PLA2 affects neurology centrally rather than peripherally.

5.3.4. Acute renal failure

This is uncommon after bites by any of the Zambian snakes, but renal failure may develop if there has been profound hypotension or rhabdomyolysis (in neglected adder bites). Complications can occur from tourniquet, haemoglobinuria or MAHA/TMA.

6. CLINICAL PROFILES OF ENVENOMING

Clinical profiles of envenoming by some of the snakes that cause bites of medical importance and / or are often implicated in snake bite cases.

6.1. Back-fanged snakes (Colubridae)

Species that have proven to be capable of causing fatal envenoming on humans in Africa are the Boomslangs (Dispholidus typus spp.) and Twig Snakes (*Thelotornis spp.).* Included among their victims are the famous herpetologists Karl P. Schmidt *(Dispholidus spp)* and Robert Mertens *(Thelotornis kirtlandii).* If these snakes are allowed to engage their rear fangs for a prolonged period, severe envenomation may result. Symptoms resulting from envenoming by *Dispholidus spp.* and *Thelotornis spp.* may be delayed for several hours (and in some cases for days) after the bite. Antivenom treatment has been successful up to several days after Dispholidus bite where clinical findings have shown an active coagulopathy.

There is nausea, vomiting, colicky abdominal pain and headache. Bleeding develops from old and recently healed wounds such as venepunctures and there is spontaneous gingival bleeding, epistaxis, haematemesis, melaena, subarachnoid or intracerebral haemorrhage, haematuria and extensive ecchymoses. Intravascular haemolysis and microangiopathic haemolysis have been described.

Most of the fatal cases recorded, were attributed to renal failure from acute tubular necrosis, many days after the bite. Local effects of the venom are usually trivial but several patients showed some local swelling and one bite by Dispholidus spp. had a massive swelling with blood-filled bullae.

Investigations reveal incoagulable blood, defibrination, elevated Fibrinogen Degradation Products (FDPs), severe thrombocytopenia and anaemia. These clinical features are explained by disseminated intravascular coagulation, triggered by venom prothrombin activators.

6.2. Stiletto Snakes – Atractaspis spp.

Only three of the 17 species of this genus are capable of causing fatal envenomation, none of which are found in Zambia. However, due to the possibility of severe swelling, fatality may occur with bites from Zambia's Bibron's Stiletto Snake (*Atractaspis bibronii*) and Congo Stiletto Snake (*A. congica*) on very small children.

Local effects are severe pain, swelling, blistering (sometimes necessitating amputation), tender enlargement of lymph nodes, local numbness or paraesthesia. The most common systemic symptom is fever.

Regional effects include sore throat as well as difficult and painful swallowing.

Mild abnormalities of blood coagulation and liver function have been described. Atractaspis venoms contain endothelin-like peptides such as sarafotoxins that can have marked cardiovascular effects. Venoms also contain haemorrhagic and necrotic factors but no true neurotoxins.

6.3. Spitting Cobras

Bites by Spitting Cobras (in Zambia: Black-necked Spitting Cobra – *Naja nigricollis* and Mozambique Spitting Cobra – *N. mossambica*) produce a distinct clinical syndrome

unlike that caused by other elapid snakes: local necrosis without neurotoxicity although mild neurological symptoms have been observed in N. mossambica bites.

There are occurrences of Spitting Cobra bites at night inside homes while people sleep. There is immediate pain, followed by vomiting within six hours and extensive local swelling, local blistering in 60% of cases and local tissue necrosis in 70% of envenomed cases. Necrosis usually involves only the skin and subcutaneous connective tissue.

There may be "skip lesions", areas of necrotic tissue separated by strips of apparently normal skin, caused by proximal spread of venom in lymphatic vessels. There is neutrophil leucocytosis with evidence of complement activation, principally via the alternative pathway. Complications of necrotic lesions include loss of function due to chronic ulceration, osteomyelitis, arthrodesis, hypertrophic scars, keloid formation and, after several years, malignant transformation (Marjolin's ulcer). Volkmanns and/or Dupuytren's contracture may occur in upper limb bites.

6.4. Spitting Cobras: venom ophthalmia

When venom of the spitting Cobras (Black-necked Spitting Cobra – *Naja nigricollis* and Mozambique Spitting Cobra – *N. mossambica*) enters the eye, there is intense local pain, blepharospasm, palpebral oedema, epiphora and leucorrhoea. In Nigeria, slit-lamp or fluorescein examination revealed corneal erosion in more than half the patients spat at by *N. Nigricollis*. It is a chemosis eye injury.

Secondary infection of the corneal lesions may result in permanent opacities causing blindness or pantophthalmids with a destruction of the eye. Rarely, venom is absorbed into the anterior chamber causing hypopyon and anterior uveitis. Seventh cranial nerve paralysis is a rare complication which results from tracking the venom from the conjunctival sac through the lymphatics posteriorly to the superficially VIIth cranial nerve.

6.5. Black Mambas

The Black mamba (*Dendroaspis polylepis*) is arguably the most feared snake in Zambia. This is partly due to exaggeration of this snake's defensiveness and physical capabilities (myths) and partly due to the fact that bites by this snake often lead to death, due to the fast-working venom.

Black Mamba venoms contain unusual neurotoxins called dendrotoxins. They are 59 amino acid proteins that bind to voltage-gated potassium channels at pre-synaptic nerve-endings, causing acetylcholine release. These toxins are responsible for a distinctive clinical syndrome of envenoming: paraesthesia, signs of autonomic nervous system stimulation and muscular fasciculations (contractions of groups of muscle fibres innervated by single motor neurones producing a rippling contraction under the skin that can be confused with shivering. They also affect the post synaptic nerve ending inhibiting acetylcholinesterase.

Rapid progressive descending paralysis can appear as soon as 15 minutes after the bite and progressing to fatal respiratory paralysis.

Black Mamba bite case in Zimbabwe

The speed of evolution of envenoming is well-illustrated by a patient seen in Harare, Zimbabwe. Within a minute of being bitten by a 3-meter-long Black Mamba, a 41-year-old man noticed tingling of the tongue and lips, followed by generalised tingling, abdominal pain and light-headedness. Within 20 minutes he was sweating profusely, had dilated pupils and was too weak to stand up. He became nauseated and vomited 30 minutes after the bite, by which time he was unable to pass urine and had detectable ptosis. He became breathless and found it difficult to clear his throat of thick secretions; 40 minutes after the bite he felt cold all over and noticed gooseflesh. His conjunctivae were congested and he was unable to open his mouth or protrude his tongue. There was then a rapid deterioration in his breathing and level of consciousness. Generalised fasciculations were noticed. He was treated with antivenom after 75 minutes. 4.5 hours after the bite, he was intubated and mechanically ventilated for 40 hours after which he made a complete recovery (Warrel, 1995).

Other features described in the literature describe severe local pain, metallic taste in the mouth, diarrhoea, excessive salivation, involuntary muscular contractions and recurrent episodes of paralysis despite antivenom treatment. Local swelling is variable and sometimes absent. The rare cases of local tissue damage usually resulted from bites on the finger and/or the use of a tourniquet. Tachycardia is also a feature.

6.6. Neurotoxic non-spitting Cobras

Bites by the species Forest Cobra (*Naja subfulva*), Snouted Cobra (*N. annulifera*) and Anchieta's Cobra (*N. anchietae*) (unrecorded: Banded Water Cobra – N. annulata stormsii) may cause local swelling at the bite site but necrosis rarely develops. Classic neurotoxic symptoms appear as early as 30 minutes after the bite and can evolve to the point of fatal respiratory paralysis within 2-16 hours after the bite.

There are signs of progressive descending paralysis, starting with ptosis (drooping eyelids), external ophthalmoplegia (causing diplopia, i.e. double vision) and weakness of the muscles innervated by the cranial nerves so that the victim cannot open the mouth, clench the jaws, protrude the tongue, swallow, protect the airways from secretions, speak, flex the neck and eventually cannot breath. When the respiratory muscles become affected, the pattern of breathing is initially abdominal or "paradoxical": the abdomen expands during inspiration due to contraction of the diaphragm. Respiratory distress increases, the patient becomes anxious, sweaty and cyanosed and will die unless ventilated artificially. Occasionally, unilateral neurological deficits have been observed.

6.7. Puff Adder – Bitis arietans

The Puff Adder is thought to be responsible for the majority of serious venomous snake bites in Zambia. Local swelling is often extensive, commonly extending to involve the entire bitten limb and spreading onto the trunk. This extravasation of plasma causes hypovolaemic shock, a common presenting feature.

Local blistering and necrosis may be extensive, requiring the amputation of the bitten digit or even part of the affected limb. Major arteries may become thrombosed or entrapped by swollen tissue in the bitten limb (and, rarely, elsewhere), increasing the local tissue damage. Compartmental syndromes may develop (estimated 2% of Puff Adder bites), especially in the anterior tibial compartment after bites on the feet and

ankles. These may lead to ischaemic necrosis of the compartmental muscles as in Volkmann's ischaemic contracture of the forearm. Direct myocardial effects, commonly sinus bradycardia, may contribute to hypotension.

Coagulopathy leading to incoagulable blood has been reported and rarely even cerebral thrombosis, (whereas in West Africa, bites can lead to spontaneous bleeding without coagulopathy). This regional variation in the pattern of envenoming is consistent with the hypothesis that there may be different species of Puff Adder in Africa.

6.8. Gaboon Adder – Bitis gabonica

Local effects of envenoming may be less severe than those produced by *B. arietans*

but swelling, bruising, blistering and necrosis are common. Systemic symptoms may be early and dramatic. Cardiovascular abnormalities, including hypotension and shock, arrhythmias and ECG changes are reported. Spontaneous systemic bleeding is a common feature while haemostatic abnormalities include thrombocytopenia and evidence of thrombin-like and fibrinolytic activities.

6.9. Night Adders – Causus spp.)

Night Adders are a common cause of snakebite in Africa and Zambia. Local envenoming (pain, swelling and lymphadenopathy) is usually the only effect. There are four species of Causus in Zambia, of which two are common within their range: Common or Rhombic Night Adder (*C. Rhombeatus*) and Snouted Night Adder (*C. defilippi).*

With C. defilippi bites there is pain, local swelling, lymphadenopathy and mild fever without necrosis.

Causus rhombeatus bites cause pain, swelling, and fever. Although necrosis and fatalities have not been reliably attributed to this species, caution is required. C. rhombeatus has elongated venom glands, extending 15-20 cm into the neck region. This results in a large amount of venom which could, potentially, cause extensive swelling and thus have a systemic impact on small children or the frail.

7. Main clinical syndromes of envenoming

Except in cases where a dead snake is brought to a hospital or photos of the snake were taken *and* can be reliably identified by hospital staff or snake experts, the identification of the snake responsible for the bite is usually difficult or impossible. It is, however, important to try to diagnose which particular snake (genus or even species) was responsible for the bite so that the likely course of envenoming and potential complications can be promptly anticipated, prevented or treated. Descriptions of the snake and the circumstances of the bite may suggest a species diagnosis but this is not a satisfactory basis for treatment. What is needed for appropriate clinical management is the reliable identification of a distinctive clinical syndrome based on epidemiological, clinical and laboratory data.

