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Fertility in dairy cattle: a review

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Table of Contents

1. GENERAL ASPECTS OF FERTILITY AND INFERTILITY

1.1. Introduction to fertility and infertility

Dairying in Ireland is changing. The removal of the milk quota system will give farmers the opportunity to expand production without purchasing quota rights for the first time in thirty years. A 50% increase in production has been set (Food Harvest 2020). This will result in "significant regional restructuring of milk production, which is likely to present some challenges to the dairy processing sector" (Läpple and Hennessy, 2012).

Dairy production in Ireland uses a seasonal grass based system. To meet the ambitious target increase it is necessary to expand cow numbers and increase milk yield/cow (Shalloo et al., 2014). The importance of fertility is greater in seasonal systems compared with other systems (Veerkamp et al, 2002). The expenses linked with decreased reproductive efficiency are larger in pasture based models. Increased calving intervals can reduce the synchrony between feed supply and feed demand. It is vital to plan your calving pattern so that feed demand is parallel with highest levels of grass growth (Shalloo et al., 2007). The current national average calving date is mid-March and it should be mid-February. This could potentially result in decreased grass utilisation and shortened lactations (Shalloo et al., 2014).Key traits that influence the economics of fertility are; increased calving intervals (Esslemont et al., 2001), increased culling (Esslemont et al., 2001), increased labour costs, increased costs associated with additional artificial insemination (AI) usage (Boichard, 1990), interventions in one form or another; veterinary/hormonal costs (Boichard, 1990)

Factors crucial to dairy herd reproductive performance are: nutrition, mating management, disease and genetics. Sub-optimal performance will result if these targets are not met. Fertility of cows has been on the decline. This decline has been shown to have links with larger herd size, genetic merit for milk production and nutritional management (Butler, 1998; Darwash et al., 1999).

1.2. Feeding Standards for Reproduction

Nutrition begins influencing the reproductive potential of the animal early in its life. Nutrient changes in utero will dictate future performance. Feeding level of the young animal or "plane of nutrition" affects the age at which they reach puberty. In mature

adult animals inadequate nutrition can reduce the production of ova and spermatozoa which can result in failure to conceive. In pregnancy there are specific nutrient requirements for maintenance and growth of the foetus. When assessing the nutrient requirements for reproduction one must remember important features of the reproductive process. Firstly, consider that reproduction may not be the only productive process. Young cattle may be expected to conceive before they have achieved their adult body weight. These animals must continue growing. The post calving cow is expected to conceive again during high milk production. Secondly, one must remember that the nutrient requirements of gestation vary. In the last weeks of pregnancy the foetus rapidly gains weight, this increases the nutrient requirements. Lastly, it is important to note that reproduction can be termed an "all or nothing" phenomenon, the results of failure can be damaging for the farmer. A cow must produce a calf to produce milk. Failure means no output and the farmer makes a loss.

1.3. Plane of Nutrition, Fertility and Fecundity

Nutrition is the primary determinant of fertility (whether the animal conceives or not) and fecundity (the number and quality of ova shed from the ovaries) in females. In the cow the ovulation rate is normally one. Twins are not encouraged. High planes of nutrition can reduce the survival of oocytes and embryos by stimulating metabolic rate. This increases the rate progesterone (establishment and maintenance of pregnancy) is degraded. Getting a cow to conceive two months post calving is a serious problem for the industry. It is recommended that cows should be regaining weight at insemination. This is easier said than done, it is difficult to ensure a positive energy balance at this time. Provision of inadequate amounts of food leads to extended calving intervals and culling. *Table 1.1*., shows the connection between selected nutrients and reproductive physiology.

Nutrient	Effects	Interaction
Phosphorus	↓metabolism ↓feed intake	
Copper	↓oestrus resumption ↑calving interval	Molybdenum
Zinc	↓spermatogenesis	
Protein	↑↑RDP ↓Embryo survival	
Starch	↑Pre-service ↓Post-service	

Table 1.1. Effects of selected nutrients on the reproductive performance

1.4. Nutritional interactions with reproductive performance in dairy cattle

At parturition milk production rapidly increases, this stress results in negative energy balance (NEB) linked to DMI and therefore BCS at calving. Optimal BCS for cows is 3.0 (Loeffer et al., 1999).The greater the loss of BCS the greater the reduction in conception rate (Butler, 2000).NEB 3-4 weeks post calving is linked with timing of the first ovulation. "The detrimental effects of [NEB]… in early lactation appear to be manifested as reduced fertility" (Butler, 2000).It's important to minimise the interval to first ovulation which provides time for multiple cycles pre-service (Butler and Smith, 1989). Minimising the time interval between calving to first ovulation has a positive correlation to conception rate (Butler, 2000).The level of progesterone in the blood increases with each oestrus (Villa-Godoy et al., 1988; Spicer et al., 1990; Staples et al., 1990). This increase is negatively affected by NEB (Villa-Godoy et al., 1988; Spicer et al., 1990). It is known that "The ability to produce and maintain optimum progesterone concentrations is important for fertility due to the effects of progesterone from one cycle to the next" (Folman et al., 1990).

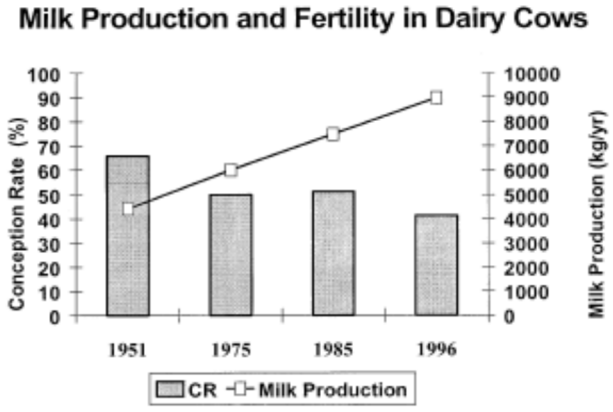

Figure 1.1. The inverse relationship between conception rate (CR) and annual milk production of Holstein dairy cows (adapted from Butler, 1998).

