A LOOK AT RECOMMENDATIONS FOR THE CONTROL OF INFERTILITY DUE TO CLOVER DISEASE IN SHEEP

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I. INTRODUCTION

Bennetts, Underwood and Shier (1946a) published the first detailed scientific report of an infertility syndrome affecting ewes grazing subterranean clover pastures which they thought to contain "... an oestrogen or an oestrogen precursor ...". The infertility was expressed as a failure to conceive and was accompanied by varying degrees of dystocia, uterine prolapse and lactation in maiden ewes. The syndrome, which included abnormalities of the urino-genital tract and lactation in wethers, subsequently became known as "clover disease" (Shier & Rossiter 1949). Several reviews of the scientific literature are available (Moule 1961; Moule, Braden & Lammond 1963; Morley 1966; Bickoff 1968; Braden & McDonald 1970; Francis; Gladstones & Stern 1970; Lindsay & Kelly 1970; Rossiter 1970; Braden & Cox 1974) and so this is not attempted here. This paper presents the recommendations that can be made to flock owners troubled by the disease and examines the basis of such recommendations.

Clover disease in its chronic form, involving severe infertility together with high incidence of dystocia, prolapse etc., is seen only rarely today. It seems confined to areas of new land development (based on highly oestrogenic cultivars of subterranean clover) where clover dominance is common in the first few years following pasture establishment. There is a growing body of evidence, however, that reproductive wastage due to clover disease is still widespread, but that it occurs as a comparatively uncomplicated infertility of more modest proportions (Davenport 1967; Davies & Mailer 1970; Davies, Rossiter & Mailer 1970; Lightfoot 1972; Wroth & Lightfoot 1972). In Western Australia some 3.5 million ewes are grazed in Shires (Local Government Areas) that contain, on average, more than 25 per cent of the highly oestrogenic cultivars of subterranean clover in the pasture. Although no areas in other States fall into this classification the present author's calculations suggest that each year approximately one million ewes of the Australian flock fail to lamb due to clover disease.

Attention must also be drawn to a second form of reproductive loss, popularly known as "temporary infertility", that occurs in ewes actually grazing oestrogenic pasture around mating time. This phenomenon, first described in Australia by Morley and co-workers, should not be confused with the permanent and progressive infertility described by Bennetts, Underwood & Shier (1946a) in which joining normally occurs some months after pastures have dried off and lost their oestrogenic potency. Because of the limited space available, discussion in the present paper is confined to the permanent form of infertility but some of the recommendations examined, in particular those in section II (c), are relevant to both.

II. RECOMMENDATIONS

Coincident with their scientific report, Bennetts, Underwood & Shier (1946b) published a number of recommendations for farmers with flocks affected by clover disease. It was the first of a series of articles to be released and

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progressively updated by appropriate authorities throughout Australia. In particular the Departments of Agriculture in both Western Australia (e.g. Shier & Rossiter 1955; Beck & Gardiner 1965; Neil, Fels & Francis 1969; Marshall 1973) and South Australia (e.g. Chamberlain 1955; Habel 1967) have been active in this regard. Methods advocated for the control of clover disease in the ewe may be divided on the basis of their modus operandi into three main classifications.

These are:

(a) Methods involving conversion to an alternative enterprise.
(b) Methods involving change in flock husbandry.
(c) Methods involving change in pasture management.

(a) Conversion to an Alternative Enterprise

Because flock infertility due to clover disease is permanent (Schinckel 1948; Underwood & Shier 1951), if lambing percentages fall to very low levels it becomes unprofitable to continue breeding, at least with stock bred on the property. Thus alternatives, such as those below, need consideration.

(i) Graze sheep for wool production only

Should low fertility force a flock owner to discontinue breeding, ewes on hand can be retained for wool production or fattened and sold for slaughter. In either event a gradual conversion to an all wether flock maintain is by purchasing replacements follows. With such a policy financial loss due to phyto-oestrogens can still occur but in the form of increased mortality among wethers due to bulbo-urethral disease (Bennetts 1947) and urinary obstruction (Gardiner, Nairn & Meyer 1966; White, Nottle & Nairn 1972). Additional economic loss due to reduced wool production in affected wethers seems likely but has not been investigated. It is significant to note, however, that the problems with wethers result from current intake of phyto-oestrogens. Strategic grazing management in conjunction with the removal of susceptible stock can therefore be adopted to reduce losses.