A syndromic approach is recommended in the majority of cases in which the cause of the bite is not certain. This has been developed and used effectively to guide algorithm treatment with poly-specific antivenoms in Southern Africa and sub-Saharan Africa as a whole. The latter includes the algorithm for the Saw-scale or Carpet Vipers (Echis spp.) which do not occur in Zambia. In these guidelines for Zambia, the algorithm of Dr. Roger Blaylock for Southern Africa is followed.

Table 2 Syndromes of envenoming

Syndrome	Description	Syndrome name	Abbreviation
Syndrome 1	Marked local swelling and intense pain	Painful progressive swelling syndrome	PPSS
Syndrome 2	Progressive and descending paralysis	Progressive weakness syndrome	PWS
Syndrome 3	Mild or negligible swelling with incoagulable blood	Bleeding syndrome	BS
Mixed syndrome (1+3)	Combination of marked local swelling and intense pain with incoagulable blood	Combination PPSS and BS	PPSS+BS

7.1. Syndrome 1: Painful Progressive Swelling

There is intense pain and rapidly progressing, local swelling, sometimes with blisters and necrosis, with coagulable blood (detected by 20WBCT (20 Minutes Whole Blood Clotting Test)) and absence of spontaneous systemic or persistent local bleeding.

It is suggestive of bites by Spitting Cobras, Puff Adder, Night Adders, Stiletto Snakes and (rare) Gaboon Adders.

7.2. Syndrome 2: Progressive Weakness Syndrome

There is no, negligible, mild or moderate swelling with progressive, usually descending, with bilateral or unilateral paralysis. It is strongly suggestive of Black Mamba or non-Spitting Cobras (neurotoxic Cobras).

7.3. Syndrome 3: Bleeding Syndrome

This is a rare syndrome. There is mild or absent local swelling with incoagulable blood (detected by 20WBCT) and often spontaneous systemic bleeding. It is suggestive of bites by Boomslang (Dispholidus spp.) or, even rarer, Twig Snakes (Thelotornis spp.).

7.4. Mixed Syndrome: PPSS + BS

There is intense pain and rapidly progressing local swelling, sometimes with blisters and necrosis, with incoagulable blood (detected by 20WBCT) and often systemic or persistent local bleeding at the bite site.

This mixture of syndromes indicates bites from Puff Adder, Gaboon Adder or Black-necked Spitting Cobra.

8. CLINICAL ASSESSMENT + SPECIES DIAGNOSIS

8.1. Bite history

A precise history of the time and circumstances of the bite and the progression of local and systemic symptoms and signs is of the utmost importance. Four initial questions should be asked as below:

8.1.1. "In which part of the body have you been bitten?"

Look where the patient points. There may be evidence that the patient has been bitten by a snake (for example: fang marks), with signs of local envenoming (for example: local swelling, bruising or continuing bleeding from fang punctures), but also evidence of pre-hospital treatment (for example: impressions made by a tourniquet or incision marks that are bleeding, suggesting the blood is incoagulable). Exceptionally, the snakebite may not have been recognised by the victim, if the bite happened at night during sleep, or in the dark, or in the water or in thick undergrowth. In such cases, suspicion of the diagnosis will depend on typical signs such as puncture marks, progressive swelling, bleeding gums or descending paralysis. Consider possible bites and stings from other animals such as scorpions, spiders, bees, etc.

8.1.2. "When were you bitten?"

Assessment of the severity of envenoming depends on the length of time between the bite and when the patient seeks treatment. The patient may seek treatment so soon after the bite that signs and symptoms have not yet developed or so late that the only signs are of late complications of envenoming, such as gangrene, renal failure, laboured breathing.

8.1.3. "What did the snake look like?"

Sometimes, the snake that bit the victim is killed and brought to the health centre. If the snake is available, its identification can be very helpful, but only if there is someone capable of identifying snakes. If the snake is identified as a harmless snake, the patient can be quickly reassured and discharged.

Note: transporting a dead snake may be unsafe. The fangs of a dead snake may still contain and inject venom when penetrating skin.

Descriptions of the snake by victims or bystanders are often unreliable and misleading. Therefore, the questions need to be guiding and closed. Instead of asking "was the snake big?" ask comparison questions such as: "was the snake longer than you?", was it thicker than your wrist, your finger?", etc.

Suggested questions:

Was the snake longer than.....?

Was the snake thicker than.....?

What was the colour of the snake?

Was the snake one colour or was there a pattern?

Was the snake short and fat-looking or long and thin?

Further questions:

Where was the snake found?

What was the victim doing?

Ask about the behaviour of the snake:

Did the snake rear up and spread a hood? (Cobras, Black Mamba)

Did it open its mouth? (Black Mamba).

8.1.4. "How and what are you feeling?"

The patient's current symptoms can point to what is likely to be the most important effect of envenoming (for example faintness or dizziness, indicating hypotension or shock; breathlessness indicating incipient respiratory failure).

Patients should be asked to describe their symptoms and should be questioned about the extent of local pain, swelling, tenderness, tender and painful enlarged lymph nodes draining the bite area, bleeding from the bite wounds, at sites of other recent injuries and at sites distant from the bite area (gums, nose, etc), motor and sensory symptoms, vomiting, fainting and abdominal pain. The time after the bite when the symptoms appeared and their progression should also be noted. Details of prehospital treatment (tourniquet, ingested and applied herbal remedies, etc) should also be recorded as these may, themselves, be responsible for some of the symptoms. If there is swelling, mark the area and write the time.

8.2. Examination

8.2.1. Tooth, teeth or fang marks

The absence of discernible tooth or teeth marks does not exclude snakebite. However, the discovery of one or more discrete, separate puncture marks, suggests a bite from a possible venomous snake. The pattern of fang punctures is rarely helpful as marks made by accessory fangs, palatine maxillary and mandibular teeth may complicate the pattern and there may have been multiple strikes/bites. The greater the distance between clear fang marks, the broader the head of the snake was.

8.2.2. Local signs

Local swelling and enlargement and tenderness of regional lymph nodes are often the earliest signs of envenoming, but factitious swelling may be caused by a venous tourniquet as well as by envenoming. Most cases of significant envenoming by African adders and spitting cobras are associated with the development of local swelling within two hours after the bite but there have been exceptions to this rule. Symptoms and signs of severe systemic envenoming from colubrids (Dispholidus spp., Thelotornis spp.) have been delayed for 15 hours or more after the bite. These species usually cause negligible local swelling. However, systemic envenoming by most African venomous snakes is associated by local swelling, although this may be negligible in the case of some bites by colubrids, Black Mambas and neurotoxic cobras.

8.2.3. Bleeding

Persistent bleeding from the fang marks, other recent wounds and venepuncture sites suggests that the blood is incoagulable. The gums (gingival sulci) should be examined thoroughly as these are usually the first sites of spontaneous systemic bleeding.

8.2.4. Shock

The signs of shock are falling blood pressure; collapse; cold, cyanosed and sweaty skin; and impaired consciousness, low urine output (<30 ml/hour), rapid pulse. The foot of the bed should be raised (Trendelenburg position) and an intravenous infusion of isotonic saline or a plasma expander or colloidal such as haemaccel, gelofuse, dextran or fresh frozen plasma should be started immediately.

8.2.5. Neurotoxicity / paralysis

The earliest symptoms of neurotoxicity after elapid bites are often blurred vision, a feeling of heaviness of the eye lids and apparent drowsiness. Whether the snake venom toxins can exert any direct central effect on the level of consciousness is controversial but it is unlikely that they cross the blood-brain barrier. The frontalis muscle is contracted, raising the eyebrows and puckering the forehead, even before ptosis can be demonstrated. Respiratory muscle paralysis with imminent respiratory failure is suggested by dyspnoea, distress, restlessness, sweating, exaggerated abdominal respiration, central cyanosis and coma. If there is any suggestion of respiratory muscle weakness, objective monitoring should be attempted by measuring peak expiratory flow, forced expiratory volume in one second (FEV1), vital capacity of forced expiratory pressure using the mercury manometer of a sphygmomanometer. Coma is usually the result of respiratory and circulatory failure.

8.3. Monitoring of snakebite victims

Patients bitten by a snake should, ideally, be observed in hospital for at least 24 hours after the bite. The intensive care unit or a high dependency bed is appropriate but rarely possible. In an open ward, the patient should be placed close to the nursing station and in full view of the medical staff. The following should be checked at least every four hours and action taken if there is any deterioration:

- **Level of consciousness**
- **Pulse rate and rhythm**
- **Respiratory rate**
- **Oxygen saturation**
- **Urine output**
- **Blood pressure** - Measure the blood pressure while the patient lies supine and after sitting up or being propped up in bed to assess any postural drop in pressure, suggesting hypovolaemia.
- **Signs of neurotoxicity** - Prescence or absence of ptosis, the early signs of neurotoxicity. Seeing droopy eyelids is not diagnostic! Ask the patient to look upward and check that the upper eyelids are fully retracted so that the pupils are fully exposed.
- **Extent of swelling and tenderness** - Keep track of swelling progression by using marker pen marks (with time and date) on the boundary of the swelling extent.
- **New signs and symptoms.**

8.4. Investigations

8.4.1. Haematology

Conduct a total blood count, as systemic envenoming is usually associated with a neutrophil leucocytosis: counts above 20×10^9/l indicate severe envenoming. Initially, there may be haemoconcentration (increased haemoglobin concentration or haematocrit) but later haemoglobin concentration and haematocrit may fall because of bleeding into the bitten limb and elsewhere, from intravascular haemolysis, microangiopathic haemolysis or from a disseminated intravascular coagulation. Thrombocytopenia is common after large adder and colubrid bites. The platelet count may fall to its lowest level after 1-2 days. The blood film may show evidence of microangiopathic haemolysis (fragmented erythrocytes also known as "helmet cells" or schistocytes).

8.4.2. Test of haemostasis: 20MWBCT

Incoagulable blood is a cardinal sign of consumption coagulopathy from envenoming by large adders and medically important colubrids. For clinical purposes, the 20 minutes whole blood count test (20MWBCT) has proven reliable. This is a simple, "all or nothing" test of blood coagulability which can be done at the bedside and correlates well with fibrinogen concentration.

Two to three millilitres of blood taken by venepuncture are placed in a new, clean, dry, glass vessel and left undisturbed for 20 minutes; then tipped over to see if the blood has clotted or not. The vessel must be glass rather than plastic to activate blood coagulation via Hageman factor (FXII). Glass vessels may not activate coagulation if they have been cleaned with detergent or are wet.

- ⇨ Use a second test vessel with blood from a person, not bitten by the same snake, for comparison.

8.4.3. Other tests of haemostasis

More sensitive laboratory tests include prothrombin time (PT), thrombin and activated partial thromboplastin (aPTT) times and measurement of FDP and D-dimer concentrations. PT is often reported as international normalisation ratio (INR).

8.4.4. Biochemistry

Biochemistry can reveal evidence of muscle damage. Serum concentrations of creatine kinase, aspartate aminotransferase and blood urea are commonly raised in patients with severe envenoming because of local muscle tissue damage at the bite site. Generalised rhabdomyolysis caused by neglected large adder bites causes a steep rise in serum creatine kinase and other muscle-derived enzymes, myoglobin and potassium concentrations. Plasma is stained brownish by myoglobin and urine will be black, dark-brown or "cola coloured" and positive for blood haemoglobin on testing with reagent sticks. This can indicate long restrictive tourniquet as well.

