CATARACTS, GOITRE AND INFERTILITY IN CATTLE GRAZED ON AN EXCLUSIVE DIET OF *LEUCAENA LEUCOCEPHALA*

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SUMMARY: Gross and histopathological changes and serum thyroxine levels were determined in 10 heifers fed an exclusive diet of *Leucaena leucocephala* from 10 months of age until slaughter, 23 months later. Normal ovarian activity and mating were observed during a 7-month mating period. Cataracts, goitre, lingual epithelial ulceration and gingival atrophy were present at slaughter. Only one of the heifers was pregnant. Histologically, severe vacuolation and disruption of lens fibres and focal hyperplasia of lens epithelium were present. Both follicular hyperplasia and colloid accumulation were found to varying degrees in the thyroid glands and serum thyroxine levels were higher than in a comparable group of animals not fed *L. leucocephala*. Morphologically normal trophoblast was present in the uteri of 6 animals even though no embryo or foetus was present. Embryonic death and resorption may have been due to the anti-mitotic effect of mimosine or the goitrogenic effect of DHP.

Introduction

Ingestion of the legume *Leucaena leucocephala*, or the administration of its toxic constituent, mimosine (β — N — (3 — hydroxy — 4 — oxo-pyridyl) — α — amino propionic acid), has been associated with reproductive disturbances and depilation in non-ruminants, with depilation in ruminants (Gray, 1968) and with cataracts in rats (von Sallman *et al* 1959). Goitre is an additional symptom in ruminants where ruminal microflora metabolise mimosine to 3-hydroxy — 4 (1H) — pyridone), (DHP), which as been demonstrated to be goitrogenic (Hegarty *et al* 1976). Holmes (1980) showed that heifers grazing *Leucaena* exlusively had poor reproductive performance. Breeding stock may graze *L. leucocephala* throughout their productive life, perhaps for 10 to 12 years. However, little information is available relating to the pathological changes in cattle ingesting *L. leucocephala* over long periods. The present study describes gross and histopathological changes and serum thyroxine levels in heifers on a sole diet of *L. leucocephala* for almost 2 years.

Materials and Methods

Animals and Management — The trial was conducted on an old stand of *L. leucocephala* (var. Peru) on sandy loam at Erap, 50 km west of Lae, Papua New Guinea, latitude 6°35'S and altitude 100 m.

Ten five-eighth-Brahman crossbred heifers aged 10 months and weighing 157 ± 8 kg (mean ± S.E.M.) were grazed on a pure stand of *L. leucocephala* at a stocking rate of 2.5 beasts/ha. Sixteen months after grazing commenced, a Brahman bull was introduced for 4 months, after which it was replaced by a crossbred Brahman Bull. Both bulls were proven sires and all animals were free of brucellosis, trichomoniasis and vibriosis. All heifers were slaughtered after a total of 23 months grazing *L. leucocephala*.

Clinical and pathological Examinations — Heifers were observed for clinical or behavioural abnormalities throughout the trial and were weighed weekly. Ovarian function and pregnancy status were assessed weekly by rectal examination for the first 3 months following the introduction of the bull and subesequently at monthly intervals.

At slaughter serum samples for thyroxin (T4) analysis were separated from blood collected from jugular veins. For comparison, serum samples were obtained from 10 animals of the same age and sex, reared on adjacent improved pasture with no access to *L. leucocephala*. These heifers were slaughtered at various stages of pregnancy to provide samples of normal pregnant uteri for histological comparisons. Thyroxine levels were determined by a specific radioimmunoassay using antibody produced in sheep, and polyethylene glycol as the separating agent (Walton and Humphrey 1979).

Both eyes, the thyroid gland and internal genitalia were removed from each animal, together with samples of liver, kidney, adrenal and parotid salivary glands. Thyroid glands were weighed, the presence and severity of lenticular opacity in each eye was assessed and pregnancy status was determined.