1.5. Dietary protein intake and reproductive performance

Due to the increase in genetic merit for milk production, nutritional demands have increased. Diets containing 17% - 19% crude protein are fed during early lactation (Butler, 2000). It has been shown that high protein diets are linked to decreased reproductive performance (Butler, 1998; Westwood et al., 1998). High protein diets have no positive influence on oestrus resumption. Evidence indicates the demands of

high milk production are linked to reduced concentrations of plasma progesterone in the early breeding period (Butler, 2000). Successful development of the embryo depends on the uterine environment. High protein diets change the uterine pH and ion concentrations resulting in poor fertility (Butler, 1998). High protein feeding is linked to increased blood ammonia and urea. Increased milk or plasma urea nitrogen is associated with a drop in reproductive performance (Butler, 1998; Westwood et al., 1998; Wittwer et al., 1999). Plasma urea is inversely related to pH of the uterine lumen. *Figure 1.2.* (Adapted from Butler, 1998) shows how changes in plasma urea affect uterine pH.

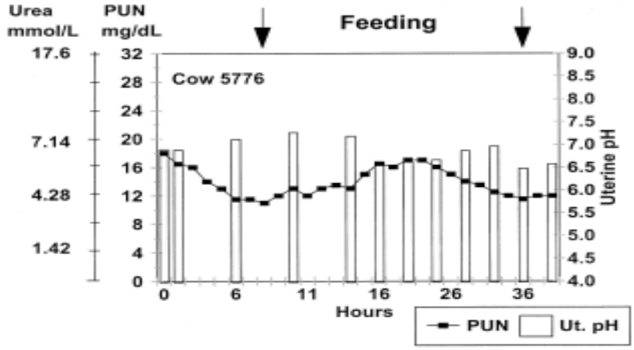

Fig 1.2. Urea concentration and its effect on uterine pH (adapted from Butler, 1998).

It can be seen above that increased levels of urea result in a more acidic uterine environment. Higher urea will also negatively affect the inductive actions of progesterone in the uterus resulting in sub-optimal embryo development (Butler, 2000). Increased urea levels change the pH gradient across cells and increases the release of PGF2α decreasing embryo development and viability (Butler, 1998).

1.6. Genetics and Fertility

"Cows that have been highly selected for milk production in recent decades have suffered a decline in… fertility" (Walsh et al., 2010). Rising milk yields, increasing herd size, changing housing standards and increases in farmers doing their own AI/stock bulls have all contributed to the difficulty in achieving high fertility (Rodriguez-Martinez et al., 2008). A study in Ireland showed that the number of AI/conception rose from 1.54 to 1.75 between 1990 and 2000, with a corresponding decrease in conception rates from 64.9% to 57.1% (Mee et al., 2004).

Relative Breeding Index focused on genetic improvement for milk. A study by (Dillion et al 2006) showed "Between 1985 and 2003, the rate of phenotypic gain in

milk production per cow per year has been 193kg for the United States, 131kg for the Netherlands, 35kg for New Zealand and 46kg for Ireland". This strategy underestimated the antagonism between milk production and fertility (Evans et al., 2002; Berry et al., 2003). Medium RBI dairy cattle were more profitable than high RBI stock when their higher fertility was noted (Veerkamp et al., 2000).AI fell in tandem with the decline in fertility; most replacements were by stock bulls. Genetic merit of the replacement heifers had stagnated (Wickham et al. 2012).Focus shifted toward "functional nonproduction traits associated with improved health and fertility" (Miglior et al., 2005). Evidence is emerging that the lowest point of cow fertility is past and improvements are being made (Crowe, 2007; Norman et al., 2009).

1.7. The Economic Breeding Index (EBI)

EBI is aimed at helping farmers identify the most profitable bulls and cows for breeding replacements. The EBI is measured against the theoretical base cow. A €1 higher EBI is expected to result in a €2 increase in profit per cow. Since the introduction of EBI in 2000, moderate but continued improvement in genetic merit for milk production has been sustained as genomic technologies are adopted by dairy farmers (Ramsbottom, 2014).

Year	**Milk Production**		**Replacement Rate**		**Net Profit**
	Yield (kg/cow)	Sales (€,000's)	Rate (%)	Cost (€,000's)	(€, 000's)
1990	5,033	126	16	21	29
1993	5,307	136	21	28	30
1997	5,629	145	25	34	32
2000	5,609	148	26	35	33
2003	5,638	150	27	37	33
Change	605	24	11	16	4

Table 1.2. Impact of EBI (adapted from Evans et al. 2006)

Sub-Index	Trait	Economic Weight	Trait Emphasis	Overall Emphasis
Production	Milk	-€0.09	10.6%	33%
	Fat	€1.04	3.4%	
	Protein	€6.64	18.9%	
Fertility	Calving Interval	-€12.43	24.0%	35%
	Survival	€12.01	10.9%	
Calving	Direct Calving Difficulty	-€3.52	2.8%	9%
	Maternal Calving Difficulty	-€1.73	1.3%	
	Gestation Length	-€7.49	4.1%	
	Calf Mortality	-€2.58	1.0%	
Beef	Cull Cow Weight	€0.15	0.7%	9%
	Carcass Weight	€1.38	5.1%	
	Carcass Conformation	€10.32	1.7%	
	Carcass Fat	-€11.71	1.1%	
Maintenance	Cull Cow Weight	-€1.65	7.2%	7%
Management	Milking Time	-€0.25	2.1%	4%
	Milking Temperament	€33.69	1.9%	
Health	Lameness	-€54.26	0.6%	3%
	SCC	-€42.49	1.8%	
	Mastitis	-€77.10	0.8%	

Table 1.3. Composition of the Economic Breeding Index.

1.8. Inbreeding in Irish Dairy Cattle

"Inbreeding is defined as the probability that two alleles at any locus are 'identical by descent' and occurs when related individuals are mated. Inbreeding produces inbred animals and the degree to which an animal is inbred is measured by its inbreeding coefficient. Concerns over increased rates of inbreeding are mounting, attributable mainly to the known deleterious effects of inbreeding depression (McParland 2007).