8.4.5. Evidence of intravascular haemolysis

Pink plasma (haemoglobinemia) suggests haemolysis, but centrifugation or storage of blood samples may cause in vitro disruption of erythrocytes. Urine may be black (as in malarial "blackwater fever") or reddish brown and positive for blood/haemoglobin on testing with reagent or urine dipsticks. Haematuria is excluded by microscopy. Distinguishing myoglobinuria from haemoglobinuria is difficult, requiring immunoassay.

8.4.6. Evidence of renal dysfunction and acid-base imbalance

Blood urea or serum creatine and potassium concentrations should be measured in patients who become oliguric, especially in cases with a high risk of renal failure (especially victims of bites by colubrids). A snake-bitten patient should be encouraged to empty his/her bladder on admission. Urine should be examined for blood/haemoglobin and protein (by reagent/ dipsticks, Stix test) and for microscopic haematuria and red cell casts. Severely sick, hypotensive and shocked patients may develop lactic acidosis (suggested by an increased anion gap). Those with renal failure will also develop a metabolic acidosis (decreased plasma pH and bicarbonate concentration, reduced arterial PCO_2) and patients with respiratory paralysis will develop respiratory acidosis (low pH, high arterial $PC0_2$, decreased arterial PO_2) or respiratory alkalosis if they are mechanically overventilated.

8.4.7. Evidence of hypoxaemia/respiratory failure

Arterial oxygen saturation will fall. Arterial blood gas analysis will confirm low PO_2, high PCO_2 and low pH. However, arterial puncture is contraindicated when there are haemostatic abnormalities or coagulopathies associated with the risk of bleeding! Arterial oxygen saturation can be monitored non-invasively by finger pulse oximeter.

8.4.8. Electrocardiographic abnormalities

Electrocardiographic abnormalities include sinus bradycardia, ST-T-wave changes and various degrees of atrioventricular block and evidence of hyperkalaemia. Shock may induce myocardial ischaemia or infarction in patients with diseased coronary arteries.

8.4.9. Chest radiography

Chest radiography is important in artificially ventilated patients who are desaturated or when there is doubt about the position of the endotracheal tube. Lung collapse, consolidation or pneumothorax may be revealed.

8.5. Diagnosis

In most patients, the history of the snakebite will be clear-cut and the clinician will have to decide which species was likely to have been responsible and whether there are signs of envenoming. However, some patients may only suspect that they have been bitten by a snake because they experienced a sharp, pricking pain while walking in the dark or through undergrowth, collecting firewood or even while asleep.

8.5.1. Differential diagnosis of snakebite

The differential diagnosis of immediate local pain and one or more puncture marks include thorn pricks, rodent bites and bites and stings from arthropods, such as scorpions and centipedes (and in the water fish bites and spine pricks).

The differential diagnosis of immediate local pain and one or more puncture marks with mild local swelling and severe systemic symptoms includes bites and stings from venomous arthropods (e.g. spiders, scorpions, centipedes).

The differential diagnosis of local swelling and inflammation, sometimes resulting in a hot, red, swollen limb with enlarged regional lymph nodes includes secondary infection (cellulitis) following cytotoxic bites (necrotic arachnidism), penetrating wounds from thorns or rodent or other mammal bites. The interval between the accident and the development of inflammatory swelling is usually more than 24 hours but in cases of Pasteurella multocida infection following mammal (especially dog and cat bites), this interval may be as short as 6-12 hours.

8.5.2. Species diagnosis

Unless the snake has been brought for identification, the snake was photographed or the circumstances of the bite are helpful, the clinician will have to rely on the clinical picture and the results of bedside and laboratory tests to make specialised diagnosis. Clinical features are rarely diagnostic and so the syndromic approach is recommended to guide (antivenom) treatment.

9. FIRST AID AND TRANSPORT TO MEDICAL CARE

9.1. Introduction

In snakebite, incorrect first aid is worse than no first aid. Many first aid measures are aimed at either denaturing the snake venom or to extract it. Neither are possible. First aid should be aimed at slowing down the spread of the venom to avoid systemic complications while at the same time getting the bite victim to a medical facility as soon as possible (if available, use cellular phone and other forms of communication to call for help). If ambulances are available, call and meet them half way.

9.2. Essential first aid procedures (basic measures)

9.2.1. Move the victim to safety

Move the victim away from the area where he or she may be bitten again (if the snake has not been observed slithering off) and remove the snake if it is still attached (which is very rarely the case), but not with your bare hands. Do not try to kill the snake if people can move away, as it wastes time and the snake may bite another person.

9.2.2. Reassure the victim

Reassure the victim who may be terrified. Reassurance is justified as most bites results in negligible or no envenoming at all and, even if the patient is envenomed by a highly venomous snakes, there is usually ample time to transport them to medical care. Death in neurotoxic Elapid bites occurs in hours, cytotoxic Adder or Elapid bites in many hours to days after the bite. Bites by Colubrids usually take 48-72 hours to lead to fatality.

9.2.3. Remove constricting items

In case of swelling, tight items such as jewellery (rings, bracelets, bangles) and clothes would cause harm. Remove any jewellery and clothing from the bitten limb.

9.2.4. Elevate the bitten limb

By elevating the affected limb, the pressure on the limb is reduced which aids in slowing down the spread of the venom somewhat and helps in reducing the pain.

9.2.5. Immobilise the patient.

Immobilise the whole patient, but especially the bitten limb (using a splint or sling). Muscle contractions anywhere in the body, but especially in the bitten limb, will promote absorption and spread of the venom from the bite site via the lymphatics and veins; all movements should be avoided as much as possible.

9.2.6. Transport to medical facility

Transport the victim as quickly as possible to the nearest facility available for medical care. Ideally, the victim is transported by stretcher, in a vehicle, on a bicycle (as passenger) or by boat, or the patient can be carried using the fireman's drill.

9.2.7. Snake species identification

Since species diagnosis is very helpful in determining the correct clinical treatment, the snake should be taken along to the medical facility if it happens to have been killed. However, if the snake is still at large, do not risk further bites and waste time by searching for it. Even snakes which appear to be dead should not be touched with bare hands but carried in a bag or dangling across sticks as some snake species may pretend to be dead and even the severed head of a snake can still inject venom.

Photos of the snake can be very helpful too, but again: only if the snake is visible and no time is wasted searching for it (and of course, without the risk of further bites).

9.3. Incorrect and harmful first aid

Avoid the many harmful and time wasting traditional first aid treatments. Cauterization, incision or excision, tattooing, immediate prophylactic amputation of the bitten limb, suction by mouth, vacuum pumps or "Venom-ex" apparatus, instillation of chemical compounds such as potassium permanganate, application of ice packs (cryotherapy), "black stones" (snake stones) or electric shocks are absolutely contraindicated as they are all potentially harmful and none have any proven benefit. Incisions provoke uncontrolled bleeding if the blood is incoagulable; may damage nerves, blood vessels or tendons; and introduce infections. Suction, chemicals and cryotherapy increase the risk of tissue necrosis.

As all above mentioned measures have no benefit and mostly cause additional harm, valuable time is wasted between the bite and effective and safe clinical care.

9.4. Advanced first aid measures

Apart from the mentioned basic first aid measures, there are several advanced measures that could be taken, which all aim at slowing down the absorption and spread of the venom.

9.4.1. Pressure pad immobilisation

Scientists at Monash University first suggested this alternative to pressure immobilisation. It is a simpler method for attempting to delay venom absorption, using local compression at the bite site. It has been studied by Tun-Pe et al, in victims of Russell's Viper bites in Myanmar. Application of a foam rubber pad directly over the bite wound delayed systemic envenoming, as assessed by measurements of venom antigenaemia. This method appears safe and effective in a preliminary field trial and could be considered in snakebites with neurotoxic envenoming.

9.4.2. Pressure-immobilisation

The pressure immobilisation technique (Sutherland et al, 1979) demands special equipment and training and is not considered practical for general use in Africa. However, it might be feasible in certain specific settings such as zoos, field work programmes, or expeditions where the necessary equipment and highly trained staff could be made available or in highly motivated communities. It is a safe method in the neurotoxic Cobra bites but can't be applied in bites in which cytotoxic or haemotoxic venom was injected. Pressure mobilisation can reduce the speed of spreading of venom of these snake species for a couple hours. However, the effects of even a correctly applied pressure immobilisation bandage are completely diminished if transport over a rough road takes longer than 15 minutes. In Black Mamba bites this technique would be ineffective as venom is transported directly in the blood circulation (see 9.4.3 Tourniquet).

9.4.3. Tourniquet

Tourniquets are a highly controversial tool in snakebite. Unlike the pressure immobilisation, which only slows down the lymphatic system (and not the blood circulation) in the affected limb, the tourniquet brings the flow of lymph and the blood circulation to a stand-still. The World Health Organisation has banned the use of tourniquets for all snakebite because in most snakebite cases they cause more harm than good.

Most venom types are absorbed into the lymphatic system. However, some of the venom particles of the Black Mamba are much smaller and are capable of entering the blood circulation via the capillaries/capillary bed. This is the reason that, in Black Mamba bites, a rapid onset of systemic symptoms and signs are observed. This access means that conventional methods such as pressure immobilisation or pressure pad immobilisation have very limited effect. In case of a Black Mamba bite, the only way to keep a patient alive (if the journey to a medical facility equipped with antivenom or ventilator will exceed 1 hour), is the application of a tourniquet. However, the tourniquet should be broad, to spread the pressure over a larger area and thus avoiding damage to nerves and blood vessels. Do not release the tourniquet until after administration of antivenom and/or the victim is placed on a ventilator.

9.5. Treatment of early symptoms

9.5.1. Analgesics in pain management

Distressing and dangerous effects of early envenoming may appear before the victim reaches a medical facility. Local pain may be intense. Oral paracetamol is preferable to aspirin or non-steroidal anti-inflammatory agents (NSAIDs) which carry the risk of gastric bleeding in patients with incoagulable blood. Severe pain should be treated with opiates but there is a danger of respiratory depression (this is particularly a risk in bites from neurotoxic cobras which also have cytotoxic venom components, especially the Brown Forest Cobra).

9.5.2. Vomiting

Vomiting is a common early sign of systemic envenoming. Lay the patient in the recovery position (on the left side), head down to avoid aspiration. Persistent vomiting can be treated with chlorpromazine by intramuscular injection (25-50 mg in adults, 1 mg/kg in children) or prochlorperazine intramuscular (dose in adults is 12.5 mg). Note that in patients with incoagulable blood, injections can lead to haematomas. Pressure dressing should be applied to all injection sites to avoid oozing. Suppositories are more

appropriate in children. Avoid if <10 kg or < 1 year. Rectally give in 2-3 divided doses: 10-13 kg, up to 7.5 mg/day; 14-17 kg, up to 10 mg/day; 18-40 kg, up to 15 mg/day.

10. EMERGENCY CLINICAL MANAGEMENT OF SNAKEBITE

10.1. Introduction

Snakebite is a medical emergency. Any snakebite victim entering a medical facility should be treated accordingly, even when there are no symptoms. Ideally, all patients bitten by a snake should be assessed by medically trained staff. Uncertainties, such as the snake species responsible, the amount of venom injected and the variable time course for development of signs, demand that the patient be kept under observation for **at least 24 hours**. Medical staff must decide quickly whether their patient has been bitten by a snake, whether there are signs of envenoming and whether antivenom or ancillary treatment is needed.