Both ovaries, oviducts and sections of the mid-region of both uterine horns and of the cervix were fixed in Bouin's solution. All other tissues were fixed in 10% buffered formalin. The posterior sclera of the eye was incised to facilitate fixation of the lens. Tissues were embedded in paraffin, cut at 6 μm and stained with haematoxylin and eosin. In addition, lens tissue was stained by the periodic acid-Schiff reaction.

Results

Clinical Examination

Immediately prior to the introduction of the first bull the mean body weight of heifers was 355 ± 29 kg and their mean growth rate during the mating period was 0.3 kg/day. Bulls showed normal libido and mating behaviour. Normal oestrus

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signs were observed in heifers and cyclic ovarian activity was present. No pregnancies were detected, although early (6 weeks) pregnancies were suspected in 2 heifers on the basis of rectal examination, but not confirmed on subsequent examination. A persistent, purulent, vaginal discharge was present in 1 animal during the mating period.

Hair loss, confined to the long hairs of the tail and poll, was observed in 4 heifers during the first 12 months of grazing. Two of these animals subsequently showed similar hair loss during the mating period. Cataracts ranging from slight cloudiness to almost complete opacity were observed in 9 heifers 18 months after the commencement of grazing. Partial loss of vision was evident from their behaviour. The severity of cataracts, rated on an arbitrary scale from 0 to 3, was not significantly correlated with growth rates ($r = 0.48$).

Gross Pathology

Mild to severe bilateral cataracts, characterised by a non-uniform, diffuse, lenticular opacity with dense reticular and stellate formations (Figure 1) were present in all animals. In severe cases pits up to 0.5 mm in diameter were present on both surfaces of the lens.

Goitre was present in all animals which grazed *L. leucocephala* and the mean weight of the thyroid gland was 123 ± 60g, (range 57 to 238 g). Two animals had severe perithyroid oedema. The thyroids of grass-fed heifers weighed 20 to 25 g.

Elongate to ovoid, transverse erosions and ulcerations were present in the dorsal and lateral lingual epithelium immediately anterior to the prominence of the tongue in 7 heifers. Mild to marked gingival atrophy, exposing up to 1 cm of the roots of the molar and premolar teeth had occurred in 8 animals (Figure 2). In severe cases food material was firmly impacted between the teeth.

Only one heifer was pregnant, with a foetus approximately 10 weeks old, which had not been detected at the pregnancy test 1 month previously. A copious, mucopurulent exudate was found in the uterine lumen of the heifer with the vaginal discharge and a clear mucoid exudate was present in the uterine lumen of another heifer. Bilateral ovarian cysts, up to 5 cm diameter, were present in a third heifer.

Histopathology

Focal abnormalities were evident in both the capsule and the substance of the lens. Although most capsular tissue appeared normal (Figure 3), gross thickening of the capsule was present in the central part of the anterior surface of the lens in one case. In the thickened region the capsule had split into 2 layers enclosing a wide band of abnormal tissue (Figure 4). The lens epithelium was flattened over most of the anterior surface of the lens, but was columnar and heavily vacuolated in the central part of this surface (Figure 5). Separation of the capsule from the epithelium (Figure 5) was widespread, but probably represented a preparation artifact. Focal degenerative changes were present in the substance of the lens, primarily in the subcapsular, cortical regions of both the anterior (Figure 5) and posterior (Figure 6) surfaces. Affected areas showed condensation of the lens substance, and replacement of lens fibres by masses of densely-stained globular bodies. The lens epithelium close to the equator, and the bow nuclei, appeared normal.

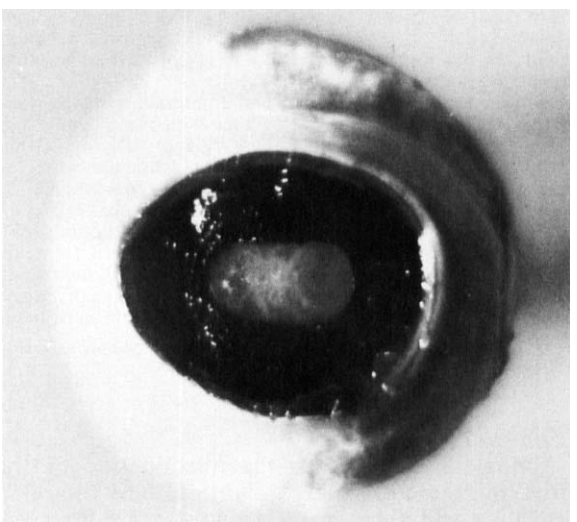

Figure 1. Eye freshly removed at slaughter, of heifer which had grazed *Leucaena* for 23 months, showing cataract formation.