Inbreeding depression refers to the reduction in mean phenotypic performance as a result of inbreeding. Inbreeding increases at a rate of 0.10%, on par with most countries. Despite the similar level of inbreeding, inbreeding depression of milk producing ability is lower in Ireland compared to others. Inbreeding depression of fertility is highest in Ireland. If short term goals are pursued at the expense of genetic diversity long term genetic gain can be impacted. "Long term control of inbreeding will rely on minimising the genetic relationships both among the population of young test bulls and between the population of young test bulls and the future breeding female population" (Mc Parland 2007)

1.9. Genetic Evaluations

To improve important traits on a given farm the genetic merit of the herd must be measured. The effects of genes and the effects of the animal's environment must be separated. This way we can discern whether an animal has desirable genes or is fed and managed well. Once the genetic merit of the cow had been ascertained a sire of suitable EBI can be selected. Once a cow has been assessed she is given Predicted Transmitting Ability figures (PTA). The animal's PTA values are a measure of the amount of a given trait she is expected to pass on. An animal's PTA is equal to half its Breeding Value, due to the fact that they only pass on half their genes. Female offspring of a sire with a PTA for milk yield of 150kg are expected to produce 100kg more milk/lactation than the female offspring of a sire with a PTA of 50kg. The actual differences between the individual female progeny will not be this exact but on-farm genetic/financial data has shown that EBI is associated with increased profit (Ramsbottom, 2014).The table below illustrates how bull selection can achieve the fertility sub-index target of €125:

Herd average fertility sub-index	€25	€50	€75	€100
Bull team average fertility sub-index	€225	€200	€175	€150
Expected heifer fertility sub-index	€125	€125	€125	€125

Table 1.4. Semen selection using EBI (adapted from Ramsbottom, 2014).

1.10. Establishment of Moorepark High/Low Fertility Herd

A study to evaluate the effects of genetic merit for fertility traits on reproduction in lactating dairy cows was established (Moore and Butler, 2014). An experimental herd was established of heifers due for first calving. The heifers had similar genetic profiles for milk production but different genetic profiles for fertility either good (Fert+) or bad (Fert-). The group represented the top 25% of the Irish herd in milk production. The herd also represented the top 20% (Fert+) and bottom 5% (Fert-) in fertility. The following parameters were measured during the herd's first and second lactation:

	Fert +	**Fert-**
Mean milk solids	436kg	424kg
Submission rates	83%	72%
Conception rate to first service	56%	33%
Services per pregnancy	1.4	2.2

Table 1.5. Impact of fertility on production (adapted from Moore and Butler, 2014)

The cows in the Fert- category needed an extra 28 days to get pregnant. This has a negative effect on milk yield. The study's results "indicated that a robust model for investigating the causes of poor fertility" (Cummins et al, 2012). A further study was undertaken to study the physiology of Fert+ and Fert- cows during the transition period (Moore and Butler, 2014). The study found that Fert+ cows out performed Fert- in the following categories; DMI, average energy balance, milk solids production, BCS circulating insulin, circulating IGF-I, circulating glucose, uterine health, milk progesterone analysis.

A further study showed “twice as many cows in the higher fertility sub-index category survived to fourth lactation and they did so on average nine months earlier than the cows in the lowest fertility sub-index category”(Ramsbottom, 2014).

A study of 18 spring calving herds had the following results:

Month of calving	**January**	**February**	**March**	**April/May**
Avg. calving date	25th Jan	15th Feb	16th Mar	22nd April
No. of cows	88	975	493	258
Milk production				
Milk solids (kg/cow)	426	398	355	322
Days in milk	292	276	245	197
Lactation Number	3.2	2.9	2.8	3.8
Genetic merit				
EBI	€132	€125	€124	€109
Milk sub-index	€14	€30	€29	€25
Fertility sub-index	€102	€85	€86	€78

Table 1.6. Calving date and production (adapted from Ramsbottom, 2014)

Cows calving in January had the highest milk yield despite having a lower milk sub-index. The biggest factor that contributed to this was a longer lactation period. Earlier calving cows had better grass utilisation. “Earlier calving cows spent longer in milk” (Ramsbottom, 2014). These findings show that the ideal calving interval of 356 days is linked to an EBI fertility sub-index value of €125.

Herd average Fertility sub-index range	**Expected calving interval range**
<€50	>377 days
€50-€100	369-377 days
>€100	<369 days

Table 1.7. Calving interval and fertility sub-index (Ramsbottom, 2014)

2. GENERAL ASPECTS OF HEAT DETECTION

2.1. Introduction

Effective mating management is vital to dairy farmers. AI programmes need accurate detection of heat in the animal. This allows the correct timing of insemination with ovulation (Walsh et al., 2011). Failure in this will hinder the success of AI schemes and lead to repeated services, more open days for the cows and impact on the farmers' profit. Observation by a knowledgeable person remains the best method of heat detection. Cows should be observed two/three times daily (morning, afternoon, evening) for signs of heat. Efficient heat detection is labour intensive and time consuming but it must not be neglected. Keep in mind that missed heats will result in economic losses.

2.2. What is Heat?

Heat or oestrus is the term given to the period that occurs roughly every three weeks (18-24 days) in sexually mature, non-pregnant females. During this time they are receptive to mounting by bulls/females. Onset is due to increased oestrogen, this alters the physiology and behaviour of the cow. Mounting/standing heat occurs in the first 12-18 hours after the onset of heat. The cow is not fertile until around 6-10 hours after, when ovulation occurs. Following ovulation progesterone is released. This prevents further ovulations/heat signs. There is a small window where fertilisation can occur. Pinpointing this window relies on accurate heat detection. Recent studies have shown that animals displaying "standing heat" decreased by 30%. Also the duration of detected oestrus fell from 15 to 5 hours (Dobson et al., 2008).