10.2. Rapid clinical assessment and resuscitation

Rapid clinical assessment and resuscitation are essential. In Zambia, people may arrive at the medical facility between hours and days after being bitten. They may, therefore, show early or late signs of envenoming or its complications. It is essential that all patients with a history of snakebite be assessed rapidly; they may be moribund but still salvageable by appropriate resuscitation.

10.3. Cardio-pulmonary resuscitation

Cardio-pulmonary resuscitation may be needed. This includes clearance of the airway, oxygen administration by face mask or nasal catheters and establishment of intravenous access to allow treatment of hypovolaemic shock with intravenous fluids and medicines.

10.3.1. Vitals check - ABC

Airway, respiratory movement (**B**reathing) and arterial pulse (**C**irculation) must be checked immediately. Vital signs must be recorded; blood pressure, pulse rate and respiratory rate and oxygen saturation.

If the patient is unresponsive and no pulse or respiratory movement is detectable, start cardio-pulmonary resuscitation (CPR) immediately (external cardiac compression, mouth to mask respiration in the ratio 30:2, check electrocardiogram for arrhythmia, defibrillate if appropriate).

In case of respiratory distress/failure: clear the airway (tongue, foreign bodies, etc), lift the chin, give oxygen by face mask or nasal catheters without assisted ventilation and consider the need for endotracheal intubation.

In case of circulatory failure/shock (impaired consciousness, cold cyanosed extremities) / hypotension, systolic pressure less than 80-90 mmHg with rapid pulse: raise the foot side of the bed on blocks (Trendelenburg position), establish intravenous access with one or two wide-bore cannulae and start infusing normal saline (0.9%) or other crystalloid or colloid as soon as possible. If intravenous access seems impossible, consider femoral venous or intraosseous access.

However, avoid excessive fluid replacement as this may result in fluid overload/ pulmonary oedema. Consider the need for a vasopressor medicine such as phenylephrine or noradrenalin or adrenalin.

10.3.2. Consciousness

The level of consciousness should be recorded and monitored if possible, using the semi-quantitative Coma Scale but in patients with advanced neurotoxicity from snakebite this is difficult to assess. These patients appear unconscious because their eyes may be closed (eyelids are paralysed, i.e. ptosis) and they may be unable to speak or move their limbs because of the descending flaccid paralysis, typical of venom-induced neurotoxicity.

10.3.3. Flaccid paralysis

In patients with generalised flaccid paralysis whose ventilation is adequately supported, full consciousness can often be confirmed by asking them to signal, in response to spoken questions or commands, by flexing a finger or toe. These movements may remain possible even when paralysis is virtually complete. In patients with complete ptosis, raising the upper eyelids manually, as they can see their surroundings, is very reassuring and may help rouse them and establish communication. Patients with full general flaccid paralysis may not be able to even flex fingers or even change facial expressions. This is called locked-in syndrome.

10.4. Urgent intervention

Patients bitten by venomous snakes may present with any of the following problems requiring urgent medical attention.

10.4.1. Profound hypotension and shock

Profound hypotension and shock may result from:

- Hypovolaemia, secondary to extravasation of plasma fluid into the bitten limb, external or concealed blood loss, persistent vomiting and failure of adequate oral fluid intake.
- Direct cardiovascular effects of the venom (for example after Adder and Atractaspis bites).
- Auto-pharmacological effects of the venom (activation/inhibition of physiological vasomotor systems, such as the angiotensin-renin-bradykinin system, by venom toxins).
- Anaphylaxis provoked by antivenom given outside of the hospital or, rarely, provoked by venom in those who have been sensitised to previous exposure.

10.4.2. Sudden deterioration from removal first aid contraptions

Sudden deterioration after release of a tourniquet or compression bandage resulting in shock, bleeding or respiratory paralysis. These bands, bandages and ligatures are often removed too hastily by the medical staff before antivenom treatment or ventilation has been initiated and appropriate staff and equipment are on hand in case resuscitation is needed. A venom storm can occur or production of muscle degradation from hypoperfusion may occur. Where, as a first aid measure, a tourniquet was applied using rope, cloth or other, the tourniquet needs replacing. This is done by applying a blood-pressure cuff above the tourniquet. The original tourniquet can then be removed. After administration of antivenom, and / or placement of the patient on a ventilator, the tourniquet can be slowly released. After antivenom (AV) administration, allow the venom to circulate the body for at least 10 minutes before slowly releasing the cuff.

10.4.3. Airway obstruction

Airway obstruction resulting from aspirated vomit or the tongue blocking the upper airway, especially in patients with evolving bulbar paralysis (which occurs in non-spitting cobras) who have not been transported to hospital in the left lateral (recovery) position. Vomiting can be the result of systemic envenoming or indigestion of emetic traditional herbal remedies.

10.4.4. Respiratory failure

Terminal respiratory failure from progressive weakness syndrome (neurotoxic) that has led to paralysis of the respiratory muscles.

10.4.5. Intercranial haemorrhage

Intercranial haemorrhage after envenoming by Dispholidus spp. There will be characteristic lateralizing signs, dysphasia, impaired consciousness (haemorrhagic stroke) or neck rigidity (subarachnoid haemorrhage). Consider a fall with head strike after the bite may precipitate a haemorrhage.

10.4.6. Cardiac arrest

Hours after the bite: cardiac arrest resulting from hyperkalaemia in patients with massive generalised skeletal muscle breakdown (rhabdomyolysis) after neglected cytotoxic bites.

10.4.7. Renal failure

Days after the bite: acute renal failure due to shock and rhabdomyolysis.

10.4.8. septicaemia

Days after the bite: septicaemia from secondary infection of necrotic bite wounds or if incisions made at the site of the bite or from complicating aspiration pneumonia.

11. Management of snakebite at different levels

In rural areas of Zambia where snakebite is most frequent, transfer to a hospital may not be feasible within a reasonable amount of time frame of a few hours. In these cases, a lower-level health facility must cope with the emergency as presented below.

11.1. At community level

1) Check history of snakebite and look for obvious evidence of a bite (fang puncture marks, swelling of bitten part).
2) Immobilise whole patient as far as possible and especially the bitten limb;
3) Mildly elevate limb (at heart level);
4) Give reassurance to keep the patient calm.
5) Arrange transport of the patient to medical care as quickly, safely and passively (patient is to remain immobile) as possible. Ideally the patient should lie in the recovery position with the airway protected to minimize the risk of shock and aspiration of vomit.
6) Discourage time wasting and potentially dangerous traditional treatment.
7) If the snake has already been killed, take it with the patient but ensure safety and avoid direct contact.
8) Contact the medical facility and alert them to prepare for the emergency.

11.2. At a rural clinic, dispensary, zonal referral centre of health post

Different levels of health care can contribute to the management of a snakebite. Since the treatment of severe envenoming is a medical emergency that may require a range of medical skills, equipment, antivenom and other medicines, referral should be to the highest level of care that is readily available.

1) Simple medical assessment: history and simple medical examination – local swelling, painful tender enlarged lymph nodes, persistent bleeding from the bite wound, blood pressure, pulse rate, bleeding (gums, nose, vomit, stool or urine), level of consciousness, droopy eyelids (ptosis) and other signs of paralysis, 20MWBCT, urine examination (appearance, stick testing for blood etc). Identify the snake if brought.
2) Assess need and feasibility to transport the patient to a higher level of health service.
3) Administer tetanus toxoid booster
4) Give analgesia by mouth if required:
    - paracetamol (acetaminophen) (adult dose 1 g – 4 g max in 24 hours; children 15-20 mg/kg, maximum 100 mg/kg/day)
    - A mild opioid (e.g. Tramadol) (adult dose 50-100 mg, max 200 mg / 24 hours; children above 2 years old: 0.5 mg/kg, max 2mg/kg per 24 hours) can be given every 4-6 hours by mouth as required (not aspirin or NSAIDs which can cause bleeding).
    - If proof of skin damage due to cuts applied post-bite is evident or if there are blisters or evident necrosis, broad-spectrum antibiotics are administered.

5) If the necessary skills, equipment, antivenom and other medicines are available, give intravenous fluids to correct hypovolemic shock and when the patient's signs and symptoms meet the criteria, give antivenom. The skills mentioned include the ability to diagnose local and systemic envenoming, set up intravenous infusion or intravenous injection, identify the early signs of anaphylaxis and treat it with intramuscular adrenalin/epinephrine. If no antivenom is available, transport to hospital.

6) If the patient has evidence of respiratory paralysis, give oxygen by mask and transfer to a hospital. It is assumed that assisted ventilation other than by a tight-fitting face mask connected to an anaesthetic (ambu) bag will not be effective at this level.

7) Discourage the use of ineffective and potentially harmful medicines (e.g. corticosteroids, antihistamines and heparin)

11.3. First level (district hospital)

Proceed as in 11.2 plus:

1) More detailed clinical and laboratory assessment including biochemical and haematological measurements, ECG or radiography as indicated.

2) If no antivenom is available, transfer to a hospital that has antivenom or treat conservatively. This may require transfusion of blood or fresh frozen plasma. Consider getting the antivenom, if required, transported to the particular healthcare facility.

3) Reassess analgesia and, if required, consider stronger parenteral opioid medicines as required all with great caution (e.g. subcutaneous, intramuscular or even intravenous pethidine, initial adult dose 50-100 mg; children 0.5-1 mg/kg or morphine: initial adult dose 5-10 mg; children 0.03-0.05 mg/kg). Facilities must be available to provide ventilatory support if necessary.

4) If the patient has blisters or evidence of local necrosis (gangrene), administer suitable/empirical antibiotics and consider surgical debridement of dead tissue. (**Note:** surgical debridement should be done at least 5-7 days after the bite, to ensure clear boundary between dead and viable tissue). *Note: the doctor may determine if and when surgery is conducted.*

5) If the patient has evidence of bulbar or respiratory paralysis, insert endotracheal tube or laryngeal mask airway. If there is evidence of respiratory failure, assist ventilation manually by anaesthetic (Ambu) bag or mechanical ventilator on ASV or SIMV mode.

6) If the patient has evidence of acute renal failure, treat with peritoneal dialysis. If this is not available, transfer the patient to a specialised hospital.

7) If the patient is bleeding severely or is already severely anaemic, consider blood and/or clotting factors transfusion.

8) Simple rehabilitation/physio (exercising of the bitten limb).

11.4. At the second level, third level and fourth level hospital

Proceed as in 11.2 and 11.3 plus:

1) More advanced surgical management of local necrosis (e.g. split skin grafting after

debridement)

2) More advanced investigations, including bacterial cultures and imaging (CT scan) as indicated.
3) If the patient has evidence of acute renal failure peritoneal or haemodialysis or haemofiltration.
4) Rehabilitation by physiotherapist

12. ANTIVENOM

12.1. Introduction

Antivenom is the only effective treatment or antidote for snakebite. Antivenom is raised in large domestic animals (usually horses, sheep, camels or donkeys), by hyper-immunising them against a single snake venom (producing a monovalent antivenom, such as the monovalent Boomslang antivenom) or against venoms of several species of snakes whose bites are common and can potentially be life threatening in humans. Several different species can be covered in some polyvalent antivenoms.