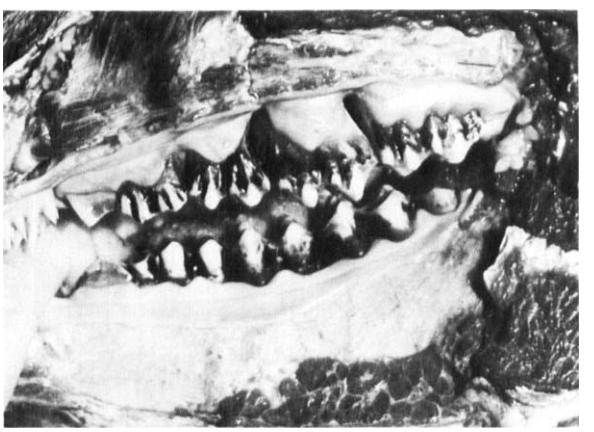

Figure 2. Atrophy of gums in left upper jaw of heifer which had grazed *Leucaena* for 23 months.

All thyroid glands showed varying degrees of both follicular cell hyperplasia and colloid accumulation. There was no flattening of the follicular epithelium. Four of the glands exhibited predominantly hyperplastic changes, whereas colloid accumulation was predominant in 3 cases.

Although the uteri of 8 of the heifers grazed on *Leucaena* appeared grossly as normal non-pregnant uteri, 6 animals showed histological development of normal foetal trophoblast, despite the absence of a foetus or embryo. In the endometrium and lumen of the uterus which con-

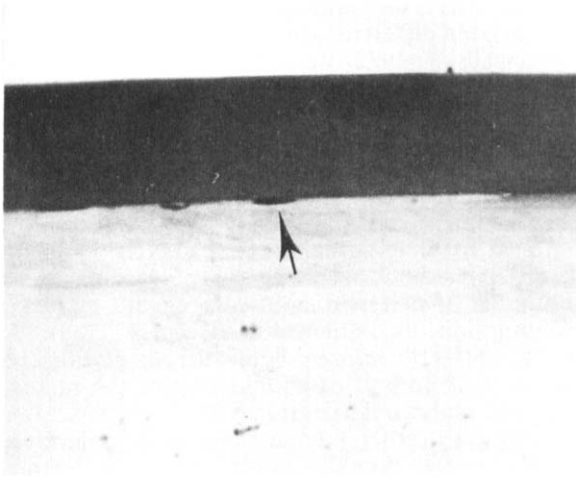

Figure 3. Normal area of capsule from the anterior surface of the lens. Beneath the capsule, which appears dark, can be seen the flattened lens epithelium (arrow). Lens substance is below this epithelium. Haematoxylin and eosin x 550.

Figure 4. Area of thickening of the capsule from the central part of the anterior surface. The capsule appears to have split into an outer (top) and inner layer, separated by a zone of bundles of fibrillar material. At this point the capsule has become separated from the lens epithelium. Haematoxylin and eosin x 550.

