Benefits of treating the individual cow:
'Oestrus not observed' ('ONO', missed heat, 'not seen bulling')

The routine veterinary visit is an important part of the management of fertility. A key part of the routine visit is the examination of cows which have not been seen in heat, but have been calved long enough that they are eligible to be inseminated. Some of these cows may have abnormal ovaries (cystic structures or ovaries that are small and inactive) or have an infection of the uterus several weeks after calving (endometritis or 'whites'). However, a large proportion of cows presented as 'not seen bulling' are likely to have apparently normal reproductive tracts and a corpus luteum (CL) on at least one ovary. The presence of a CL indicates that the cow has probably been in heat and ovulated within the last 5-17 days. If cows which have cycled are not treated then they are likely to carry on cycling, coming in heat roughly every 21 days, until they get pregnant. However, it is likely to be at least seven to ten days before they come into heat again, and, as the previous heat behaviour was missed, it is quite probable that subsequent heats will be missed too.

Missing heats has become an increasing problem in modern dairy herds because, as cows have been bred for increasing milk yields, there has also been a significant decrease in the length of time over which cows show heat. This time can be as short as 3 hours in the highest production cows and it is therefore very easy to miss these heats. Looking at inter-service intervals can identify a problem at the herd level with missed heats (see Fig 1).

It is also possible that the CL is abnormal and is a persistent CL that will not disappear as quickly as a normal one. These CLs are more common in cows with endometritis, which stops the normal breakdown process of the CL (called 'luteolysis'), but they can occur in otherwise normal cows. Diagnosis of a persistent CL is not possible on a single examination but the standard treatment is exactly the same as for a normal CL - prostaglandin F\(_2\alpha\) (PG), the hormone which is responsible for natural luteolysis.

The aim of treatment with PG is to remove the CL and thereby stimulate the cow to come on heat and to ovulate. Non-responsive cow (i.e ones that are not seen in heat) can be retreated 11/14 days later and oestrus observed again or fixed time AI can be used (72 and 96 hours after injection).

PG treatment has to be used strategically - to be effective treatment needs to reduce voluntary waiting period (the interval between calving and the first time a cow is inseminated) (Archer et al 2015 [link](#)). Delaying treatment and reducing the number of inseminations before a cow is culled for failing to conceive increases cost per pregnancy (Fig 2) and reduces the benefit of treatment.

One commonly used alternative to PG treatment alone is the use of a progesterone device alongside PG treatment - with the device inserted for 7 days and PG

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Fig 1: In a herd with good oestrus detection, over 50% of the intervals between services should be 18-24 days. In this herd there are a lot of cows with longer intervals, so heats are being missed. Treating cows that have not been seen bulling will reduce the chance of them being missed the next time. © TotalVet (QMMS/SUM-IT).

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given 24 hours before device removal. Compared to PG alone, the combined treatment is likely to improve the proportion of cows inseminated first time as oestrus behaviour tends to be stronger in cows treated with progesterone, perhaps because it supplements progesterone (which may be low in high producing cows) and also because PG treatment is given at a time when the CL is more likely to be responsive. Fixed time AI can also be used after the device removal (48 and 72 hours). Thus combining P4 and a progesterone device is particularly useful in herds where oestrus detection is poor.

Another alternative in herds with poor oestrus detection is using the Ovsynch programme, which combines GnRH with PG, to tightly control ovulation resulting in a single fixed time AI. The best treatment option will vary between farms based on your goals and your underlying fertility problems so discuss with your vet what is best for you.

Endometritis

After calving, all cows have a uterus which is contaminated with bacteria, which in most cases is eliminated within a few weeks. However in a minority of cows, this contamination is not eliminated and the uterus becomes infected. In most cases the infection is mild but chronic, meaning it doesn’t affect the cow but does results in infertility. Some cows may have an obvious vulval discharge, but many will not.

Only two treatments have shown any evidence of effectiveness – prostaglandins and intra-uterine antibiotics. Antibiotics have the best evidence of an economic benefit, and seem to be effective in cows and without a CL, whereas the data suggest that PG works best in cows with a CL. There is no good evidence that injectable antibiotics are useful for the treatment of endometritis.