Several solutions have been implemented. Tail painting and visual inspection is simple and economical but its heat detection efficiency ranges from 25-96% (Mee et al., 2002), pedometers demonstrated higher rates of detection; 80-100% (Roelofs et al., 2010).Accelerometer systems were also studied (Fricke et al., 2014). Their findings are illustrated in the table below:

Activity and ovulation responses of cows after induction of luteolysis	**%**
Cows with oestrus activity	**71%**
Cows that ovulated	95%
Cows with no ovulation	5%
Cows with no oestrus activity	**29%**
Cows that ovulated	35%
Cows with no ovulation	65%

Table 2.1. Summary of accelerometer study (adapted from Valenza et al., 2012).

Several risk factors have been identified for poor expression of oestrus, many of them are listed here:

- Silent or anovulatory anoestrus
- Parity (number of times a female has given birth)
- Milk production (Sangsritavong et al., 2002)
- Health (lameness) (Bergsten, 2001; Walker et al., 2008)
- Nutrition (NEB)
- Housing (Tied/untied stall, pasture)
- Season (Heat stress)
- Number of herd mates in oestrus simultaneously (Roelofs et al., 2010)

2.3. Signs of Heat

The most definitive sign of heat is when the cow allows her herd mates to mount her. She will be restless and will mount other cows. The following secondary signs can confirm heat:

- Roughened tail head. This indicates recent mounting.
- Dirty marks on hips, sides and shoulders from the hoofs of herd mates.
- Nervousness or restlessness. The cows may search for a bull she may also call out.
- Grouping together, animals in heat will gather in groups of three to five animals.
- A clear, thick mucus discharge from the vagina will be present.
- Swollen vulva, on close inspection the vulvar lips will be swollen and reddened.
- Bloody discharge, this occurs at the end of estrus and indicates a missed heat (Diskin and Sreenan 2000).

2.4. Heat Detection Aids

Several aids to heat detection are commercially available. None of these aids are a replacement for the traditional methods.

- *Adhesive heat pads;* a detector is glued along the spine between the hip bones. Mounting will cause either a visual change/audible signal to be emitted.
- *Chin ball markers on vasectomised bulls;* When the infertile bull detects a cow in heat and mounts her he will mark her back.
- *Tailhead chalking/painting*; when the chalk is rubbed off this indicates mounting.
- *Pedometer*; determines how far the animal has walked. The readings are entered into a data base (Diskin and Sreenan, 2000).

2.5. Checklist for Heat Detection Success

In order to achieve a good conception rate, a well-organized heat detection program is necessary, which should be organized based on the following points.

1. Identify each animal and track individuals throughout their life cycle.
2. Establish good record keeping.
3. Adopt SOP and follow them. Designate someone to be in charge of heat detection.
4. Regular inspections of the herd for a minimum of thirty minutes three times daily.
5. Animals expected to come into heat should be grouped together two weeks before the start of the programme. This allows the animals to fall into a natural rhythm and allows the farmer to tailor feeding to the animals if required. (BCS).
6. Make note of any grouping activity.
7. Use heat detection aids wisely. They are aids not replacements for observation.
8. Synchronise with prostaglandins. Allows for greater heat detection.
9. Treat lameness immediately. Lame cattle will not show standing heat signs.
10. Document all activities and make note of dates. (Diskin and Sreenan, 2000; DuPonte, 2007).

3. PUBERTY AND FIRST INSEMINATION

3.1. Introduction

The onset of puberty in cattle is influenced by nutrition. The quicker the animal grows the sooner it reaches sexual maturity. In cattle the onset of puberty is governed not by age but by size/weight. Energy rich diets induce puberty earlier.

Plane of Nutrition		**At puberty**			
		Age (months)	Weight (kg)	Height at the withers (cm)	Empty body fat (%)
High	11MJ ME/kg DM 210g CP/kg DM	9.3	282	110	7.4
Medium	10.1 MJ ME/kg DM 181g CP/kg DM	10.8	282	112	7.2
Low	9.5 MJ ME/kg DM 135g CP/kg DM	16.5	316	119	7.0

Table 3.1. Age and size at puberty of Holstein cattle on different planes of nutrition (adapted from Chelikani et al. 2003.)

Body size is the most important factor that decides breeding time. Animals are considered too small for breeding at puberty. They are not mated until 15 months old. The female will have the nutrient demands of pregnancy and growth. Inadequate nutrition during pregnancy will likely stunt the foetus/retard growth of the mother. It can be dangerous if the mother has incomplete skeletal development. Narrow birth channels can result in the death of the calf/cow.

It is advantageous for the farmer to breed animals that reach breeding size early. This reduces the portion of the animals' non-productive life. There are some drawbacks to

rapid growth in breeding stock i.e. fat deposition. In dairy cows, fatness in early life may hinder production of mammaries. There is some evidence that rapid growth reduces the useful life of cows. It is best practice to feed animals for rapid increase in size without excessive fat accumulation (Mc Donald et al 2010).

3.2. Breeding maiden heifers

Maiden heifers generally represent the highest genetic material in the herd, and it is therefore logical to breed these high merit animals to high EBI AI sires to continue genetic progress into future generations. Teagasc recommends the following programme be implemented to optimise breeding. Inseminations can be carried out following observation of a standing heat and/or removal of tail paint (or activation of a heat mount detector), or as part of a synchronisation protocol.

Prostaglandin synchronization protocols work very well for heifers that have started cycling. Tail paint all heifers, and inseminate following observation of oestrus during the first 6 days of the breeding season. All heifers not inseminated in the first 6 days receive a prostaglandin injection on day 7, and are inseminated following observation of oestrus in the next 3 – 5 days.

Heifers that failed to come into heat following the first injection of prostaglandin receive a second injection 10 days later. Heifers are again inseminated at a standing heat, or receive fixed time AI at 72 and 96 h after the second injection. This protocol generally results in submission rates close to 100% and conception rates to first service of 70%. All heifers should be observed for repeat heats, and a stock bull introduced 5 to 6 weeks after the start of the breeding season (Pryce et al 2002).