(ii) Regular purchase of replacement ewes

A breeding programme can be maintained on severely affected properties if based on the regular replacement of existing stock with ewes purchased from non-oestrogenic clover areas. Bennetts, Underwood & Shier (1946b) noted that such ewes would lamb normally for at least one year after transfer and in many cases a second lambing was possible before fertility was markedly affected. The concept is supported by published evidence of the rate of the fertility decline (Davies and Maller 1970; Davies, Rossiter & Maller 1970; Marshall et al. 1971) and rests on the fact that purchased ewes can be joined without previous exposure to oestrogenic pasture. In contrast, replacements bred on the property may have grazed oestrogenic pasture for two seasons, both as a lamb and a hogget, prior to being joined for the first time.

(iii) Sell sheep and buy cattle

Although there are many instances in the literature of reproductive disturbances in cattle receiving oestrogenic forages (Reviews - Moule, Braden & Lammond 1963; Bickoff 1968) a permanent infertility, resulting from prolonged intake of phyto-oestrogens, does not appear to have been reported. While it is unlikely that major infertility as seen in the ewe will develop, it is possible that a measure of reproductive wastage is induced but definitive experiments of sufficient sensitivity to detect the reduction have yet to be conducted.

(b) Changes in Flock Husbandry

In situations where flock fertility has not declined to the point at
which breeding becomes unprofitable a range of management practices, involving manipulation of the stock rather than the pasture, have been recommended.

(i) Grazing management

Early recommendations for the prevention of clover disease included advice not to graze breeding ewes on dominant stands of oestrogenic clover during the growing season. This finds less application today due to the practice of running comparatively high stocking rates that leave little choice of alternative grazing. Similarly, past recommendations to reserve dominant clover pastures for hay have less relevance to today's sheep farming practice. In addition it has been shown that such hay, if cured rapidly, may retain a high proportion of its original oestrogenic potency (Davies & Dudzinski 1965).

The principle implicit in the original recommendations for grazing management is seen more recently in advice to graze the least susceptible classes of stock on the most oestrogenic pastures (Table 1).

### TABLE 1

Theoretical example of the effects of strategic grazing on fertility

<table>
<thead>
<tr>
<th>Age of flock at joining (years)</th>
<th>&quot;Control&quot; farm</th>
<th>&quot;Oestrogenic&quot; farm*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Theoretical fertility</td>
<td>Random grazing</td>
</tr>
<tr>
<td></td>
<td>(a)</td>
<td>(b)</td>
</tr>
<tr>
<td>1.5</td>
<td>70</td>
<td>60</td>
</tr>
<tr>
<td>2.5</td>
<td>85</td>
<td>65</td>
</tr>
<tr>
<td>3.5</td>
<td>95</td>
<td>65</td>
</tr>
<tr>
<td>4.5</td>
<td>95</td>
<td>55</td>
</tr>
<tr>
<td>Average</td>
<td>86</td>
<td>61</td>
</tr>
</tbody>
</table>

* Assumptions:

. The example assumes a farm with 5 paddocks containing either 0, 25, 50, 75 or 100 per cent oestrogenic clover. Merino ewes are run in flocks according to age, first joined at 1.6 years and sold following the fourth lambing. Theoretical age-fertility relationships are shown in (a) above. For simplicity deaths have been ignored.

. A permanent depression in the percentage of ewes that conceive (relative to the theoretical inherent level) is expressed at joining due to the cumulative effects of grazing oestrogenic pastures over previous seasons.

. The depression resulting from one full season's grazing on paddocks containing either 0, 25, 50, 75 or 100% oestrogenic clover are 0, 5, 10, 15 or 20 per cent ewes lambing respectively.

. Grazing management during the growing season

. (b) The ewes are grazed without consideration to pasture composition, and are moved between paddocks frequently.

. (c) The youngest ewes are allocated the paddocks containing the most clover.

. (d) The youngest ewes are allocated the paddocks containing the least clover.

The strategic allocation of flocks to pastures rests on the likelihood that not all paddocks on a property will be equally oestrogenic. Variation in oestrogenic potency will result from differences in the species and cultivar group, the
proportion of oestrogenic components in the sward and phosphate status. Because the infertility of clover disease is permanent and cumulative, young ewes, in terms of their total life time productivity, are more susceptible than old ewes. There may be other aspects that affect susceptibility such as the presence of circulating progesterone (Morley 1966; Lindsay & Francis 1969) but these have not been proven.