Antivenom is only produced to neutralise the venom of snake species which could cause serious, life threatening harm to humans. In Zambia, the venom of Night Adders (Causus spp.), Stiletto Snakes (Atractaspis spp.) and Garter Snakes (Elapsoidea spp.) are not included in the venom mix for antivenom production (WHO 2023), (Van Driel, 2022).

12.2. Antivenom production

The venom of a single species of snake may vary in composition and antigenicity. As a result, pooled venom from many individual specimens of each snake species should be used for antivenom production. These individuals should come from different parts of the geographic range and should include some younger (smaller) specimens to take these factors into account.

After host animals have completed the immunisation schedule, plasma is collected, preferably by plasmapheresis (so that the red blood cells can be returned to the donor animal) and is passed through several processes designed to produce either refined whole IgG antibodies or IgG antibody fragments such as F(ab')2 or Fab, which are free of other plasma proteins such as albumin, fragments such as Fc, aggregates (a major cause of antivenom reactions), pyrogens and microbes. It is then either lyophilized or stored as a liquid.

Lyophilized antivenom has a longer shelf life and is cheaper and does not require cold chain storage but general medicine storge standards. Liquid antivenom in glass ampoules should be stored at 2-8 °C (not frozen).

Polyvalent antivenom is derived from animals hyperimmunized against the venoms of several snake species (those to be of the greatest medical importance in the area where the antivenom is intended to be used), while monospecific antivenom is derived from animals that are immunised against the venom of one snake species.

Polyvalent antivenom allows for syndromic management of snakebites which is especially helpful in cases where the snake that delivered the bite is not known (which is in most cases). However, with the venom of more species in the mix, the required quantities of antivenom are significantly higher than is the case with monovalent antivenom. There is also increased antigenicity or risk of allergy with polyvalents because there are more different types of antibodies in them.

12.3. Antivenom use

Antivenom neutralises a fixed amount of venom. Since snakes inject the same amount of venom into adults and children, the same dose/volume of antivenom must be administered to children as to adults. There is no paediatric dose!

Antivenom can be effective provided the venom is still active in the patient's body, causing symptoms of systemic envenoming. These may be persistent for several days or even weeks after the bite (e.g. incoagulable blood).

12.4. Precautions

As antivenom is scarce, expensive and might have potentially serious side effects, it should be administered only if there is a threat to life or limb. Administration may be associated with acute life-threatening adverse reactions (anaphylaxis), pyrogenic (feverish) reactions, or late immune complex disease (serum sickness). The former may be treated (and prevented) with epinephrine (adrenalin) and the latter with antihistamines and corticosteroids.

12.5. Producers and suppliers

There are currently two polyvalent antivenoms available for Zambia. Both cover bites from the snake species: Black Mamba, Puff Adder, Gaboon Adder and all six cobra species.

The gold standard in antivenom was always the SAIMR antivenom from the South African venom Producers (SAVP). Recently, the PANAF antivenom from Premium Serums and Vaccines (India) has been approved as safe and effective by the World Health Organisation. This antivenom is effective, has so far shown indication of a highly reduced risk of adverse reactions due to its modern manufacturing process and is available on the Zambian market via the International Drug Company Limited.

Table 3: Antivenom

SAVP Polyvalent antivenom	PANAF Polyvalent Antivenom
$ 250 per ampoule	$ 60 per vial
Requires cold chain	Doesn't require cold chain
Shelf life 36 months	Shelf life 48 months
Liquid	Lyophilised
Shortage in Zambia	Available in Zambia
High incidence rate of adverse reactions, including anaphylactic shock	Highly reduced incidence rate of adverse reactions
Black-necked Spitting Cobra not included but has limited effectiveness	Black-necked Spitting Cobra included

13. ANTIVENOM TREATMENT

13.1. Appropriate use of antivenom

The most important and urgent decision to be made concerning any patient bitten by a snake is whether or not to give antivenom, the only specific antidote to venom.

There are various reasons why antivenom should never be used routinely, indiscriminately or carelessly, but only when indicated. The reasons are discussed below.

- All commercial antivenoms carry a risk of potentially dangerous early anaphylactic reactions.
- Antivenom is not always necessary; some patients are bitten by non-venomous snakes and many of those that are bitten by venomous snakes are not envenomed.
- Antivenoms have a defined range of specific and para-specific neutralising effect but are useless for venoms outside that range.
- Antivenom is very expensive, usually in short supply and has a limited shelf life.
- The healthcare facility must be able to handle anaphylaxis.

13.2. Indications for antivenom

Antivenom is indicated in all cases of systemic and severe local envenoming. In the table below, the antivenom indications are included per syndrome.

Table 4: Antivenom indication

Painful Progressive Swelling syndrome (PPSS)		
Extensive or rapidly progressive swelling: if the swelling reaches:	Bite on foot	Bite on hand
	Ankle within 1 hour	Wrist within 1 hour
	Knee within 3-4 hours	Elbow within 3-4 hour
	Groin within 8 hours	Shoulder within 8 hours
	Torso	Torso
Swelling progression is > 10 cm / hour		
Progressive Weakness Syndrome (PWS)		
Neurotoxicity		
5 Ps Pain at bite site Paraesthesia of tongue and lips Ptosis Pupillary abnormalities Descending flaccid paralysis	5 Ss Swallowing difficulties Slurred Speech Sweating Secretions Salivation	
If there is 1 P and 2 Ss or 1 S and 2 Ps observed, antivenom should be administered.		

Further, if descending flaccid paralysis has set in or in case of cardiovascular abnormality; marked respiratory effort or lack thereof, hypotension, shock, arrhythmia, abnormal electrocardiogram, antivenom is administered.
Bleeding Syndrome (BS)
Spontaneous systemic bleeding
Incoagulable blood (20MWBCT)

13.3. Contraindications to antivenom

There is no absolute contraindication to antivenom when a patient has a life-threatening systemic envenoming. However, patients with an atopic history (severe asthma, hay fever, etc) and those with a history of previous reactions to equine antisera (e.g. anti-tetanus serum) have an increased risk of severe reactions. Pre-treatment with subcutaneous adrenaline is justified to prevent or diminish the reaction. There is no time for even rapid desensitisation.

13.4. Hypersensitivity testing

Intradermal, subcutaneous or intraconjunctival tests with diluted antivenom are NOT predictive of early anaphylactic or later serum sickness type antivenom reactions and should no longer be used. The reason is that most of these reactions are not IgE based, type hypersensitivity reactions of the kind that might be predicted by prick skin tests or radioallergosorbent tests (RAST). Most early anaphylactic reactions to antivenom result from direct activation by aggregates of IgG or its fragments.

13.5. Timing of antivenom treatment

Antivenom should be administered as soon as possible once signs and symptoms of systemic or severe local envenoming are evident (see table above). It is almost never too late to try antivenom treatment for persistent systemic envenoming. However, the earlier the better and the least amount is required. Administration to avoid or reduce tissue damage resulting from cytotoxic venom (PPSS) is futile from 6 hours after the bite, as by then the damage has been done. After six hours, antivenom would only have influence on potential systemic envenoming or to avoid complications such as a Puff Adder bite showing heamotoxic systemic effects where swelling and tissue damage is obvious but over 6 hours post bite.

13.6. Antivenom administration

Antivenom is most effective when given intravenously. Freeze dried (lyophilized) antivenom should redissolve quickly (less than 10 minutes) in sterile water. Difficulty dissolving means faulty manufacture or expired antivenom. Antivenom is diluted in normal saline to a total volume of 200 ml and is given by intravenous injection over 30-60 minutes at a rate of 200-400 ml/hour. Instructions for reconstitution and/or addition to a bag of suitable dilutant fluid for infusion will be based on the insert or manufacturer guidelines or local intravenous reconstitution policy for administration.

The incidence and severity of adverse reactions was the same with these methods. The advantage of intravenous infusion is ease of control, but intravenous “push” injection requires less expensive equipment, is quicker to set up and ensures that someone remains at the patient’s bed site during the crucial first 10-15 minutes after the start of the treatment, when early reactions are most likely to occur.

When intravenous administration is impossible, antivenom can be given, as a last resort, by deep intramuscular injection at multiple sites in the anterior and lateral

aspects of the thighs, followed by massage to promote absorption and application of pressure dressings to limit haematoma formation. **Intramuscular injection is not ideal and not generally recommended** as absorption is very slow. Absorption from intragluteal injection is very unreliable. There is a limit to the volume of antivenom that can be given by this route and there is a risk of haematoma formation in patients with incoagulable blood.

Based on experiences in South Africa (Hardcastle, 2023), the recommendation on antivenom administration, with possible adverse reactions in mind are as follows:

1) Premedicate with 0.25 ml adrenalin subcutaneously
2) Administer antivenom
3) Monitor response, especially adverse reactions (Stridor!)
4) If adverse reaction occurs, halt administration of AV and administer 0.5 ml adrenalin intramuscular.
5) Once adverse response dissipates, continue antivenom administration.
6) Monitor for adverse reaction. If no adverse reaction occurs, continue AV administration. If an adverse reaction re-occurs, consider ending AV administration and treat symptomatically.

13.7. Antivenom dosage

In the table below the recommended dosage of antivenom per snake species or group of snake species is given. The initial dose, however large, may in some cases not be enough to neutralise the depot of injected venom (especially if copious amounts were injected) at the site of injection or prevent redistribution of venom from the tissues. Patients should therefore be observed for several days, even if they show good clinical response to the initial dose of antivenom.

Table 5: Antivenom dosage

English name	Antivenom type	Recommended minimal initial dose SAIMR	Recommended initial minimal dose PANAF
Puff Adder	Polyvalent	50 ml	50 ml
Gaboon Adder	Polyvalent	50-200 ml	50 ml
Black-necked Spitting Cobra	Polyvalent	50 ml	200 ml
Mozambique Spitting Cobra	Polyvalent	50 ml	200 ml
Black Mamba	Polyvalent	80-120 ml	100 ml
Brown Forest Cobra Snouted Cobra Anchieta's Cobra	Polyvalent	80-120 ml	200 ml
Boomslang	Monovalent	20 ml	n/a

For both polyvalent and monovalent: 1 ampule is 10ml

Continuing absorption of venom from the bite-site depot and redistribution of venom from the tissues may cause recurrent neurotoxicity or haemostatic problems after therapeutic antivenom has been eliminated. This process may be enhanced by resuscitation: correction of hypovolaemia and restoration of blood pressure may improve tissue perfusion at the bite site, resulting in further absorption of venom from the site of the injection. The average initial dose of antivenom for treating bites by a particular species may vary throughout the geographic range.

Response to antivenom treatment

Neurotoxic signs often change slowly, after several hours, or unconvincingly. Cardiovascular effects such as hypotension and sinus bradycardia (for example after B. arietans bites) may respond within 10-20 minutes. Spontaneous systemic bleeding usually stops within 15-30 minutes and blood coagulability is restored within about 6 hours provided the adequate amount of antivenom is administered. The 20MWBCT should be used to monitor the dose of antivenom in patients with coagulopathy. If the blood remains incoagulable after 6 hours, the initial dose should be repeated and so on, every 6 hours, until blood coagulability is restored.

