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RYEGRASS STAGGERS: CLINICAL, PATHOLOGICAL AND AETIOLOGICAL ASPECTS

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Abstract

This paper briefly introduces animal disease aspects of ryegrass staggers (RGS) and describes the occurence and the clinical signs of the disease. Recent suggestions for the production of a reversible biochemical lesion in the central nervous system are mentioned in relation to the apparent lack of specific morphological lesions found in sheep. The recent isolation of novel potent neurotoxins, the lolitrems, from toxic pasture material is reviewed. There is now strong circumstantial evidence that the lolitrems produce the neurotoxic disease of RGS and also that the lolitrems are elaborated in the close association of perennial ryegrass with its parasitic fungus, *Lolium* endophyte, in pastures. Under what conditions the lolitrems are produced, or their precise locus within the association, are not yet known.

INTRODUCTION

Ryegrass staggers (RGS) affects principally sheep and cattle, but also horses and deer, grazing pastures in which perennial ryegrass (*Lolium perenne* L.) is dominant (Cunningham & Hartley, 1959; Byford, 1978). Outbreaks occur throughout New Zealand, are confined to the summer and autumn, and they are usually but not always associated with close grazing of swards during, or subsequent to, prolonged warm dry conditions (Byford, 1978; Keogh, 1973, 1978).

These factors differentiate RGS from the hypomagnesaemic staggers of cattle which occur in the spring and also from the similar disease of paspalum staggers in cattle (and occasionally sheep) which occurs on rank undergrazed pastures in the warmer regions when ergot- (*Claviceps paspali*) infected seedheads of *Paspalum dilatatum* are eaten by livestock in summer.

CLINICAL SIGNS

In an outbreak of RGS many animals in a flock or herd may be affected, yet losses are usually not severe. These are generally occasioned by accidental deaths, falling over bluffs or drownings in water courses or troughs. In drought conditions, when feed is short and debility occurs, there may be many deaths from dehydration and starvation of incapacitated stock which are unable to range and forage.

Within a flock or herd there is a wide range of susceptibility to the disease. This is seen in effects ranging from animals showing no obvious clinical signs to those unable to stand. On casual examination of animals resting quietly or grazing undisturbed, affected animals may show little abnormality. However when disturbed and made to run the clinical signs immediately become apparent. As forced exercise is continued the signs increase in severity until a maximum response is reached which indicates the extent and severity of the disease present in the mob.

growth rates between those lambs moderately affected with ryegrass staggers and those unaffected. On a property in Cheviot where stock liveweights were measured, ewe lambs lost 4 kg from December until March. Because the stock are forced to graze close to the ground, the animals are then subjected to a greater endophyte challenge. Many farmers can identify with this apparent problem, however, it is difficult to know whether to attribute this loss to ryegrass staggers or a lack of high quality feed. Unfortunately for farmers ryegrass staggers and feed shortages generally occur together.

FARMER ACTION

Several alternatives are available to farmers to reduce the incidence of ryegrass staggers. The obvious answer is to stop grazing those areas with a high endophyte level – the infected ryegrass pastures. Farmers can attempt to move stock to 'safe' areas such as lucerne, grass species other than ryegrass, or summer forage crops. With the majority of the property in ryegrass, pasture and all stock being moved to a small area of 'safe' pasture applies considerable grazing pressure to this area. Farmers can continue to stock the areas infested with the endophyte, but to do this, considerable inputs of supplements such as silage, hay or grain must be considered. Fungicides have been investigated and have been largely found unsatisfactory. Some initial work with seaweed derived products has shown a decline in the incidence of ryegrass staggers but not a cure.

Perhaps the bright light at present in the long term, is the selection of resistant stock. Obviously if selection for resistance can be made, and these animals identified, it will still take time before the gene can be introduced into commercial flocks.

COST TO THE FARMER

The property considered in this example runs 2000 ewes in an area which is severely affected by ryegrass staggers. The only cost which is directly attributable to ryegrass staggers is increased stock deaths. Deaths over and above those normally experienced can be increased by 2-10%.

Deaths increased by 4% 80 head @ $18/hd	$1,440

This represents about half of the farmer's total expenditure on animal health for the year. Other tangible costs which may be attributable to ryegrass staggers include additional supplementary feeding, loss of stock condition and the labour requirement for increased stock surveillance.

Supplementary feed fed at the rate of 1% bales/l 00 for 2 months 1800 bales @ $3/bale	$5,400
Stock production loss – 4 kg liveweight loss causes a reduction in lambing percentage of 10% 200 lambs @ $18/hd	$3,600
Additional labour requirement at $8 per hour	?

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It has been shown experimentally that sheep develop clinical signs within 7-14 days of being placed on toxic pastures (Byford, 1978; Mortimer et al. 1982). The mildest clinical signs are a slight trembling of the head and fasciculation of the skin muscles of the neck, shoulder and flank regions (Keogh, 1973). As the neuromuscular disorder progresses there is head nodding and jerky limb movements. Interference with postural reflexes follows, seen as swaying while standing or staggering during movement. As the condition worsens a stiff-legged stilted gait may develop with short prancing steps usually resulting in collapse to the ground. Sheep roll into lateral recumbency with head extended, arched back and rigid extended limbs held in a tetanic spasm of several minutes duration. This is followed by sudden muscular relaxation and apparent recovery, the animal then slowly regains its feet and walks away, often still showing tremors but with very little locomotory into-ordination.

