THE ROLE OF PHYTOESTROGENS in pseudopregnancy of goats

Alice Fraser, SVS Laboratories, Hamilton, and **Vicki McLean** of the Dairy Goat Co-operative, discuss a case involving an increased rate of pseudopregnancy in a North Island dairy goat herd.

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INTRODUCTION

Pseudopregnancy is the abnormal accumulation of sterile uterine fluid in the absence of pregnancy due to persistence of corpus luteal function (Harwood and Moeller, 2018). The condition is sometimes termed hydrometra, but this term is also used to describe excess uterine fluid accumulation during pregnancy. Pseudopregnancy occurs in several species, but is particularly common in goats, with incidences in milking herds sometimes greater than 10%.

To the owner, the affected animal does appear to be in-kid following oestrus (with or without mating), with gradual abdominal distension and no return to oestrus. In non-lactating does, some later mammary development occurs. The condition is realised at scanning, or, less commonly, due to natural luteolysis leading to sudden expulsion of copious uterine fluid (hence the colloquial name 'cloudburst'). Luteolysis can occur before term (usually in unmated does), at term or beyond term (in mated does). Pseudopregnancy is an important pathological condition, as it represents one of the main causes of temporary infertility in dairy goats (Souza et al., 2013).

The aetiology and pathophysiology have not clearly been determined, but may include:

1. early embryonic death, due to toxoplasmosis, border disease virus, etc
2. consumption of oestrogenic compounds in pasture or feeds (clover species, beans)
3. use of oestrus-controlling hormones in breeding management (eg, gonadotrophin-releasing hormones)
4. high prolactin levels in milking goats. Although disproved by some workers (Wittek et al., 1998), the ability of does to continue lactating without regular pregnancies may be linked to the higher incidence of pseudopregnancy in this species.

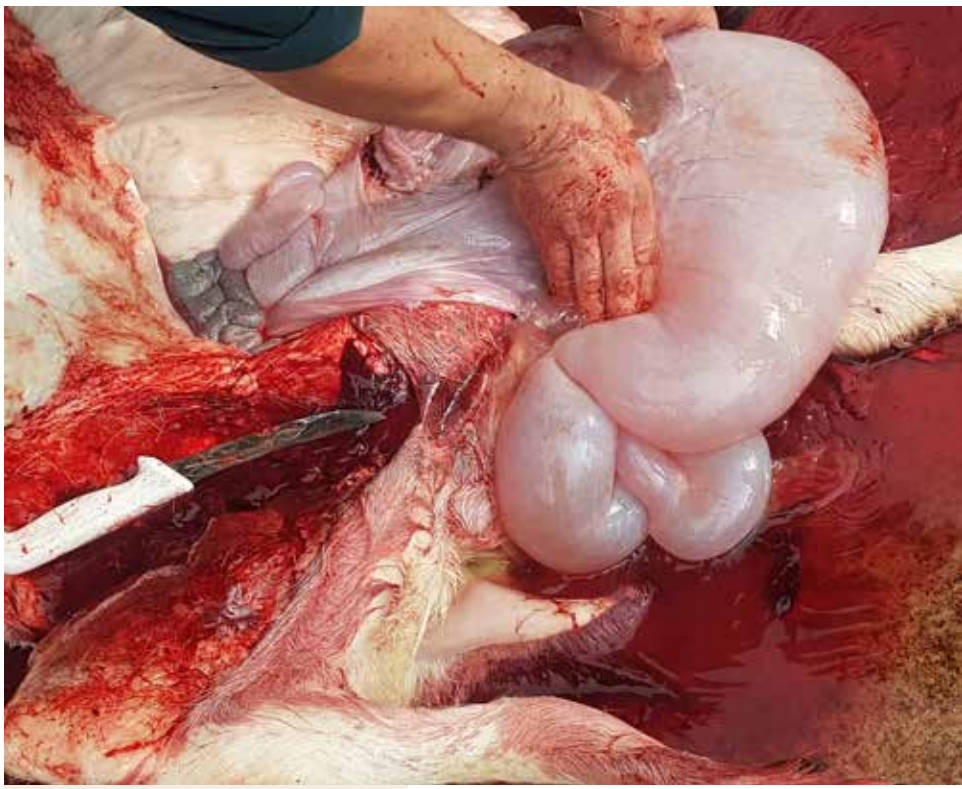

FIGURE 1: Postmortem of doe with pseudopregnancy, large fluid-filled uterus.