It must be emphasised that the administration of polyvalent antivenom in the acute phase of neurotoxic snake envenoming will usually not prevent progression of neurotoxic effects, most noticeably respiratory paralysis and consequently the patient will not survive without life support. Respiratory support is the only life-saving treatment modality in neurotoxic snake envenoming. However, intravenous administration of adequate doses of antivenom will decrease the time course of muscle paralysis and recovery. Neurotoxic Zambian snakes do not damage the synaptic motor end plates such as the Cape cobra and a smaller adder (Berg Adder, Bitis Atropos) found further south on the continent than Zambia. Similarly, in cytotoxic envenoming, administration of polyvalent antivenom will not reverse but may limit future tissue damage. On the other hand, the haemostatic effects of Boomslang envenoming are rapidly reversed by its specific antivenom at *any time* after the bite.

13.8. Antivenom reactions

13.8.1. Early reactions

Early reactions begin 3-60 minutes after starting intravenous administration of antivenom. Cough, tachycardia urticaria (especially of the scalp), fever, nausea, vomiting, and headache are common symptoms. More than 5% of patients with early reactions develop systemic anaphylaxis: hypotension, bronchospasm and angio-oedema. However, there are few reports of deaths reliably attributed to these reactions. The incidence of these reactions varies from 3-54% depending on the manufacturer, refinement, dosage, and route of administration. The vast majority of early anaphylactic antivenom reactions are not immediate type I hypersensitivity reactions but result from complement activation by aggregates of IgG or its fragments present in the antivenom.

Adrenaline (epinephrine) 0.1% (1 in 1000) should be given intramuscularly in a dose of 0.5 – 1.0 ml for adults, 0.01 mg/kg for children. This should be followed by an intravenous injection of an H1 antagonist (antihistamine) such as chlorpheniramine maleate (10 mg for adults, 0.2 mg/kg for children) or promethazine (25 mg intramuscularly in adults; contraindicated in children < 2 years of age; in children 5-10 years: 6.25-12.5 mg and in children 10-16 years old: 12.5-25 mg intramuscularly).

13.8.2. Pyrogenic reactions

Pyrogenic reactions result from pyrogenic contamination of the antivenom during the manufacture. They begin within 1-2 hours after administration. There is an initial chill with cutaneous vasoconstriction, gooseflesh and shivering. Temperature rises sharply during the rigors and there is intense vasodilation, widening of the pulse pressure and eventually fall in mean arterial pressure. In children, febrile convulsions may occur at the peak of the fever. Patients should be laid flat to prevent postural hypotension. Their temperature should be reduced by fanning, tepid sponging and antipyretic medicines such as paracetamol (15 mg/kg) given by mouth or via nasogastric tube.

13.8.3. Late reactions

Late (serum sickness type) reactions occur 5-24 (average 7) days after antivenom treatment. There is itching, urticaria, fever, arthralgia, periarticular swelling, proteinuria and sometimes neurological symptoms. Antihistamines are used for milder attacks but in severe cases, including those with neurological symptoms, a short course of prednisolone should be given.

13.9. Specific issues about antivenom

13.9.1. Antivenom in pregnancy

After envenomation, pregnant patients may develop uterine vasoconstriction during compensated hypovolaemic shock, even though maternal vital signs may appear normal. As a result, the foetus may become hypoxic while the mother has normal tissue oxygenation. Adequate fluid resuscitation and oxygenation of the mother are therefore essential. Uterine and foetal heart rate monitoring are recommended to detect asymptomatic premature labour and foetal distress. If there is coagulopathy, retroplacental haemorrhage may occur, causing high maternal and foetal mortality.

Early, adequate doses of antivenom are therefore essential if there is any suggestion of anti-haemostatic disorders. Labour (for example induced by a snakebite) in a woman with snake venom-induced haemostatic abnormalities may be complicated by massive post-partum haemorrhage.

13.9.2. Antivenom in children

Venous access may be a challenge. The intraosseous route may be required. Due to high venom to body mass ration both morbidity and mortality are higher than in adults. Swelling travels faster up their bodies and coagulopathy occurs sooner as does weakness and respiratory failure due to a faster evolution of envenomation. Frequent reassessment of snake bitten children is necessary. Should the indication for antivenom administration be followed, then children receive antivenom sooner and more frequently than adults, but in the same initial dose quantities as adults.

13.10. Snakebite and traditional practices

Traditional practices and healers are held in high esteem in most African communities and play a large role in the village-based treatment of many illnesses, including snakebite.

There is need to educate traditional practitioners in evidence-based snakebite management and to make use of the trust and belief community members have in them.

It should be emphasised that in many cases of snakebite, traditional healing procedures have resulted in delayed transfer of victims to health facilities, thus increasing the risk of death and permanent sequelae. Traditional healers should therefore be encouraged not to delay the victim's transfer to a health-care facility. They should further be discouraged from engaging in practices that may endanger lives, especially where efficacy has not been established. These include incisions, applying black stones and tight tourniquets, and administering unproven herbal remedies.

To date, no herbal or traditional remedy for snakebite has proven effective in a clinical trial. To validate efficacy of traditional treatments, properly designed scientific research should be instigated.

14. Ancillary treatment

14.1. Treatment of local envenoming

14.1.1. Tetanus toxoid

It is appropriate to give a prophylactic booster dose of tetanus toxoid to all snakebite victims where skin was breeched. This is also a safe and useful placebo for those who are (possibly) not envenomed but need the reassurance of being given some sort of therapy.

14.1.2. Wound infection

Although most local effects of snakebite are attributable directly to cytotoxic and other activities of the venom itself, the bite may, in very rare occasions, introduce bacteria and the risk of local infections greatly increases if the wound has been incised with an unsterile instrument, tampered with in some other way or if it contains necrotic tissue. The potential risk of tetanus must be addressed by boosting immunity. However, this must be delayed until after resolution of any coagulopathy to avoid unpleasant haematomas.

The pattern of bacterial flora may vary but is usually Gram-negative aerobic bacteria (Enterobacteriaceae) or Gram-positive aerobic cocci (Staphylococcus and Streptococcus). Antibiotic treatment should be delayed until there are definite signs of infection, such as a hot, fluctuant local swelling resembling an abscess, when blisters form or if the wound is necrotic. Appropriate blind antibiotic treatment is with amoxicillin or Flagyl with clavulanic acid. Subjective to the severity of the condition, upscaling may be required. Prophylactic antibiotics are not appropriate unless the wound has been grossly interfered with or is frankly necrotic.

14.1.3. Care of the bitten limb

The wound should be cleaned with an antiseptic. Blisters and bullae should be left intact unless there are signs of infections. Snake bitten limbs should be nursed in the most comfortable position, in a slightly elevated manner.

The wound should be checked regularly for evidence of necrosis: blistering, blackening or depigmentation of the skin, loss of sensation and a characteristic smell of putrefaction.

14.1.4. Debridement of necrotic tissue

Necrotic tissue should be debrided by a qualified medical practitioner under general or local anaesthesia. However, this is preferably done 5-7 days after the bite time to ensure clear boundary between dead and viable tissue. Skin appearance may be deceptive, for necrosis can undermine apparently normal skin. Large areas may be denuded of skin; recovery can be accelerated by applying split skin grafts immediately after debridement, provided that the wound is not infected. Debrided tissue, serosanguinous discharge and pus should be cultured and the patient treated with appropriate antimicrobials. Fluctuant areas, suggestive of an underlying abscess, should be aspirated and opened for drainage. Inexperienced surgeons may mistake bruised for necrotic muscle. In some cases, muscle fibres damaged by snake venom myotoxins (Phospholipases A_2) may regenerate if the muscle is left intact and so debridement should be restrained.

14.1.5. Compartment syndrome

Compartment syndrome is an uncommon and over-diagnosed complication. However, if they occur, they require urgent attention. The clinical appearance of snake-bitten

limb often suggests compartment syndrome as the signs are very similar to those of painful progressive swelling syndrome. There may be severe pain, tense, tender swelling, cold, cyanosed anaesthetic skin, pain on passive stretching of the muscles and apparently absent pulses. However, these appearances are usually misleading and when the intercompartmental (tissue) pressure is measured directly (for example with a Stryker monitor) pressures are found to be below the threshold of danger for ischaemic necrosis of the intercompartmental muscles.

Compartment syndromes of hands and feet tend to self-decompress via the bite site. If a compartment syndrome in a limb is suspected, the pressure should be measured directly as this is the only reliable way of confirming raised intra-compartmental pressure and justify fasciotomy.

However, many surgeons seem reluctant to measure the pressure. The normal intercompartmental pressure is 0-10 mmHg. An intercompartmental pressure of more than 45 mmHg is usually associated with compartment syndrome but there may be a risk of intra-compartmental ischaemia at lower pressures if mean arterial pressure (perfusion pressure; **mean arterial pressure = diastolic pressure + 1/3 [systolic -diastolic pressure**] is reduced, for example, in an elevated limb.

If the pressure is raised but mean arterial pressure is more than 30 mmHg higher than compartmental pressure, the patient may be treated conservatively for one hour with steep elevation of the affected limb combined with the appropriate antivenom and mannitol 100 g (500ml of 20% solution in adults, less for children).

Should conservative treatment fail, open full fasciotomy should be performed, providing there is no coagulopathy or gross thrombocytopenia. However, animal studies have shown that fasciotomy is ineffective in saving envenomed muscles.

Provided that adequate antivenom treatment is given as soon as possible after the bite, fasciotomy is rarely, if ever, needed. However, bites involving the finger pulps are frequently complicated by necrosis. Expert surgical advice should be sought, especially if the thumb or index finger is involved.

14.1.6. Vessel entrapment syndrome

This is uncommon and is usually due to massive swelling compressing the femoral vessels beneath the inguinal ligament. It presents as a cool, blister-covered leg with absent distal pulses. Provided there is no coagulopathy and the leg is still viable, division of the inguinal ligament and multiple fasciotomies are required.

14.1.7. Nerve entrapment

Nerve entrapments (e.g. median carpal tunnel syndrome, femoral nerve i.e. meralgia paraesthetica) are treated conservatively.

14.1.8. Muscle haematomas

Muscle haematomas (E.g. iliacus haemorrhage causing unilateral weakness of hip flexion as patient with haemophilia) are treated conservatively after correction of the haemostatic disorder with antivenom and, in cases, clotting factors.

14.1.9. Vascular thromboses

Deep vein thrombosis may be suspected when the swelling of a leg fails to subside after 2-3 weeks. Arterial and venous thromboses are rare complications reported after bites by Adders (Puff Adder, Gaboon Adder).

Arterial thrombosis is suspected when agonising pain rapidly develops in a limb, there is a sharp demarcated cold distal area and arterial pulses prove undetectable even by doppler. Once haemostatic abnormalities are corrected, the limb might be investigated by arteriography with the possibility of angioplasty, thrombectomy or reconstructive arterial surgery.

14.1.10. Amputation

Amputation of doomed digits and limbs is the last resort but the decision must be made and agreed upon by the patient and family before life-threatening septicaemia, gas gangrene or tetanus supervenes.