4. FACTORS INFLUENCING EARLY EMBRYO MORTALITY

The ultimate test of the oocyte is the ability to be fertilised, develop to a blastocyst, establish a pregnancy and produce a live calf. Embryonic mortality is a major cause of reproductive failure (Walsh et al., 2011). Embryo mortality is divided into three stages. Foetal mortality occurs between day 46 and parturition (Committee on Bovine Reproductive Nomenclature, 1972).

4.1. Very early embryonic mortality (Day 0-7): post conception and the animals at risk are mainly the cows with high genetic merit for milk production (Snijders et al., 2000), lactating animals (Leroy et al., 2005) and cows with low progesterone levels (Diskin and Morris, 2008). Progesterone has no direct effect on the embryo but alters the endometrial secretions to promote embryonic development (Clemente et al., 2009).

4.2. Early embryonic mortality (7-24 days): the composition of the microenvironment of the uterus is critical to continued development (Rizos et al., 2002). Factors causing mortality at this stage are:

- Low concentrations of progesterone and IGF's (Leroy et al., 2008).
- Pathogenic bacteria (Sheldon et al., 2006).
- Small embryos (low interferon tau production) (Spencer et al. 2008).
- Gross chromosomal abnormalities (Peters, 1996).

4.3. Late embryonic and early foetal mortality (24-285 days)

"The death of the embryo between days 25 and 45 of gestation and days 46 until parturition" (Committee on Bovine Reproductive Nomenclature, 1972). Loss in this period is lower relative to the earlier stages. Keep exposure to stressors/pathogens at an absolute minimum during this period to avoid abortion/still births (Walsh et al, 2011). Cows with higher milk production/lactation have a higher chance of losing embryos at this stage than lower yielding cows (20% vs. 7%) (Vasconcelos et al., 1997). Factors associated with losses in this period are: genetic**,** environmental**,** physiological, hormonal (Diskin and Morris, 2008). Bacteria, viruses, fungi and protozoa are linked with infertility/abortion during this period (Givens and Marley, 2008).

4.4. Neonatal death, calf mortality

Death of the calf "within 48 hours of parturition following a normal gestation" (Walsh et al, 2011) is linked with difficult calving (dystocia) in over 50% of cases (Meyer et al., 2001; Berglund, 2008).Risk factors associated with stillbirths: (Meyer et al., 2001; Murray et al., 2008).

- Feto-pelvic incompatibility (most common (Berglund, 2008))
- Inbreeding (cross breeding alleviates (Berglund, 2008))
- Twin calves (one/both calves stillborn in 28.2% of twins (Snodgrass et al., 1986)

Neonatal calf mortality is also associated with: Rotavirus, Coronavirus, enteropathogenic E. coli, Salmonella spp., Cryptosporidium infections (Snodgrass et al., 1986).

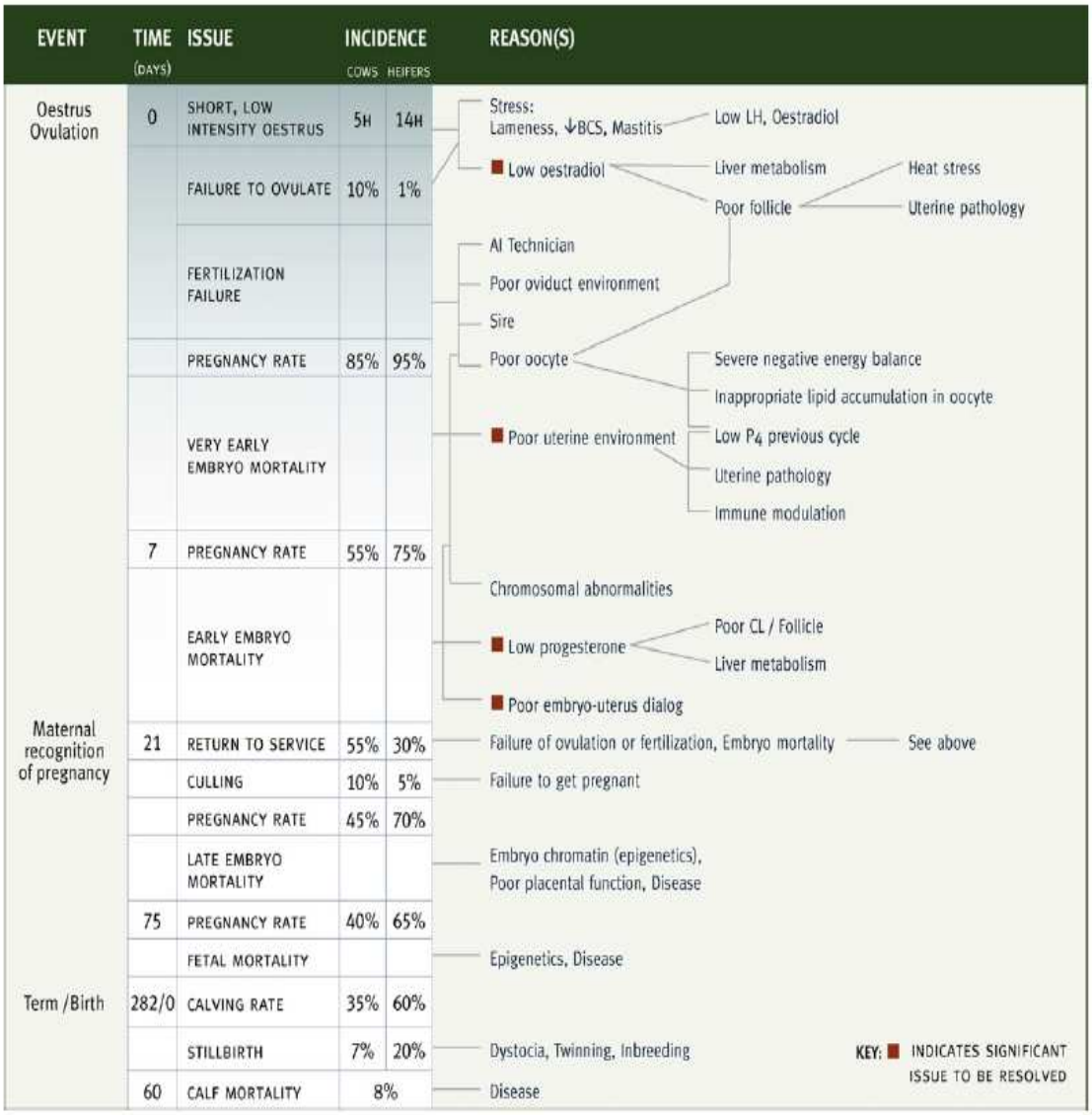

Fig 4.1. Major problems leading to low fertility during pregnancy (Walsh et al. UCD 2010).