Variations between cows in the severity and chronicity of endometritis means that there are no simple calculations as there are for treating missed heats, as the response is cow dependent. However, in large scale studies, antibiotic treatment of cows with endometritis has been shown to decrease calving to first service interval, increase first service conception rates, and decrease calving to conception intervals. Based on these results it would be a reasonable expectation that cows with endometritis that are treated with intra-uterine antibiotics get pregnant 10 days earlier than untreated cows - a return of £20 for an £8 cost.

The key to effective antibiotic treatment is to not treat too early or too late. Treatment under 10 days after calving is unlikely to be beneficial as many treated cows would have had normal fertility (due to ‘self-cure’) and in some cows may do more harm than good. If treatment is delayed until after 56 days then it will be less effective, partly because the uterus has less time before breeding to become normal, but also because the longer a cow is infected for, the less responsive to treatment the endometritis will be.

PG treatment is cheaper than antibiotic treatment, but whereas intrauterine antibiotics seem to work whatever the ovarian status of the affected cows, PG seems to work most effectively in cows with a CL. Recent work in New Zealand has shown that overall impact on profitability is less as ‘normal’ cows are far more common than abnormal ones.

**Fig 2 : Effect of number of inseminations after treatment on the benefit of treatment. The cost per pregnancy decreases as more treated cows become pregnant.**

Treating cows early with PG makes economic sense. Waiting (‘giving the cow another chance’) costs money. If PG is used as a last chance treatment (i.e. the cow isn’t inseminated again after treatment insemination, the benefit per treated cow is only £3.08 - less than the cost of the prostaglandin.

These benefits do not include the benefits from treating abnormal cows with persistent CLs, which are greater than for cows with missed heats. Treatment of abnormal cows often has a better cost-benefit than treating ‘normal’ cows; but the
treating cows with a CL with PG and treating the rest with antibiotics was as effective as treating all cases with an antibiotic. Such a protocol takes more time but it suits a UK situation where treatment is focussed on individual cows better than the seasonal New Zealand system and also has the benefit of reducing antibiotic use.

No matter what treatment is used, the fertility of cows with endometritis will still be worse than that of their normal untreated compatriots. It is important, therefore, to focus on preventing endometritis by ensuring transition cows are managed well, i.e. BCS is neither too high nor too low, dry matter intakes are high in the last 2-3 weeks and the risk of metabolic disease, particularly milk fever, is reduced. Dystocia is another crucial risk factor, particularly in heifers. To reduce the risk of dystocia avoid over-fat cows and choose bulls which score highly for calving ease.

Cystic Ovaries

After endometritis, the most common abnormality diagnosed in cows presented to veterinarians at routine visits is the ovarian cyst. These are large structures that persist on the ovary and prevent normal function. In most cases, the result is a cow which doesn't show heat; occasionally, an affected cow will come into heat every two or three days (nymphomania), but such cows are rare. As with persistent CL, a single examination is not sufficient to confirm that an ovarian structure is persistent, so most cows are diagnosed as ‘cystic’ on the basis of size and clinical signs alone.

From a treatment perspective there are two types of cyst - those that will just respond to stimulation of ovulation ('thin-walled' or follicular) and those which require luteolysis ('thick-walled' or luteal). However, they can be difficult to separate and clinically there is often little difference, therefore most common treatment regimes both induce luteolysis and stimulate ovulation.

Cystic ovaries can spontaneously cure without treatment; this occurs when ovarian function begins again, even though the cyst may still be present. But the numbers are small - one study showed 50% recovering within 60 days - and the recovery can take a long time (on average 30 days). So, not treating is not a good option.

Lactating dairy cows need to be exposed to progesterone before ovulation in order to ovulate and produce a CL. (Gumen, Sartori et al 2002, Wilbank, Gumen et al 2002, Gumen and Wilbank 2005). Therefore, progesterone is the main component of treatment for cystic ovarian disease, this can be a combination of inserting a progesterone device ('PRID Delta' or 'CIDR') and using a GnRH injection to help form a CL and let the cow produce her own progesterone. The progesterone device should be inserted for 7 to 12 days. These protocols allow for a FTAI and therefore ensure the cow is served with no lost time.