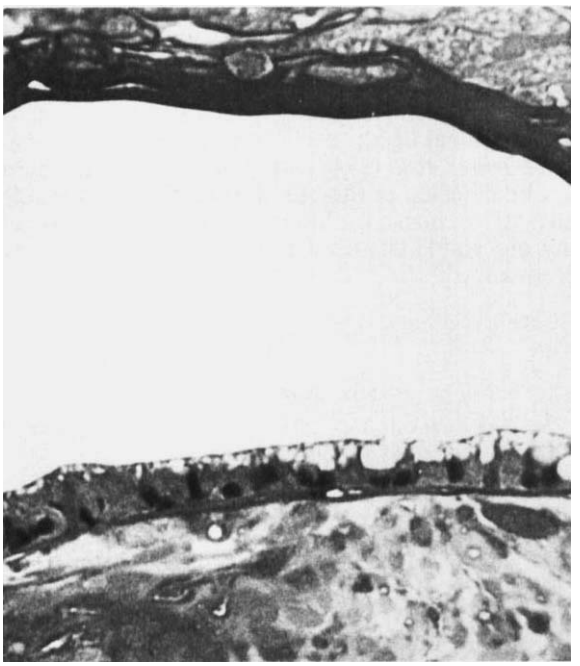

Figure 5. From the central part of the anterior surface of a lens, showing tall columnar lens epithelial cells whose cytoplasm is heavily vacuolated. The thickened capsule has separated, probably as a preparation artefact, and can be seen at the top of the picture. Many globular bodies are present in the lens substance beneath the epithelium, at the bottom of the picture. Haematoxylin and eosin x 440.

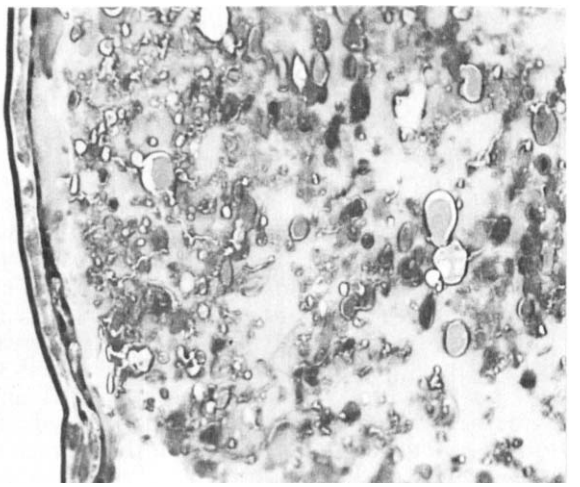

Figure 6. From the posterior surface of a lens, showing a focal area in which the lens fibres have been replaced by numerous deeply-staining globules, many of which showed some basophilia. The capsule is at the left. Haematoxylin and eosin x 220.

tained purulent exudate a heavy infiltration of neutrophils was present. The morphology of the endometrial glands and the cervix and oviducts was normal in all animals.

There were no significant histological changes in liver, kidney, salivary or adrenal gland tissues examined.

Serum Thyroxine Analysis

The mean serum thyroxine concentration of the 10 heifers grazing *L. leucocephala* (107 nmol/l) was significantly higher ($P<0.05$) than the level in animals grazing improved pasture (85 nmol/l).

Discussion

The lenticular changes found in the present study are not identical with the cataracts which developed in a few days in rats fed a diet containing mimosine (Von Sallmann *et al* 1959). The metabolism of mimosine and DHP in the eye is unknown. Cataracts can be produced by quinone derivatives of dinitrophenol, which undergo substitution reaction with side chains of amino acids. Reaction with 2 different protein molecules results in formation of insoluble aggregates which scatter light (Ogino and Yasukura 1957). Possibly, mimosine or DHP can undergo an analogous change and cause similar cross linking.

Thyroid glands in the present study showed both follicular cell hyperplasia and colloid accumulation. Predominantly hyperplastic tissue changes were described in thyroid glands of cattle fed *L. leucocephala* (Hegarty *et al* 1976) and of newborn calves of heifers fed *L. leucocephala* (Donaldson *et al* 1970). Such changes are consistent with DHP interfering with organic binding of iodine within the follicle, as suggested by Hegarty *et al* (1976), resulting in reduced thyroxine levels, subsequent release of thyroid stimulating hormone from the anterior pituitary and follicular cell hyperplasia. Reduced thyroxine levels have been found in cattle grazed for 3 months on a *Leucaena* and grass pasture (Jones *et al* 1976) or fed exclusively on *Leucaena* (Jones *et al* 1978). Conversely, Falvey (1976) found increased thyroxine levels in cattle allowed access to *L. leucocephala* and Donaldson *et al* (1970) found no changes in plasma bound iodine (PBI) levels in cows on a sole diet of *L. leucocephala*, whereas levels in their calves were elevated for the first 35 days post-partum. In the same study PBI and thyroxine levels in ewes were unaffected by feeding *L. leucocephala*, whereas both parameters were elevated in their lambs at birth and declined to normal levels by 6 weeks of age. In the present study the mean thyroxine level was increased compared with similar animals that had never grazed *L. leucocephala*. The occurrence of elevated thyroxine levels and the presence of a predominantly colloid goitre in the thyroid glands of 3 animals in the present study suggest a complex aetiology in the development of goitre in animals grazing exclusively on *L. leucocephala* for a prolonged period of time. This may be related to fluctuations in mimosine concentration in *Leucaena* in different seasons.