Cattle usually collapse onto their brisket with legs splayed, but generally remain upright either on their brisket or in a dog-sitting attitude.

PATHOLOGICAL AND FUNCTIONAL CHANGES

The absence of consistent specific pathological changes and lesions in the organs and tissues of RGS affected sheep, including the central nervous system, has been the general finding in New Zealand (Cunningham & Hartley, 1959; Mortimer, 1978). These negative findings when considered together with the apparent rapid recovery of animals within minutes from bouts of severe inco-ordination, suggest a very temporary derangement. The incapacity is probably in the transmission of nerve impulses between the brain and the functional groups of skeletal muscles whose co-ordinated activities maintain precise balance and smooth movement during locomotion.

Very recently, some evidence has been obtained from biochemical studies of tissues taken from the cerebral cortex of 'the brain of sheep severely affected with RGS. These studies indicate that in the nerve endings (synaptosomes), isolated from this site, there is an increased spontaneous release of neurotransmitter amino acids (Mantle, 1982). It is possible that the neurotoxins present in toxic pastures may, when eaten, produce a reversible biochemical derangement in nerve endings which upsets nerve-impulse transmission, yetwithout permanent injury to the cells of the nervous system. Although this hypothesis based on biochemical evidence is an attractive one it is at present speculative, for it could be that the changes found are the effect of the nervous derangement rather than the cause of it.

THE CAUSE OF RYEGRASS STAGGERS

It has been suspected for many years that a toxic substance in or associated with pasture was responsible for RGS (Cunningham & Hartley, 1959). Alkaloids produced by pasture plants were at one time incriminated in Australia (Aason et al, 1969). More recently in New Zealand and elsewhere, tremorgenic neurotoxins produced by fungi (mycotoxins) associated with both soil and plants have been extensively researched as the cause of RGS (Mantle & Penny, 1981).

Convincing evidence for the presence of tremorgenic neurotoxins in samples of ryegrass obtained from RGS outbreaks emerged from the recent painstaking work of Dr E.P. White at the Ruakura Animal Research Station. Extracts of 25 g samples of ryegrass collected from widespread RGS outbreak sites in New Zealand,

when sufficiently concentrated (x 10,000 to x 30,000) and purified, produced characteristic tremors and into-ordination when injected into mice. That the mouse tremors produced by injections of toxic grass extracts were qualitatively distinguishable from those produced by certain known fungal tremorgens isolated from *Penicillium* spp. cultures (e.g. Mantle & Penny, 1981) was also recently recognised (Mortimer & White, 1980). These minor but important differences in neurological responses in injected mice cast serious doubts that known *Penicillium* tremorgens being investigated were the neurotoxins responsible for RGS.

Further chemical purification and concentration of ryegrass neurotoxic fractions led to the isolation of two tremorgens with different chromatographic characteristics and with higher molecular weights than any of the then-known fungal tremorgens. The two tremorgens (Table 1) from toxic ryegrass samples were new to science and the names lolitrem A and 8 were proposed for them (Gallagher et al. 1981).

Table 1: TREMORGENS (NEUROTOXINS) ISOLATED FROM STAGGERS-PRODUCING PERENNIAL RYEGRASS

Tremorgen	Molecular Weight	Formula
Lolitrem A	701	$C_{42}H_{55}NO_8$
Lolitrem B	685	$C_{42}H_{55}NO_7$

Injected into mice, each produces tremors and into-ordination.
Fungal or plant origin? – at present unknown.

The first positive association of the *Lolium* endophyte of perennial ryegrass (Neill, 1940) with the lolitrems and with natural outbreaks of RGS in sheep was to be provided by the historic DSIR Lincoln outbreak in 1981 (Fletcher & Harvey, 1981). Pasture samples collected from these pure ryegrass plots at the time of the outbreak, when extracted, chromatographically evaluated and injected into mice, gave good correlation between presence of the lolitrems, mouse neurotoxic activity and subsequent findings of extent of endophyte infection of ryegrass in the plots (Mortimer et al. 1982).

Strong substantiating evidence for the same association soon followed from the 1982 RGS sheep grazing trials conducted at Ruakura. Here, on the low endophyte ryegrass plots no RGS developed and lolitrem levels were subsequently found to be low, while on the high endophyte plots all sheep developed RGS and subsequent samples from these plants yielded higher levels of the lolitrems (Mortimer et al. 1982; Mortimer, di Menna and Gallagher, unpublished findings).

CONCLUSIONS

Although unquestionable verification is still needed there is now convincing evidence that the lolitrem neurotoxins, elaborated within the perennial ryegrass/*Lolium* endophyte association, are responsible for producing the disease of RGS in susceptible livestock species. Some factors in the occurrence of RGS are

as yet not well understood. In particular the interplay of factors and conditions which may trigger the ryegrass/endophyte association to produce the lolitrems in some seasons but not in others needs to be known. Nor is the precise origin of the lolitrems currently known. Are they of plant origin or fungal origin? All this is vitally required information which is likely to have a bearing on recognising the onset of toxicity in pastures and control of the disease.

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