CHAPTER 1 : GENERAL INTRODUCTION

Background

Southern Africa is well known for the diversity and beauty of its flora. Ironically, about 600 plants in the subcontinent are toxic and a large proportion of these are potentially poisonous for livestock [10,29,30,35]. In most of the Region (Fig. 1), livestock is traditionally kept under extensive conditions on veld that is frequently denuded by drought, burning and overstocking. Under these circumstances, animals may be forced to eat poisonous plants that they would normally avoid. Devastating outbreaks of poisoning have been reported under such conditions. During 1926 and 1927 for example, more than 600 000 sheep were affected by plant-induced photosensitization in the Northern Cape Province, while in the period 1969 to 1970 up to 70 000 sheep died of photosensitivity in the Middelburg district of the same province [10]. In addition to plant poisonings, mycotoxicoses such as diplodiosis have also been recognised as of economic importance for livestock production in Southern Africa [10,11].

Fig. 1: Countries within the southern African Region and provinces of South Africa (L = Lesotho, Z = Zwaziland)

In a recent study, the economic importance of plant poisonings and mycotoxicoses in livestock in South Africa was estimated [13]. The annual total
cost of these intoxications to the livestock industry was conservatively estimated at ZAR 104 million. The figure did not include hidden losses such as diminished production, reproductive failure, and the cost of not utilising toxic pastures and the fall in price of infested land. Specific data for neighbouring countries is to the best of our knowledge not available.

Kellerman and others [13] determined the six most important plant poisonings and mycotoxicoses in ruminants in South Africa (Table 1). Poisoning by plants containing cardiac glycosides caused the greatest economic loss in cattle. In sheep and goats, the hepatogenous photosensitivity diseases ‘geeldikkop’ and ‘dikoor’ collectively were regarded as the most important.

The detection, isolation and identification of toxic compounds biosynthesised by plants and fungi is an important research field in veterinary toxicology. Investigations into the biochemistry of these toxins are essential to elucidate mechanisms of action, define toxin-induced effects, develop analytical assays, and assist in the design of management protocols to control and prevent poisonings. These preventative measures are based upon accurate prediction of the variation in toxin level associated with factors such as plant species, growth stage, and environmental change [5]. With these aims in mind, research in South Africa and more specifically at the Onderstepoort Veterinary Institute and Faculty of Veterinary Science, University of Pretoria, Onderstepoort has mainly focused on the most important plant toxicoses and mycotoxicoses that occur in the subcontinent (Table 1). It is therefore not surprising that toxic natural products of all except two of these plants and fungi listed in Table 1, have been isolated and characterised by South African scientists.

A number of poisonous plants and fungi may cause nervous signs and death in ruminants in southern Africa. With the exception of diplodiosis, these poisonings are not of major economic importance and occur sporadically in most instances. These intoxications are often associated with particular feeding practices, and sometimes occur on farms in remote areas where veterinary assistance is not freely available and case material difficult to obtain for study. An example of such rare neurological condition is poisoning by the plant Helichrysum argyrosphaerum in sheep and goats. Outbreaks of intoxication have been restricted to Namibia and occurred in South Africa for the first time after abnormally high rainfall ended a 9-year period of drought in the North West Province (Fig. 1).

The toxic principle(s) of most of these neurotoxicoses have not been determined and chemical analysis to achieve a diagnosis is not available. Their diagnosis therefore, is based on a detailed history, characteristic clinical signs, identification of toxic plants that have been consumed or specific epidemiological factors on the property, and especially the recognition of histological lesions, if present, in the nervous system. Detailed descriptions of the histological and ultrastructural lesions of most of these neurotoxicoses are lacking [10].
Table 1: The six most important plant poisonings and mycotoxicoses in South Africa in cattle and small stock [13].