Vohradsky (1972) described inflammation and erosions of the oral mucosa of cattle fed *Leucaena* exclusively for 20 days. Jones *et al* (1976) observed deep erosions of the lingual mucosa and gums of cattle which grazed *Leucaena* for several months. The present observations demonstrated further progression of this condition.

In a previous grazing trial, heifers grazing *Leucaena* had poor reproductive performance and a number of heifers diagnosed pregnant by rectal examination did not calve (Holmes 1980). A similar effect recorded here, together with the presence of normal trophoblast lining the uterus, suggests embryonic death up to 3 months after conception rather than failure to conceive. Mimosine is a known anti-mitotic agent (Montagna and Yun 1963; Hegarty *et al* 1964; Pritchard and Court 1968) and the inhibition of mitosis could be expected to result in aberrations in uterine or foetal membrane developments inimical to normal pregnancy. Foetal death and resorption in pregnant rats were produced by feeding dried *Leucaena* leaves, or by dosing orally with a water extract of the leaf (Joshi 1968). Although this indicates mimosine as the anti-fertility agent, in cattle a different agent, perhaps DHP, may be acting, since Jones *et al* (1978) state that mimosine could not be detected in the blood of cattle fed on a sole diet of *Leucaena*. Alternatively, the abnormal thyroid status of the heifers may be interrupting pregnancy.

Acknowledgment

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BOOK REVIEW

PRACTICE MANAGEMENT

This publication* is intended for practitioners engaged in medicine, dentistry and veterinary science who wish to improve their practice management and for those wishing to set up practice.

The book is divided into 2 sections: the first deals with establishing a practice, the second with day to day running of a practice.

Any practitioner contemplating establishing a practice by purchase of an existing practice will find good information in Chapters 2 and 3. However, I feel that the section on goodwill payment is not directed forcefully enough to veterinary practice and one is left wondering what criteria should be used.

For those veterinarians venturing into practice by commencing a new practice there is an overview of the many points for consideration. These sections are well worth reading, even if only to remind oneself.

Leasing of premises is dealt with well in succinct point by point form.

Construction of premises is discussed, and in general terms covers the salient points. The practice designs are rather superficial and anyone contemplating construction would need to research the subject more extensively.

Chapter 6 deals with partnerships and presents a wide range of methods of this business structure, including agreements and employment clauses.

The second part of this book is well worth reading for the many suggestions relating to running a practice. I feel many practitioners will benefit reading this section as there are many tips on sharing workload, delegating responsibility, employment of good staff, telephone technique, business and medical records, credit and debit control. All of which help to make for a day with less interruptions, better cash flow, less paperwork and generally better practice management.

There is a chapter on the Australian Taxation System. Appendices deal with the Medical Records System of the Royal Australian College of General Practitioners, Published Report on Appointing Systems of the Royal College of General Practitioners, Calculation of Interest, and there are Glossaries of Medical Terminology and of Business Terms.

I recommend this book for all veterinarians in practice, bearing in mind that there are some sections which do not deal adequately with the more specific topics for veterinarians.

R. G. Pedrana

**Practice Management*, F. Baverstock and D. Eve. Australia and New Zealand Book Co., Sydney, 1980. Pp. 156. Review copy from ANZ Book Co., Cross St., Brookvale, New South Wales. $14.95.