(ii) Joining husbandry

The infertility in ewes affected with clover disease is associated with a failure of sperm transport through the ewe's genital tract leading to reduced egg fertilization rates (Turnbull, Braden & George 1966; Lightfoot, Croker & Neil 1967; Kaltenbach & Davies 1970). This suggests that sperm transport, and therefore conception, may be improved by increasing the number of services per oestrous ewe. A field trial (Lightfoot & Smith 1968) with clover affected ewes showed that increasing the number of rams joined at mating produced considerably more lambs. An association between periods of high ram/ewe ratio during joining and high fertilization rates in a flock affected with clover disease has also been noted (Fels and Neil 1968). Experiments with flocks grazing non-oestrogenic pastures have clearly shown that, except with two-tooth rams, there is little advantage in using high ram percentages at joining (Lightfoot & Smith 1968; Dawe et al. 1970). In clover affected flocks the evidence indicates that more rams may be justified, but there is still insufficient knowledge for budgeting and specific recommendations.

(iii) Lambing husbandry

A high incidence of dystocia in lambing ewes leading to excessive mortality among both ewes and lambs are features of the clover disease syndrome (Bennetts, Underwood & Shier 1946a). The dystocia was observed to be of maternal origin and primarily due to uterine inertia, although the latter observation has been questioned by Maxwell (1970).

Three points are of significance with regard to the treatment of the dystocia caused by clover disease. First, constant vigilance is necessary to identify ewes affected by dystocia in the lambing flock as they engage in only a very brief period of labour before abandoning further expulsive effort (Bennetts, Underwood & Shier, 1946a). Secondly, dystocia is most commonly seen in young ewes lambing for the first time. Thirdly, losses due to dystocia occur most frequently in "good clover years" often characterised by an early germination of pastures (Bennetts, Underwood & Shier 1946a; Chamberlain 1955; Bull 1951; Bennetts 1956). The practical implications of these points are that if help is to be given an intensive lambing system may prove essential to facilitate the identification and assistance of affected ewes (Maxwell 1970). As not all classes of ewes are equally affected it may only be necessary to involve young ewes in the system, and even then, perhaps only in years when pastures germinate early.

(iv) Selection of breeding stock

Based on evidence that the infertility of clover disease was both progressive and permanent (Schinckel 1948; Underwood & Shier 1951), recommendations were made that ewes in affected flocks should be culled if they fail to lamb in two successive years. Such recommendations are contrary to the findings of several investigations in sheep grazing non oestrogenic pastures (Reviewed by Turner 1969) and assume a higher "repeatability" of barrenness in ewes affected by the disease (Barrett, George & Lammond 1965). However, analysis of individual lambing records in recent studies comparing fertility on pastures of varying oestrogenicity clearly demonstrates that the practical value of culling "twice dry" as a means of improving fertility on clover affected properties is limited (Table 2).
The question of culling for barrenness in flocks affected with clover disease raises, in its antithesis, another interesting concept, namely, selection for fertility. Data such as that presented in Table 2 show that some ewes in a flock grazing oestrogenic pastures are capable of maintaining normal fertility although flock lambing performance is severely affected. The basis of this phenomenon remains to be identified. Limited evidence (Obst, Seamark & McGowan 1971) that "resistance" to clover disease is associated with blood haemoglobin type was not supported by results (Wroth et al. 1973) from experiments cited in Table 2.

Early reports (Bennetts, Underwood & Shier 1946a,b) suggested that some British Breeds and their crosses appeared less susceptible than Merinos to the dystocia and infertility of clover disease but the latter claim was subsequently discounted (Shier & Rossiter 1955). More recent evidence with Border Leicester x Merino cross ewes (Davies, Rossiter & Mailer 1970; Kaltenbach & Davies 1970) revives interest in the original argument. Whether or not crossbreds are in fact more resistant, or as is more likely they are just inherently more fertile, remains to be seen. A significant point, however, is that there may be advantages in running more fertile breeds or strains under oestrogenic situations as total lamb production should be higher and a longer period could elapse before breeding becomes unprofitable.

Methods Involving Change in Pasture Management

The following section deals with methods that reduce the quantity of phyto-oestrogen ingested by sheep through the induction of qualitative changes in the pasture. As such it is technically independent of section (b), but in practice a combination of techniques from both sections may frequently provide the most effective measure of control.