Treatment involves injection with prostaglandin injection to stimulate luteolysis and return to oestrus.

A CASE OF INCREASED INCIDENCE OF PSEUDOPREGNANCY

An increased incidence of pseudopregnancy occurred on a dairy goat farm in the upper North Island, in which 60 of a mob of 700 does were affected (8.6%).

Five adult bucks had been joined with this group of does. All stock were on a grass-based diet (cut and carry), plus a proportion of the diet (<20%) was made up of fava beans (or faba beans, *Vicia faba* L. var. minor) that were grown on the property. Pseudopregnancy was noted in affected does at pregnancy scanning, carried out at approximately 50 days after the bucks were removed. The does responded well to an injection of 250ug of cloprostenol, occasionally requiring an additional 20i.u. of oxytocin to ensure fluid clearance (for does being milked twice daily, exogenous oxytocin is not usually required). The does had not received premating gonadotrophin treatment, ruling this out as a possible underlying cause of pseudopregnancy.

FIGURE 2: Uterus 1, uterine endometrial cyst (12mm diameter).

In order to investigate causes of this increased incidence of pseudopregnancy, three does were euthanased and postmortems carried out on site (Figure 1). Fresh uteri were submitted for further gross evaluation and sampling for histopathology at SVS Laboratories, Hamilton.

OBSERVATIONS

All three uteri were enlarged and contained copious amounts of clear to straw-coloured fluid.

Uterus 1 had multiple variable cysts (3–12mm diameter) protruding from the endometrial surface (Figure 2). The ovaries had multiple developing follicles, a single 4mm cystic follicle protruding from the surface of one ovary and a prominent dark, corpus luteum (CL) bulging from the ovarian surface. Uterus 2 was the most enlarged uterus, with multiple developed uterine caruncles on the endometrial surface (Figure 3). The ovaries had multiple follicles and several prominent dark CL. Uterus 3 was mildly enlarged, with an unremarkable endometrial surface. There was a dark CL bulging from the surface of one ovary.

The uterine endometrial surfaces were otherwise normal intact mucosae, with no gross evidence of embryonic or fetal membrane remnants. The gross findings were consistent with pseudopregnancy in all uteri examined. In addition, uterus 1 showed cystic endometrial hyperplasia.

HISTOLOGICAL EXAMINATION OF THE UTERINE TISSUES

Uterus 1 revealed marked endometrial oedema and congestion. The endometrial glands were markedly hyperplastic, with moderate to marked glandular branching and dilatation (Figure 3). The endometrial cysts were lined by intact, variably thickened epithelium, with areas of mild inflammatory cell infiltration (lymphocytic) and areas of fibroplasia.

Uterus 2 had diffusely oedematous and congested endometrium and subendometrial tissues. The caruncle regions were thickened, with central endometrial necrosis and mixed inflammatory cell debris (neutrophils and lymphocytes) suggesting some spontaneous involution of these caruncular sites. Intervening endometrial tissue had plentiful scattered stromal lymphocytes.

Gross and microscopic findings revealed no evidence of early embryonic death as an underlying cause of the pseudopregnancies. The presence of cystic endometrial hyperplasia was consistent with the effect of persistent oestrogenic stimulation. The inclusion of fava beans in the diet was investigated further as a source of oestrogenic compounds due to their high levels of phytoestrogens.

Fava beans (Figure 4) had been included year-round in the diet for approximately five years without previous fertility issues. Such beans are a valuable source of protein and energy for production animals. They are also known to contain phytoestrogens, plant oestrogenic compounds that are structurally and/or functionally similar to mammalian oestrogens and their active metabolites. The levels of several phytoestrogens in fava beans have been analysed, including daidzein, genistein and glycitein, which were found to be higher than in pea seeds, although a fraction of the content in soyabean meal (Gatt et al., 2013).