14.1.11. Late complications of local envenoming

Late complications may include incapacitating and deforming hypertrophic and keloid scars, muscle and tendon contractures, equinus deformity, destroyed or arthrodesis in joints, osteomyelitis, chronic ulceration with or without malignant change and consequences of intra-compartmental syndromes, such as Volkmann's ischaemic contracture. These are treated according to standard guidelines.

14.2. Treatment of systemic envenoming

14.2.1. Haemostatic abnormalities

Once adequate doses of antivenom have been given to neutralise venom anti-haemostatic factors, recovery of normal haemostatic function may be accelerated by giving fresh whole blood, fresh frozen plasma, cryoprecipitates or platelet concentrates. However, this is unnecessary unless trauma such as imminent childbirth or emergency surgery are anticipated.

NB: Heparin and antifibrinolytic agents should never be used in snake bitten patients. Heparin doesn't inhibit the abnormal thrombin generated by snake venoms and it exaggerates, sometimes fatally, the haemostatic disturbances.

14.2.2. Neurotoxic envenoming

The airways must be protected in patients developing bulbar and respiratory paralysis. Once secretions begin to pool in the pharynx, a cuffed endotracheal tube or laryngeal mask airway must be inserted.

Non-invasive assisted ventilation by special facemask has proven difficult to use in snakebite patients. Mechanical ventilation is usually required for only a few days but exceptionally patients have recovered after 10 weeks of mechanical ventilation and 30 days of manual ventilation by ambu-bag or anaesthetic bag. Antivenom can't be relied upon to reverse neurotoxicity or prevent its progression to respiratory paralysis.

14.2.3. Anticholinesterases

Neuromuscular blockade by post-synaptic neurotoxins may be partly overcome by administration of anticholinesterase medicines. Neostigmine (prostigmine, Prostigmin$^{tm)}$ has been used successfully to treat patients with severe neurotoxic envenoming following bites by Naja annulifera (Snouted Cobra), Naja subfulva (Forest Cobra) and Dendroaspis viridis (Green Mamba) and in a patient envenomed by Naja Nivea (Cape Cobra) there was improvement in motor response to command and electromyographic response after administration of this medicine.

All patients with neurotoxic symptoms, except for those thought to have been bitten by Black Mambas, should be given anticholinesterase test. Ideally, edrophonium is used because the "tensilon" (edrophonium) test is used in patients with suspected

myasthenia gravis. However, edrophonium is rarely available but neostigmine and glycopyrronium are widely used by anaesthetists to reverse non-depolarising (competitive) neuromuscular blockade.

Atropine sulphate (0.6 mg for adults, 50ug/kg for children) is given by slow intravenous injection to block the unpleasant and potentially serious muscarinic effects of acetylcholine such as colic. This is followed by edrophonium chloride (10 mg in adults, 0.25 mg/kg in children) by slow intravenous injection. If edrophonium chloride is not available, use neostigmine bromide or methyldulphate (Prostigmine) by intramuscular injection (0.02 mg/kg for adults, 0.04 mg/kg for children) together with atropine as above.

Patients who respond convincingly, by demonstrating increased muscle power or improvement in ptosis, can be maintained on neostigmine (0.5-2.5 mg every 1-3 hours up to 10mg/24 hours maximum for adults and 0.01-0.04 mg/kg every 2-4 hours for children) by intramuscular or subcutaneous injection together with atropine as above. It is important to note that atropine must always be given concurrently with cholinesterase inhibitors (e.g. neostigmine) in order to prevent serious muscarinic effects.

Since Black Mamba venom contains an anticholinesterase (fasciculin), it is theoretically inappropriate to use the Tensilon test in suspected or proven victims of Black Mamba bites.

14.2.4. Hypotension and shock

Specific antivenom can reverse the direct myocardial and vasodilating effects of some venoms, but in patients who have leaked large amounts of blood and plasma into the bitten limb and elsewhere, a plasma expander is needed to correct hypovolaemia. As an emergency, the foot of the bed can be raised to improve cardiac filling while an intravenous infusion is set up. Ideally, central venous pressure should be monitored to prevent fluid overload. Other causes of hypotension, such as massive, concealed haemorrhage or effects of venom toxins in the physiological mechanisms controlling blood pressure (e.g. ACE-inhibiting and bradykinin potentiating peptides) should be considered.

14.2.5. Renal failure

Acute renal failure may be caused by haemorrhage, ischaemia resulting from hypotension, disseminated intravascular coagulation and renal vasoconstriction, pigment nephropathy caused by haemoglobinuria or myoglobinuria, direct nephrotoxicity and immune complex glomerulonephritis caused by serum sickness reactions to antivenom.

Renal failure is not a common complication of envenoming by any Zambian snake, but cases have been reported after bites by Puff Adder, Twig Snake species and Boomslang species. This complication can occur in any case of severe envenoming especially if there has been prolonged profound hypotension. If the urine output falls below 400 ml in 24 hours, central venous pressure should be monitored, and a urethral catheter inserted. Cautious rehydration with isotonic fluid (to increase the central venous pressure to +10 cmH_2O) can be followed by high dose of frusemide (up to 100 mg intravenously) and finally dopamine (2.5 ug/kg/minute) by continuous infusion into a central vein. If these measures fail to increase urine output, patients should be managed conservatively until dialysis is indicated.

14.3. Snake venom ophthalmia

The two spitting Cobra species in Zambia (Black-necked Spitting Cobra and Mozambique Spitting Cobra) can cause intense conjunctivitis and bullous corneal erosions complicated by secondary infection, anterior uveitis, corneal opacities and permanent blindness. It is a chemosis reaction.

First aid consists of irrigating the eye or other affected mucous membrane as soon as possible with copious amounts of water or any other bland fluid for at least 15 minutes. To facilitate irrigation, a single application of local anaesthetic eye drops to overcome tightly closed eye lids may be used. Unless a corneal abrasion can be excluded by a slit lamp examination or a fluorescein staining, the patient should be treated as for a corneal injury with a topical antimicrobial agent (tetracycline and chloramphenicol).

Topical or systemic antivenom treatment is not indicated. Adrenalin (0.1%) eye drops or 10% phenylephrine eye drops relieve the burning sensation instantaneously. However, these eye drops can cause a rise in blood pressure and tachycardia and should be used with caution in older patients.

14.4. Snakebite in pregnancy

During the last trimester of pregnancy avoid the supine hyposensitive syndrome by resuscitating the mother while she sits up or place her in the left lateral decubitus position or raise the left hemipelvis.

Envenoming by the large Adders may cause ante-partum haemorrhage and precipitate miscarriage at any stage of pregnancy. Pregnant women should be questioned about and examined for evidence of vaginal bleeding and, in the third trimester, foetal heart rate and uterine contractions should be monitored. Foetal bradycardia may indicate foetal envenoming. Late deceleration of foetal heart rate in relation to uterine contractions indicates foetal distress. Envenomed pregnant women are at risk of ante- and post-partum haemorrhage, premature labour, foetal distress and stillbirth. Early adequate antivenom treatment is indicated, its benefits outweighing the risks to the mother and foetus e.g. of anaphylactic antivenom reactions.

14.5. Snakebite in children

Children may be more prone to morbidity and mortality due to the disadvantageous venom-to-body mass ratio. The indications for antivenom arise sooner, which tends to mitigate this. The dose of antivenom is the same as for an adult.

14.6. Snakebite in the elderly

The elderly are not different from younger patients when it comes to snakebite. However, they may be more prone to hypotension, therapeutic fluid overload and adverse effects of adrenaline (epinephrine) and are more likely to be suffering from intercurrent and unrelated chronic illnesses such as hypertension and other cardiovascular diseases, chronic obstructive bronchitis and diabetes mellitus. These possibilities should be considered in treatment.

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ANNEX 1

Venomous snakes of Zambia, not included in chapter 2 but which can inflict a harmful bite. Classification, distribution, habitat and clinical

Elapidae – Cobras, Mamba and Garter Snakes

The Elapids are generally long and slender snakes. In Zambia, they include the Cobras and the Black Mamba.

Genus and species	English name	Distribution	Clinical toxinology
Naja annulata stormsii	Storms Water Cobra	Shores of Lake Tanganyika and lake Mweru	Potently neurotoxic and cytotoxic. No recorded bites.

Viperidae – Adders and Vipers.

There is no difference between adders and vipers. They are two names for the same snakes in the family Viperidae. In Zambia, this family contains four genera: Bitis, Atheris, Proatheris and Causus. Several of the species in the Bitis and Causus genera are common. The species in the genera Proatheris and Atheris are rare, seldom encountered and do not feature in snakebite in Zambia. All snakes in this family have a potent cytotoxic venom, in the Atheris and Proatheris species combined with potent and fast working heamotoxins. They all deliver venom through enlarged front-placed fangs which can hinge in position to deliver a bite. With exception of the Causus species, they all have a very stocky build with a large head and distinct, thinner neck. They are mostly vividly patterned.

Atheris - Bush Vipers and Proatheris – Floodplain Vipers.

Relatively small, stocky snakes with a big head. They are usually found in or under bushes. Their venom presents as cytotoxic but recent study revealed that it is also highly haemotoxic, making these snakes potentially deadly (Frye, 2022).

Genus and species	English name	Distribution	Clinical toxinology
Atheris katangensis	Katanga Bush Viper	Gallery forests, sometimes adjacent woodland	Cytotoxic and potently haemotoxic
Atheris rungweensis	Rungwe Bush Viper	In bushes or on the ground in montane forests	Cytotoxic and potently haemotoxic
Proatheris supercilliaris	Floodplain Viper	Floodplains and adjacent grasslands	Cytotoxic and potently haemotoxic

Causus – Night Adders

Relatively small adders that don't exceed a meter. Lack the typical broad head. Usually, a prominent V on the head, facing forward. Unlike all other adders and vipers, Night Adders have enlarged, symmetrically placed head scales and the body scales are smooth. Predominantly terrestrial but can also be found in small bushes.

Causus bilineatus	Two-striped Night Adder	Marshy habitats, moist savanna and forest-savanna mosaic	Cytotoxic. Local pain, swelling, necrosis, lymphangitis
Causus lichtensteinii	Forest Night Adder	Predominantly forests; swamp forests, degraded habitats	Cytotoxic. Local pain, swelling, necrosis, lymphangitis
Causus rasmusseni	Rasmussen's Night Adder	Moist miombo woodland	Cytotoxic. Local pain, swelling, necrosis, lymphangitis

ANNEX 2

Essential medicines and supplies for managing snakebite at a district hospital.

For health workers to deal effectively with cases of snakebite, it is important that certain essential supplies are available in their health facilities and that they are trained in the best methods for using them. Below is a list of recommended essential supplies for the management of snakebite. It can be modified to suit the needs of local health workers, depending on their specific training and aptitude in dealing with snakebite.