Treatment with a progesterone programme improves performance by reducing the interval between calving and conception. On average, treatment reduces calving to conception interval by around 60 days - a £120 benefit for a £12-£16 cost. Of course this benefit is reduced by the high proportion of treated cystic cows which don't get pregnant (around 30-40%), so the actual treatment costs for the £120 benefit are ~£20. Furthermore there may also be a benefit in terms of culling rate,
with treated cows tending to be less likely to be culled for infertility. Although this effect is small (~2% in herds with heat detection rates >60%), the cost of an individual cull is so high (£1000) that the benefit of reducing culling is equivalent to £20/treated cow for every 100 treated cows (if treatment costs £12/cow). As with treating missed heats this level of benefits depends on identifying and treating ovarian cysts early, so that treated cows have plenty of time to get pregnant. It is important to only treat cows that are, or soon will be, eligible for mating as very early treatment (<10 days after calving) will result in the unnecessary treatment of normal cows.

As with endometritis, prevention is more effective than cure. Minimising energy deficiency after calving is crucial - monitor BCS and respond to excess losses by increasing the quantity and quality of feed.

### Treating Anoestrus Cows

**Fig 4:** The most important cause of anoestrus is poor body condition. Monitor your cows score and feed so they meet the target of 2.5 to 3.0 at calving and 2.0 to 2.5 60 days later [1].

Anoestrus means not ovulating; cows in anoestrus are therefore not cycling normally and not ovulating. There are two kinds of anoestrus cow: 1) Deep anoestrus where nothing is happening on the ovary; and 2) shallow anoestrus where the ovary is functioning but none of the follicles ovulate. The former kind is much more difficult to treat but less common. Poor body condition, particularly excess loss of body condition between calving and mating, is the key factor underlying prolonged periods of anoestrus post-calving. Management of the transitional cow is crucial in reducing the need to treat anoestrus with hormones.

In the US, where synchronisation programmes are more commonly used than in the UK, a wide range of programmes have been tested as treatments for anoestrus. The evidence suggests that the best results are achieved by a combination of a GPG (‘Ov-synch’) programme with a progesterone device. The GPG programme alone stimulates ovulation in most cows, but conception rates are often poor. It is likely that this is because of a lack of progesterone priming in anoestrus cows (as they haven’t had a period of high progesterone before they are inseminated). The addition of a progesterone device to the programme primes the brain, ovaries and uterus, increasing conception rate. Another hormone, equine chorionic gonadotrophin (‘ecG’) is often used in anoestrus cows as it has been shown to increase conception rate.

**Fig 5:** Progesterone-devices that sit in the vagina are an important part of the treatment protocol for anoestrus cows as their use tends to improve conception rates.

As anoestrus cows are much less likely than cows which have ovulated to come into heat in the next 21 days, the benefit of treatment of anoestrus cows per treated cow can be greater than that for missed heats. Nevertheless, compared to cows that have ovulated, anoestrus cows will have lower conception rates (often <25%) and thus take longer
to get pregnant. Coupled with the fact that, compared to a single PG that is effective within 72 hours, anoestrus treatment takes 10 days to work this means that the expected benefit is only around 10 days reduction in calving to conception interval - a £20 benefit for a £24 cost. The benefit of oestrus treatment therefore depends on culling fewer cows - good data are not available but it is likely that results will be similar to those for cystic ovaries with 2% fewer culled cows or a £20 benefit per treated cow. These figures reflect the fact that prevention of anoestrus is much more effective than treatment.


### Summary

The routine veterinary visit on a weekly or fortnightly basis is a good opportunity to identify and treat cows that are eligible for breeding but have not been inseminated. Such cows can be abnormal (endometritis, anoestrus or cystic) or apparently normal but just not observed in heat. Treatment of such cows will result in earlier conception, decreasing the inter-calving interval. The economics of such treatment are based on identifying and treating cows early, as the cost/benefit is closely related to the number of treated cows which get pregnant, so the longer a cow has to get pregnant the better the cost benefit.