5. FACTORS INFLUENCING FERTILITY IN THE POSTPARTUM PERIOD

5.1 Poor fertility in high producing dairy cows

The following points must be considered post-partum if we are to increase the reproductive performance of the herd:

1. Minimise NEB and resolve any infection of the post partum uterus.
2. Expression/detection of oestrus followed by insemination (day 0).
3. Ovulation and fertilisation of a high quality oocyte (day 1).
4. An early increase in progesterone secretion from the corpus luteum (days 3–7).
5. The uterine endometrium must produce an early and appropriate environment to stimulate embryo development (days 6–13).
6. A large embryo producing adequate quantities of interferon tau (days 14–18) that alters uterine prostaglandin secretion and signals maternal recognition of pregnancy (days 16–18) (Walsh et al. 2010).

5.2. Metabolic state

5.2.1 Body condition score loss and negative energy balance.

Between 4-8weeks post-partum dairy cows experience a major increase in energy requirements due to the increased daily milk yield. The cow's needs in this period can only be partially met by increased feed intake the remaining requirements are met by mobilising energy reserves. As a result the animal enters NEB (Grummer, 2007). NEB has potentially dangerous consequences including the risk of developing metabolic diseases, reduced immune function and a reduction in fertility (Roche et al., 2009).

Body condition score is defined as "an internationally accepted, subjective visual and tactile measure of body condition" (Berry et al., 2007). Temporal changes in BCS are used to monitor the nutritional and health status of animals during their productive cycle (Berry et al., 2007). It has been associated with fertility both phenotypically (Buckley et al., 2003) and through genetics (Berry et al., 2003a).

Cows with a low BCS at calving, or who suffer excessive BCS losses, are: less likely to ovulate, have reduced submission rates to AI, reduced conception rate to first service, lower six week in calf rate, increased risk of pregnancy loss, increased calving to conception interval (Berry et al., 2007; Roche et al., 2009)

The abovementioned problems are shown to be linked to impaired oocyte competence associated with a low BCS of 1.5-2.5 on the 5 point scale (Snijders et al., 2000).Cows that are over conditioned at calving (BCS of ≥ 3.5) suffer from compromised fertility. This is due to their lower DMI intake pre-calving and their slower increase in DMI post calving. This reduction in DMI compared to cows of ideal BCS results in greater fat mobilisation. This results in a more severe NEB (Roche et al., 2009).It has been shown that heat stress can exacerbate NEB in cows (Shebab-El-Deen et al., 2010). But this is of little importance to Irish farmers.

Effective monitoring of BCS is vital to maximising the efficiency of a herd. BCS pre/post calving gives an insight into nutritional/management systems. It ensures that the unavoidable NEB post calving will be mild. It also prevents "carry over" into the lactation (Roche, 2006; Chagas et al., 2007). It is important to remember that "minimising the BCS loss in the first few weeks post partum is an imperative. It is recommended that cows have a BCS of 2.75-3.0 (scale 0-5) at calving and that they are managed to suffer a BCS loss not more than 0.5 between calving and first service" (Crowe, 2008).

5.2.2 Metabolic disorders

During the transition period (2 weeks pre-calving- 4 weeks post-calving) the dairy cow in under the influence of a number of stressors. These result in the cow entering NEB accompanied by several endocrine, metabolic and physiological changes (Walsh et al., 2010). The abovementioned stressors along with further oxidative stress brought on by mobilisation of fat stores lead to a state of decreased immunity and inflammatory response in the cow (Walsh et al., 2010; Sordillo and Aitken, 2009). When immuncompromised cows are at risk of developing:

- Acidosis
- Fatty liver disease
- RFM
- Displaced abomasums
- Clinical hypocalcaemia (milk fever)
- Hypomagnesaemia
- Ketosis (Roche, 2006; Mulligan and Doherty, 2008)

Cows that suffer from metabolic disorders in the peri-parturient period are more likely to have mastitis, lameness and endometritis (Roche, 2006). These conditions all result in impaired reproductive performance, economic losses and animal welfare issues (Ouweljes et al., 1996; Ahmadzadeh et al., 2009).

NEB can further affect fertility due to decreased insulin. Low insulin has a knock on effect (decreased IGF-I) resulting in the uncoupling of the somatotropic axis (Lucy, 2008). This results in the prevention of ovulation of the dominant follicle (Beam and Butler, 1999) and the delaying normal cyclic function (Gutierrez et al. 1999). On the other hand if cows have a greater plasma IGF-I concentration following pregnancy they have a shorter gap between calving and commencement of luteal activity (Patton et al., 2007).

There has been speculation over the benefits of a high starch diet, a so called glucogenic diet or insulin promoting diet, and its ability to speed up resumption of cyclic activity (Gong et al., 2002). Questions have been raised concerning its possible harmful effects on embryo survival (Fouladi-Nashta et al., 2005). Further research has suggested that a combined approach may be the way forward; a glucogenic diet is fed early post partum to encourage follicle maturation and resumption of cyclic activity. This is followed by a lipogenic diet during the breeding period (a diet rich in fats). The higher levels of fatty acids aid oocyte quality and embryo development (Garnsworthy et al., 2009).

A nutrition strategy should be implemented in the dry and post-partum periods to minimise the risk of metabolic diseases (Walsh et al., 2010). This should avoid the potential occurrence of metabolic disorders, resulting in a cow in optimum health, with no problems getting in calf and no detriment to lactation (Roche, 2006; Chagas et al., 2007; Thatcher et al., 2010).