1) Antivenom (with sterile water for reconstituting lyophilized antivenom).
2) Tetanus toxoid.
3) Epinephrine (adrenaline) injection 0,1% (1:1,000) (1 mg/ml).
4) Parenteral antihistamine and hydrocortisone.
5) Pain killers, e.g. paracetamol, codeine, mild opioids such as tramadol. NOT aspirin or non-steroidal anti-inflammatory agents.
6) Antipyretics (paracetamol tablets, syrups and suppositories).
7) Local anaesthetic agents (1-2% lidocaine).
8) Intravenous (IV) fluids e.g. normal saline (0.9% NaCl).
9) Vasopressor drugs, e.g. phenylephrine, adrenaline, nonadrenalin.
10) Atropine and edrophonium or neostigmine (Prostigmine) for “tension test”.
11) Fresh frozen plasma or cryoprecipitates.
12) Blood platelets.
13) Oxygen cylinders with spanners, gauges, necessary connectors.
14) Antibiotics (chloramphenicol, benzylpenicillin, flucloxacillin, metronidazole, gentamicin, amoxicillin-clavulanic acid).
15) Laryngoscope (adult and paediatric sizes) with spare batteries and bulbs.
16) Cuffed endotracheal tubes (various sizes).
17) Ambu bag with connectors to endotracheal tube and face mask that fit.
18) Face masks and oral airways.
19) Suction apparatus and catheters.
20) Urine dip sticks.
21) New, clean dry glass vessels for 20WBCT.
22) Syringes, needles, intravenous cannulae.
23) IV administration set.
24) Sticking plaster.
25) Scissors.
26) Splints.
27) Urethral catheters.
28) Bathroom type weigh scales.
29) Stretchy, elasticated crepe bandage and splint or, better: smart bandage.

LIST OF PARTICIPANTS FOR THE DEVELOPMENT OF THE GUIDELINES

SPECIAL THANKS GO TO THE FOLLOWING FOR THEIR DEDICATED WORK IN THE DEVELOPMENT-GUIDELINES:

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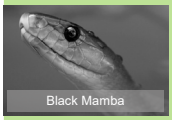
REPUBLIC OF ZAMBIA

MINISTRY OF HEALTH

GUIDELINES FOR THE MANAGEMENT OF SNAKEBITE IN ZAMBIA

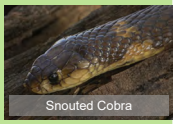
SNAKES

NEUROTOXIC

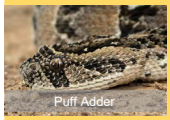

Black Mamba

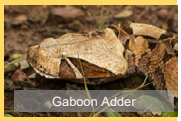

Brown Forest Cobra


Anchieta's Cobra

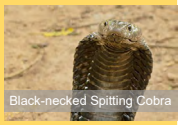

Snouted Cobra

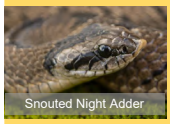
CYTOTOXIC


Puff Adder

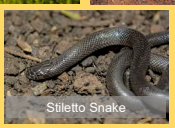

Gaboon Adder


Mozambique Spitting Cobra

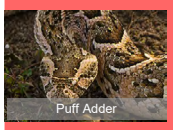

Black-necked Spitting Cobra

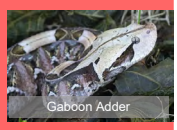

Snouted Night Adder

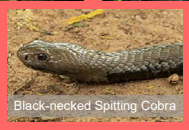

Rhombic Night Adder


Stiletto Snake

MIXED CYTOTOXIC AND HAEMOTOXIC

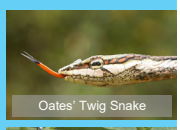

Puff Adder

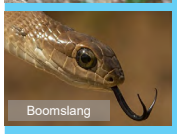

Gaboon Adder

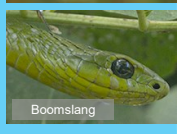

Black-necked Spitting Cobra

HAEMOTOXIC


Oates' Twig Snake


Oates' Twig Snake


Boomslang


Boomslang

DOMINANT CLINICAL PRESENTATION OF VICTIM

Pain at bite site, Paresthesia of tongue and lips, Ptosis, Pupillary abnormalities, Descending flaccid paralysis, Swallowing difficulties, Slurred Speech, Sweating	**Intense local pain and swelling**	**Intense local pain and swelling + Active and/or systemic bleeding**	**Late onset of symptoms Active and/or systemic bleeding**

IDENTIFICATION SYNDROME

PROGRESSIVE WEAKNESS SYNDROME (PWS)	**PAINFUL PROGRESSIVE SWELLING SYNDROME (PPSS)**	**COMBINED PPSS & BS**	**BLEEDING SYNDROME (BS)**

SYMPTOMS AND TREATMENT

PRE-HOSPITAL TREATMENT

Non-spitting Cobra bite: Keep victim calm Apply pressure immobilisation bandage **Positively identified Black Mamba bite:** Keep victim calm, apply arterial tourniquet. Protect airway. Artificial respiration. Immobilise victim	Keep victim calm Do **not** apply tourniquet or Pressure Immobilisation bandage Remove jewellery, clothes and shoes from bitten limb Elevate limb	Keep victim calm Do not apply tourniquet or pressure immobilisation bandage Remove jewellery, clothes and shoes from bitten limb Elevate limb	Keep victim calm Do not apply tourniquet or pressure immobilisation Elevate limb

EVERY SNAKEBITE VICTIM SHOULD BE TAKEN TO HOSPITAL FOR OBSERVATION
EVERY SNAKEBITE IS TREATED AS A MEDICAL EMERGENCY
EVERY SNAKEBITE VICTIM TO RECEIVE TETANUS TOXOID BOOSTER
ANTIBIOTICS: NO PROPHYLACTIC USE. AS TREATMENT ONLY WHEN INDICATED

SUPPORTIVE TREATMENT

PROTECT THE AIRWAYS, OXYGEN BY MASK OR VENTILATION (c)	INTRAVENOUS FLUIDS, ELEVATE BITTEN LIMB (a), ANALGESIA	INTRAVENOUS FLUIDS, ELEVATE BITTEN LIMB (a), ANALGESIA, BLOOD OR BLOOD COMPONENT THERAPY	BLOOD OR BLOOD COMPONENT THERAPY (b)

ANTIVENOM

PERCENTAGE BITES IN WHICH ANTIVENOM IS INDICATED

50-70 %	**< 10 %**	**80-100 %**	**80-100 %**

CONTENT SOURCE CREDIT: African Reptiles & Venom

DEVELOPED BY:

REPUBLIC OF ZAMBIA
MINISTRY OF HEALTH

GUIDELINES FOR ADMINISTRATION OF ANTIVENOM IN ZAMBIA

SNAKE SAFETY ZAMBIA

THESE ARE THE PRESCRIBED INITIAL DOSAGES PER SNAKE GROUP:

PUFF ADDER /GABOON ADDER: **50 ML** (5 VIALS) POLYVALENT AV

BLACK MAMBA : **100 ML** (10 VIALS) POLYVALENT AV

COBRA: **200 ML** (20 VIALS) POLYVALENT AV

BOOMSLANG: 20 ML MONOVLENT AV

—-DOSAGE IS IRRESPECTIVE OF SIZE OR AGE OF THE VICTIM!—-

ANTIVENOM ADMINISTRATION

1) Prepare 1 syringe with 0.25 ml adrenaline + 2 syringes with 0.5 ml adrenaline each (1:1000).
2) Dissolve lyophilised AV in recommended amount (see above!) of sterile water for injection
3) Infuse AV in 200 ml normal saline
4) Premedicate with 0.25 ml adrenaline
5) Administer AV via dripline (200 ml – 400 ml per hour)
6) Monitor for adverse reaction (stridor!)

ADVERSE REACTION

1) Adverse reaction (1): stop AV, inject 0,5 ml adrenaline
2) When stabilized (30-60 min): continue AV administration at slower rate
3) Adverse reaction (2): stop AV, inject 0,5 ml adrenaline
4) Consider stopping AV and treating symptomatically

ANTIVENOM ADMINISTRATION—REPEAT DOSAGE

1) MONITOR PATIENT
2) Active bleeding 30 minutes AFTER AV administration: repeat dosage
3) Coagulopathy still present (20 MWBCT) 6 AFTER AV administration: repeat dosage
4) Neurotoxic signs do not reduce after 2 hours: repeat dosage

CYTOTOXIC ENVENOMATION

Antivenom is only administered if:

1. There is rapid progressive swelling + within 6 hours after the bite. After 6 hours, the damage is done and AV does NOT reverse damage to tissue.
2. There is systemic envenomation
3. If systemic envenomation expected

NEUROTOXIC ENVENOMATION

Antivenom may be accompanied with:

1. Atropine in Black Mamba Bite (Neostigmine contra-indicated!)
2. Atropine and Neostigmine in Neurotoxic cobra bites

If antivenom is not available, Neostigmine can be used in Cobra bites

CONTENT SOURCE CREDIT: African Reptiles & Venom

DEVELOPED BY: SNAKE SAFETY ZAMBIA

REPUBLIC OF ZAMBIA

INDICATIONS FOR ANTIVENOM ADMINISTRATION IN ZAMBIA

SNAKE SAFETY ZAMBIA

NEUROTOXIC ENVENOMATION

CYTOTOXIC ENVENOMATION

HAEMOTOXIC ENVENOMATION

ANTIVENOM NOT ABSOLUTELY INDICATED

ANTIVENOM INDICATED

PROGRESSIVE WEAKNESS (PW)
(Black Mamba and Non-Spitting Cobra bites)
[polyvalent AV indicated 50-70% bites]

PAINFUL PROGRESSIVE SWELLING (PPS)
(Puff Adder, Gaboon Adder, Spitting Cobras, Night Adder, stiletto Snake)
[polyvalent AV indicated 20% bites]

BLEEDING (B)
(Boomslang, Twig Snake)
[monovalent Boomslang AV indicated 80-1005 bites. No AV for Twig Snakes]

&

MIXED PPS & B
(Puff Adder, Gaboon Adder, Black-necked Spitting Cobra)

SEVERE ENVENOMATION ANTICIPATED—ANTIVENOM INDICATED

The triad of pins & needles with or without metallic taste, profuse sweating and excessive salivation—Black Mamba

Or: 3 or more from:

5 Ps:
Pain at bite site
Paraesthesia tongue + lips
Ptosis
Pupillary abnormalities
Descending flaccid paralysis

5 Ss:
Swallowing difficulties
Slurred Speech
Sweating
Secretion
Salivation

Swelling extending at 10 cm or more per hour.

Extremity bites: swelling reaches: wrist or ankle within 1 hour or knee or elbow within 3-4 hours or Shoulder or groin in 8 hours or Torso

Unstoppable bleeding from fang punctures and/or severe head-aches, dizziness, fainting or convulsions

SEVERE OR LIFE-THREATENING ENVENOMATION PRESENT—ANTIVENOM INDICATED

Shortness of breath due to weakness in the absence of PPS (Black Mamba)

Inability to swallow saliva

Generalised weakness in the presence of PPS (Non-spitting Cobras)

Drooping eyelids, dilated pupils or squint may not be followed by respiratory distress per see.

Extremity bites—swelling of a whole limb within 8 hours

Swelling threatening the airway

Associated unexplained shortness of breath

Associated abnormality of blood clothing (see B syndrome)

Very tense limb (compartment syndrome) or compressed major blood vessel

Active systemic bleeding (not bruising of the bitten limb alone)

Non-clotting blood after 20 minutes in an undisturbed, new, dry, clean test tube (use blood from a healthy person as a control)

Significant laboratory evidence of a blood clothing abnormality

CONTENT SOURCE CREDIT: African Reptiles & Venom

DEVELOPED BY: SNAKE SAFETY ZAMBIA