<table>
<thead>
<tr>
<th>Name of intoxication and incriminated plant(s)/fungus (in brackets)</th>
<th>Toxin(s)</th>
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<tr>
<td><strong>Cattle</strong></td>
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<td>2. Seneciosis (<em>Senecio</em> spp., esp. <em>S. latifolius</em> and <em>S. retrorsus</em>)</td>
<td>2. Pyrrolizidine alkaloids [20,34]</td>
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<td>5. <em>Lantana</em> poisoning (<em>L. camara</em>)</td>
<td>5. Pentacyclic triterpenes [14,15,16]</td>
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<td><strong>Sheep and goats</strong></td>
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<td>1. ‘Geeldikkop’ (<em>Tribulus terrestris</em>) and ‘Dikoor’ or <em>Panicum</em> photosensitivity (<em>Panicum</em> spp.)</td>
<td>1. Steroidal saponins in <em>T. terrestris</em> [12,24,25] and possibly in <em>Panicum</em> [22,23]</td>
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<tr>
<td>2. ‘Vermeersiekte’ (<em>Geigeria</em> spp.)</td>
<td>2. Sesquiterpene lactones [1,6]</td>
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<td>3. Acute intoxication with cardiac glycoside-containing plants e.g. ‘tulp’ (<em>Homeria</em> and <em>Moraea</em> spp.), ‘slangkop’ (<em>Urginea</em> spp.) and ‘Witstorm’ (<em>Thesium lineatum</em>); and chronic poisoning with cardiac glycoside-containing plants or ‘krimpsiekte’ (<em>Cotyledon, Kalanchoe</em> and <em>Tylecodon</em> spp.)</td>
<td>3. Non-cumulative bufadienolides in ‘tulp’ and ‘slangkop’ [7,17,18,19,26,27,31,32,33] and cumulative bufadienolides in ‘krimpsiekte’-containing plants [2,3]</td>
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<td>5. ‘Gousiekte’ (<em>Pachystigma, Fadogia, and Pavetta</em> spp.)</td>
<td>5. Pavetamine [8,9,28]</td>
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Aim and outline of this study

In this study the clinical signs and pathology of five plant poisonings and a mycotoxicosis affecting the nervous system of domestic ruminants in southern Africa are described. For comparative purposes, an inherited storage disease (β-mannosidosis) and a drug-induced neurotoxicosis (closantel overdosage) are also presented. A common feature in the nervous tissue of these conditions is some degree of myelin and/or cellular vacuolation. Case material of these conditions was collected during outbreaks of disease and, in three of the poisonings, also during subsequent feeding trials with toxic plant material.

The study had three aims in mind:

- To document the pathology of those conditions where detailed descriptions were lacking,
- To study the appearance and/or pattern of the lesions from a differential diagnosis perspective and
- To consider the mechanisms underlying the nervous lesions.

The conditions in this thesis are grouped into three categories:

- Lysosomal storage diseases (Chapter 2.1),
- Myelinopathies (Chapter 3.1) and
- Neuronopathies and axonopathies (Chapter 4.1).

Although most lysosomal storage diseases in animals are inherited and characterised by the accumulation of sphingolipids, glycolipids, oligosaccharides, or mucopolysaccharides within lysosomes in multiple cell types, a few are induced by the ingestion of toxic plants. A novel lysosomal storage disease in goats caused by *Ipomoea carnea* is reported (Chapter 2.2). β-Mannosidosis in Hereford calves is documented, a breed not previously known to be affected by this inherited disorder (Chapter 2.3). The ultrastructural lesions and lectin histochemistry in *Solanum kwenense* poisoning in cattle, a plant toxicosis characterised by the development of lesions in the cerebellum suggestive for a storage disease, are also described (Chapter 2.4).

Four myelinopathies are described in this thesis:

- *Helichrysum argyrosphaerum* poisoning which induces blindness, nervous signs, status spongiosis, optic neuropathy and retinal degeneration in small stock (Chapter 3.2),
- Closantel intoxication in small stock (Chapter 3.3),
- A novel toxicosis causing blindness and myelin vacuolation following exposure to *Ornithogalum prasinum* and *O. saundersiae* in cattle (Chapter 3.4) and
- *Crotalaria sparthioides* intoxication in cattle, an example of hepatic encephalopathy (Chapter 3.5).
Ingestion of the fungus *Aspergillus clavatus* may induce a tremorgenic condition in cattle. In Chapter 4.1 and 4.2, the pathology of acute and chronic *A. clavatus* poisoning in cattle are reported, respectively. Based on the nature of the lesions in this neuromycotoxicosis, the condition is described in the category of neuronopathies and axonopathies.

**References**

Chapter 1

with crude steroidal saponins from *Tribulus terrestris*. Onderstepoort J Vet Res 58:47-53