The use of clovers low in phyto-oestrogens

Three major developments during the 1960's contributed substantially towards the identification of subterranean clovers that are considered safe with regard to clover disease in grazing stock. First was the demonstration that subterranean clover strains differed markedly in their oestrogenic potency (Davies & Bennett 1962; Millington, Francis & McKeown 1964; Davies & Dudziński 1965; Bennett, Morley & Axelsen 1967). Second was the recognition that although different cultivars of subterranean clover contained widely varying amounts of three closely related phyto-oestrogens, Genistein, Biochanin A and Formononetin,
only formononetin (subsequently metabolised to equol in the rumen) was important with regard to long term oestrogenic effects in grazing sheep. It is reassuring to note that much of the early evidence on this point derived from bioassay and metabolic research (reviewed by Braden & Cox 1974) is now supported by data on ewe fertility from grazing experiments (Davies, Rossiter & Maller 1970; Neil, Lightfoot & Fels 1974; Marshall 1974; Rossiter & Marshall 1974). The third was the development of analytical techniques that permitted rapid determinations of phyto-oestrogen levels in plants (Beck 1964; Francis & Millington 1965a).

Progress until comparatively recent times in plant breeding to obtain cultivars free or low in formononetin was reviewed by Francis, Gladstones & Stern (1970) and McWilliam (1972). The work involved differing approaches, including production and broad scale screening of mutants (Francis & Millington 1965a,b) and selection among naturally occurring biotypes or among their cross-breds (Gladstones 1967; Morley & Francis 1968). Despite much progress in the rationalisation of objectives and development of techniques only three "new" low formononetin subterranean clovers (Uniwager, Daliak and Seaton Park) have been certified and released for commercial use. It is an apparent enigma that the achievement of lower formononetin levels is now one of the easiest of the many criteria that must be satisfied in the selection and approval of new cultivars.

Certainly in W.A., and perhaps also in other states, the greatest deficiency in the range of certified subterranean clovers is in the lack of cultivars earlier than Daliak for use both in the drier fringes of the wheatbelt and on sandy soils in areas of slightly higher rainfall. Uniwager, a mutant almost totally devoid of phyto-oestrogens and of early maturity (Francis 1968) has failed to impress in either production or persistence. Geraldton, the standard for such areas is now recognised as highly oestrogenic (Davies, Rossiter & Maller 1970). Continued recommendations for sowing this cultivar seem pointless as agronomic success is positively correlated with risk of ovine infertility. Northam A, which is low in formononetin and earlier than Geraldton, appears to be a satisfactory alternative. Several promising crossbreds, all low in formononetin and including some that flower up to 7 days earlier than Geraldton, and others of subspecies yanninicum which show specific adaptation to waterlogging while retaining the winter vigour of Yarloop, are undergoing agronomic evaluation (Francis 1973a).

Progress has also been made in the breeding and field evaluation of alternative legume species such as the rose and cupped clovers (Beale & Crawford 1972; Rossiter, Taylor & Anderson 1972), serradella (Gladstones & Devitt 1971) and medics (Poole 1970). It is interesting to note that whereas many of the Medicago sp. may contain quite high levels of phyto-oestrogens, particularly in the presence of foliar pathogens (Francis & Millington 1971), infertility among ewes grazing these species has not been reported in Australia.

(ii) Replacement of undesirable cultivars

With the availability of suitable low formononetin cultivars the question of how to replace existing oestrogenic pastures assumed importance. Some of the highly oestrogenic subterranean clovers, in particular Dwalganup and Yarloop, are well adapted to their established environments and have often built up large reserves of hard seed in the soil. The principle of replacement therefore centres about first reducing the seed bank by successive years of cropping. Devitt (1970) has proposed programmes that involve spraying or heavy spring grazing of the undesired cultivar to reduce clover seed set, followed by at least two successive crops. The replacement cultivar can be undersown in the final crop.