5.3. Postpartum resumption of cyclic ovarian function

5.3.1. Postpartum anoestrus in dairy cattle

Fertility of the postpartum period is negatively influenced by the incidence of anoestrus characterized by the absence of oestrous behaviour, which may be an indication of suboptimal conditions (e.g., inadequate peripartum nutrition) or pathologic conditions (e.g., chronic diseases or uterine/ovarian diseases). Although initiation of ovarian follicular growth in the postpartum period is generally not affected, subsequent development (deviation) and the fate of the dominant follicle are the primary factors

that affect reestablishment of cyclicity. Anoestrus can be classified based on the three functional states of follicular development; follicle emergence, deviation, and ovulation.

Prevention of anoestrus is preferable to treatment and can be achieved in part by maintaining a healthy periparturient period. To better understand the aetiology of anoestrus and its prevention, research is urgently needed in the following three areas: the role of peripartum diseases that influence reproduction, genes involved in ovulation, and the influence of proteins (e.g., leptin) that appear to be important links between metabolic signals and the neuroendocrine axis.

The "normal" post partum dairy cow is defined as "one which has resolved uterine involution, resumed ovarian follicular development, ovulated a healthy dominant follicle early post partum and continues to have normal oestrus cycles at regular intervals at approximately 21 days, coupled with homeostatic concentrations of insulin, IGF-I and glucose" (Roche et al., 2006; Walsh et al., 2011). This definition is the ideal. It has been shown in studies that as many as fifty per cent of modern dairy cows will display abnormal oestrus cycles post partum resulting in larger gaps between calving and first insemination (Opsomer et al., 1998) as well as having lower rates of conception (Garnsworthy et al., 2009).Several risk factors for delayed first ovulation have been identified:

- Primiparous cows (Tanaka et al., 2008; Lucy, 2001).
- Cows with periparturient disorders. (Crowe, 2008; Garnsworty et al., 2008).
- Season of calving. (Crowe, 2008; Garnsworty et al., 2008).
- Management system (Crowe, 2008; Garnsworty et al., 2008).
- Mastitis (Crowe, 2008; Garnsworty et al., 2008).
- Lameness (Crowe, 2008; Garnsworty et al., 2008).
- Severe BCS loss (Crowe, 2008; Garnsworty et al., 2008).
- Clinical endometritis (Opsomer et al., 2000).
- Severe NEB (Diskin et al., 2003).
- Heat stressed animals (De Rensis and Scaramuzzi, 2003).

5.3.2. Ovarian Follicular Cysts in Dairy Cows

Ovarian follicular cysts are anovulatory structures that occur in 10 to 13% of cows. During the oestrous cycle of cows, two to four waves of follicular growth occur. From a cohort of recruited follicles, one is selected for continued growth and dominance while

the others undergo atresia and regress. Cysts have long been thought to be static structures that persist for extended periods. Although cysts can persist for extended periods, most regress over time and are replaced during subsequent follicular waves. The next dominant follicle either ovulates or develops into a new cyst. The recruitment of a cohort of follicles from which a cyst develops and the growth rate of cysts to ovulatory size are similar to ovulatory follicular waves, but the cyst continues to grow for a longer period. The interval between waves of follicular growth is longer for cows with cysts than for cows with normal oestrous cycles. Each wave is preceded by a transient increase in circulating FSH. Near the time of cyst development and persistence, the concentration of FSH is not different from that during normal oestrous cycles. Serum concentrations of LH and estradiol-17β are higher in cows that develop cysts than in cows that do not. Conversely, hypothalamic content of GnRH is lower in cows with cysts. Thus, cysts are dynamic structures, and their development and lifespan are likely associated with altered hypothalamic-hypophysial-ovarian function (Gaverick 1997).

5.3.3. Hormonal manipulation of ovarian activity

To achieve useful control of the oestrus cycle of cows one must control the life span of the corpus luteum and the follicle wave status at the conclusion of treatment. The growth of antral follicles in cattle occurs in waves during the ovarian cycle and also during the post-partum anoestrus period. The commencement of each new wave of follicle growth is stimulated by a passing spike in follicle stimulating hormone (FSH). The life cycle of each follicular wave is around 7-10 days. During that time it ascends through the following stages: Emergence, Selection, Dominance, Atresia (degeneration) or ovulation (Diskin et al., 2002).

A dominant follicle will emerge from each follicular wave it is remarkable in its “enhanced capacity to produce oestradiol, the maintenance of low intrafollicular concentrations of insulin- like growth factor binding proteins -2, -4, -5 and follistatin and an increase in free intrafollicular concentrations of IGF-1 As well as an increase in size” (Diskin et al., 2002).Different techniques can be used to control the activity/rhythm of the oestrus cycle:

1. Use of luteolytic agents (PGF2α or one its analogues)
2. Use of gonadotropin releasing hormone (GnRH) to control follicular wave emergence and regress the corpus luteum (CL)
3. Synchronisation of the previous follicular wave followed by induced luteolysis.

5.4. Uterine pathology, udder health and lameness

5. 4.1.Uterine pathology

At parturition it is normal for the cow to become contaminated, "80-100% of animals [had] bacteria in the uterine lumen in the first two weeks post-partum" (Sheldon et al., 2006). These bacteria coupled with reduced immunocompetance in NEB can result in infections.

The most common pathogens were: Escherichia coli, Arcanobacterium pyogenes, Fusobacterium necrophorum, Prevotella melaninogenica and Proteus spp.

These cause endometrial inflammation and purulent vaginal mucus (Sheldon et al., 2009a). In 80% of these cases the cows will control the infection. The remaining 20% will develop metritis within 21days post-partum. Infection with pathogens for three weeks or more results in clinical endometritis in 15-20% of the herd (Sheldon et al., 2009a). Animals at increased risk are: cows with twins, stillbirths, dystocia, RFM (LeBlanc, 2008).A meta analysis (Fourichon et al., 2000) showed that:

- Endometritis increased mean days open by 15
- Decreased the relative risk of pregnancy at 150 days in milk by 31%
- Reduced the rate which cows became pregnant by 16%

Even following successful treatment animals will have 20% lower conception rate and 3% of animals will be permanently infertile (Sheldon et al., 2009a).