The effects of phytoestrogens are hotly debated in the medical industry due to the growing inclusion of plant protein, notably soyabean,

PSEUDOPREGNANCY IS AN IMPORTANT PATHOLOGICAL CONDITION, AS IT REPRESENTS ONE OF THE MAIN CAUSES OF TEMPORARY INFERTILITY IN DAIRY GOATS.

in lieu of meat protein. Whether or not phytoestrogens are considered beneficial or harmful depends on many factors still being investigated, but in essence they are endocrine disruptors. In ruminants, ingestion of feeds and pastures high in phytoestrogens has been associated with cystic endometrial hyperplasia, due to the prolonged oestrogenic stimulation (Radi, 2005). The hyperplastic effects on the uterus are thought to inhibit production of the luteolytic hormone, prostaglandin F2alpha, leading to persistence of the CL, increased progesterone levels and pseudopregnancy (MacLachlan, 1987).

Since fava beans had been part of the goats' diet for several years without previous untoward effect, it is possible that variation in plant phytoestrogenic levels had increased due to stress (drought, etc) or there was an accumulative effect over the years of phytoestrogen consumption. The effects of the phytoestrogen on the bucks' fertility is currently being investigated.

The effects of phytoestrogens in ruminants have been investigated previously in New Zealand, in relation to certain red clover cultivars. An investigation of red clover consumption by Kelly et al., (1980) found that the high phytogenic content caused temporary reduction in fertility (clover disease) of ewes grazing it. Although the persistence of old 'oestrogenic' ecotypes of subterranean clover (*Trifolium subterraneum*) in pasture still remains a risk, genetic improvement has successfully lowered the production of phytoestrogens such as isoflavone by these species, such that clover disease infertility has been greatly reduced (Reed, 2016). VS

FIGURE 3: Uterus 2, endometrial surface, uterine caruncle.

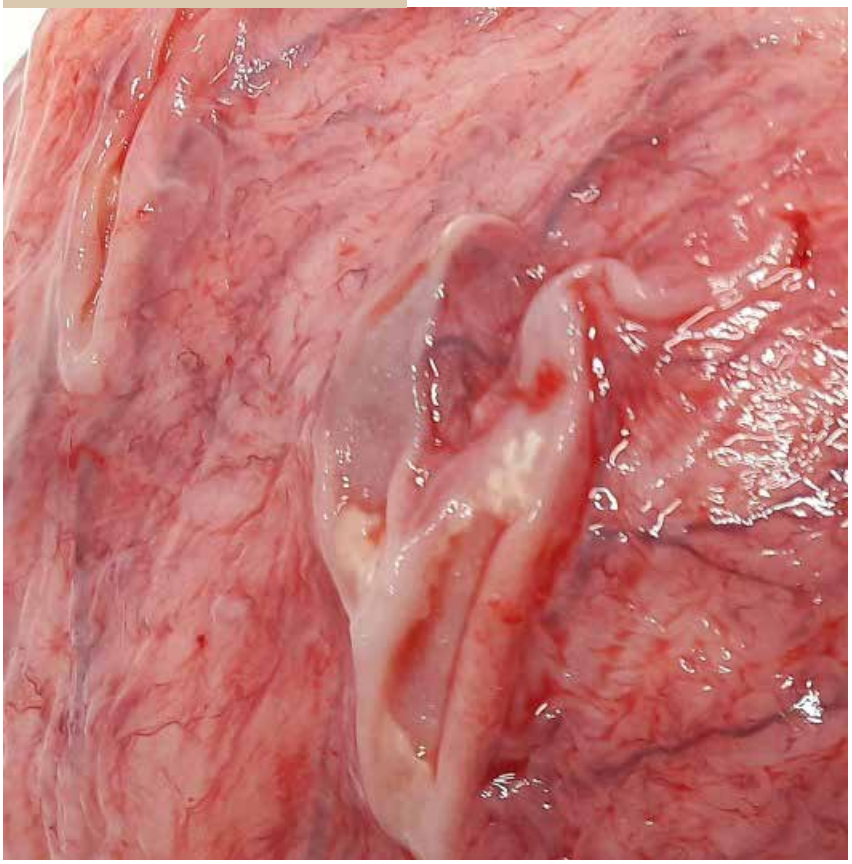

FIGURE 4: Fava beans are known to contain phytoestrogens, an endocrine disruptor.

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