Although much research remains to be done, particularly with regard to the use of selective herbicides and establishment techniques (Poole & Gartrell 1970; McGowan & Williams 1973) it is apparent that the agronomic success of such replacement programmes will depend heavily on the relative "competitive abilities"
of the original versus the replacement cultivars. There is, however, little
published evidence on this question. Rossiter (1966) presented results to
suggest that at Kojonup, W.A., Seacon Park can maintain reasonable purity when
sown on old Dwalganup land and that in the absence of waterlogging Yarloop can
be displaced by a range of cultivars. Following a chance contamination, Daliak
was also observed to increase substantially in Dwalganup pastures under
conditions of high grazing pressure (Davies, Rossiter & Maller 1970). A range
of experiments in which interactions in mixtures of clover strains is being
examined in relation to a number of factors (including initial seeding rate and
grazing intensity) are currently in progress (Rossiter & Francis, personal
communications). Results to date indicate that in some situations both Northam A
and Daliak are successful when grown with Dwalganup whereas Uniwager is not.

Evaluation of all new low formononetin strains for persistence and competitive
vigour under full scale grazing conditions, preferably involving a range of
stocking rates, is essential if recommendations are to be soundly based in the
future. The importance of this phase, although previously recognised (Rossiter
1966; Francis, Gladstones & Stern 1970), cannot be over emphasised.

(iii) Dilution of oestrogenic cultivars in the pasture

The earliest recommendations for prevention of clover disease included
advice to introduce or encourage species other than subterranean clover in order
to reduce the percentage of the clover in the sward. In particular the sowing
of annual rye grass or the use of "scratched in" crops of oats were strongly
advocated. More recently the use of nitrogenous fertilizers or herbicidal
sprays to achieve the same effect have been considered. The success of these
operations is difficult to ascertain. Experiments to evaluate the sowing of a
mixture of oats and rye grass into previously clover dominant paddocks indicated
marked reductions in the percentages of clover (Anon. 1948) but data on
persistence were not reported.

The success of programmes aimed at reducing the proportion of oestrogenic
clover in a pasture will depend on the relative intakes of alternative
components by the sheep, an animal renowned for its ability to graze
selectively. Early reports on clover disease stated that green subterranean
clover was unpalatable to sheep and argued that increasing the proportion of
non oestrogenic species in the sward would favour the selection of a "safe"
diet; Recent evidence (Francis 1973b) suggests that some cultivars containing
high levels of flavonoid glucosides may be unpalatable to sheep, and Rossiter
(personal communication) has observed that both Dwalganup and Yarloop were not
selected in common grazing with a range of low formononetin cultivars. For
practical purposes, however, as stocking rate increases so the relative intakes
of grass versus clover will approach the ratio of those species in the sward.
There is also evidence that the oestrogenicity of a pasture is directly related
to the proportion of oestrogenic clover present (Davies & Maller 1970). As
moderate to high stocking rates are a feature of the wool industry in southern
Australia it is likely that pastures containing as little as 30 per cent
oestrogenic clover cannot be considered as "safe" in the long term.

(iv) Fertilizer Applications

The fact that individual isoflavone levels for any one strain were found
to vary over a 2-fold range suggested that environmental and/or growth stage
effects could be important determinants of oestrogenic activity in subterranean
clover. In a concerted attack on the problem (Reviewed by Rossiter, 1970),
Rossiter with Beck and other colleagues studied the influence of a variety of
factors including temperature, light, moisture stress and defoliation. They
found that whereas extreme levels of each of these factors influenced
formononetin concentration in the leaves they were unlikely to have any major
influence on the occurrence of clover disease in the field. Of considerably
more importance were the findings that deficiencies of the major plant nutrients,
phosphate, sulphur and nitrogen can almost double the concentration of formononetin in Dwalganup leaves. The practical significance of this research, at least with regard to phosphate, has been confirmed by sheep bioassay (Neil & Marshall 1970) and supports earlier recommendations that especially on newly sown pastures, phosphate be applied right up to the optimal level for maximum economic return.

III. CONCLUSIONS

The treatment of infertility due to clover disease depends principally on the level to which lambing percentages have fallen and the opportunity to effect changes in flock and/or pasture management. In extreme cases, seen only rarely today, conversion to an alternative enterprise may be justified. More usually, grazing, joining and lambing procedures can be modified to minimise the effects of the phyto-oestrogens present in existing pastures. Concurrently, programmes designed to reduce the oestrogenicity of the pasture may be instituted. It is unfortunate that whereas the recommended procedures offer success in the biological sense, in some cases the economics of the situation are open to doubt. Care must be exercised to ensure that total farm profitability is not reduced as fertility should not be considered in isolation.

IV. ACKNOWLEDGEMENTS

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V. REFERENCES


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