5.4.1.1. Metritis

The depth of inflammation is used to distinguish between metritis and endometritis. The term metritis is often used to cover different uterine conditions; puerperal metritis, endometritis, pyometra and other findings. In 2006 Sheldon et al. defined metritis (puerperal metritis) as; inflammation of the uterus resulting in systemic signs of sickness, including fever, red-brown watery foul-smelling uterine discharge, dullness,

inappetance, elevated heart rate and low production. It primarily occurs in the 1st week after calving. A link has been shown between the behaviour, feed intake and metritis (Huzzey et al., 2007). It was shown that cows with severe metritis ate 2-6kg DM less than healthy cows in the 2-3 weeks preceding clinical signs. The most common bacterial isolates from cows suffering form metritis were E. coli as well as a variety of other anaerobic bacteria (Drillich et al., 2007). The biggest single risk factor for metritis is RFM, conditions that impair feed intake or immunity are also predisposing factors.
Cows with metritis display a moderate/severe illness and require systemic antibiotics. Based on current information the SOP should be to treat cows with at least two symptoms; RFM, rectal temp. >39.5C, dullness/inappetance, and fetid uterine discharge with 3-5 days of systemic cetiofur or penicillin (LeBlanc 2007).

5.4.1.2. Clinical endometritis

Endometritis is defined as uterine inflammation without systemic signs (LeBlanc 2007). Characteristic signs are muco-purulent/purulent uterine discharge associated with chronic bacterial uterine infection, occurring later than 3 weeks postpartum. Utilising histology it can be seen that endometritis is characterised by disruption of the endometrial epithelium, infiltration of inflammatory cells and accumulation of lymphocytes, vascular congestion, and stromal edema (Bonnett et al., 1991; Bondurant, 1999).

The clinical approach to diagnosis is to examine cows between 2 and 8 weeks after birth to assess if they are involuting correctly. Inspections should allow for normal uterine involution, yet allow for treatment before breeding. Cows that had twins, RFM or metritis but not veterinary assistance were more likely to have clinical endometritis (LeBlanc et al., 2002b).Cows with milk fever resulting in recumbence at calving were at substantial risk of developing clinical endometritis. There are several methods utilised to diagnose clinical endometritis; inspection, vaginoscopy and palpation of the cervix, uterus and ovaries. Palpation per rectum lacks the accuracy to identify cows with reduced fertility (Miller et al., 1980 Kristula and Bartholomew, 1998). Vaginoscopy proves to be more sensitive in predicting infection (Miller et al 1990). Endometrial biopsy is accurate but is linked to lower fertility (Miller et al 1990., Bonnet et al., 1993).

The prevalence of clinical endometritis is on average 10.1% (Kelton et al., 1998). A meta analysis of endometritis found; it increased mean days open by 15, decreased pregnancy by 150 DIM by 31% and reduced the conception rate by 16% (Fourichon et

al., 2000). Impacts of clinical endometritis include; reproductive inefficiency, culling, treatment costs, milk discard, labour and risk of residues in food products. Studies have shown that cows showing muco-purulent or purulent uterine discharge 5 weeks before the breeding season were 10-19% less likely to be pregnant by 56 days into the breeding season, also the average time to pregnancy was 8-18 days longer than in cows with no or clear mucus in the vagina (McDougall et al., 2006).

Treatment strategies include; systemic/local anti-biotics and systemically injected PGF2α. The aim is to reduce the bacterial load and boost uterine defence/repair mechanisms halting and reversing inflammatory changes in the uterus.

5.4.1.3. Subclinical endometritis

No clinical signs are associated with subclinical endometritis. Diagnosis relies on cytology. It affects cows in the period between 35 and 60 DIM at the relatively high rate of 35-50% of cows. It has been linked with reduced pregnancy rate, increased average time to pregnancy by 30-88 days and increased number of cows that fail to become pregnant by 300 DIM by 20% (Kasimanickam et al., 2004; Galvao et al., 2007).

Diagnosis of subclinical endometritis is more difficult than other uterine infections. Ultrasound can be used to diagnose in some cases. (Kasimanickam et al., 2004). Cytology is the most reliable method but is quite cumbersome to perform under field conditions. Cytobrush may be simpler than lavage (Kasimanickam et al., 2005b). Treatment with either cephapirin IU or PGF2α improved the pregnancy rate in cows with subclinical endometritis (Kasimanickam et al., 2005a).

5.4.2. Mastitis and fertility

Cows with clinical mastitis (visible abnormalities in milk) in the first 28 days post calving had delayed oestrus behaviour (91 days) compared to healthy cows (84 days)”(Walsh et al., 2011; Huszenicza et al., 2005). 30 days post birth an incidence of 23% was reported (Zwald et al., 2004). A link between high yields and mastitis was shown (Ingvartsen et al., 2003). The effect of mastitis on fertility is summarised below:

- More services/conception than healthy cows (2.1 vs. 1.6) (Ahmadzadeh et al., 2009)
- Number of days to first AI was greater (Barker et al., 1998)

- Cows with mastitis between AI-50 days of pregnancy had lower conception rates and were more prone to embryonic death (Chebel et al., 2004; Santos et al., 2004).
- Increased embryonic loss in cows that had mastitis after 50 days of pregnancy (Santos et al., 2004).

5. 4.3. Lameness; its relationship with fertility.

Lameness has been linked with sub-fertility in the following ways:

- Increased number of services/conception (Hernandez et al., 2001; Melendez et al., 2003).
- Lower conception rates to first service (Hernandez et al., 2001;Melendez et al., 2003).
- Cows that were lame 30 days post calving were likely to develop cysts. (Melendez et al., 2003).
- Cows with lameness were half as likely to conceive as cows without in the first 150 days of lactation.

Melendez et al (2003) proposed that lameness and its effect on fertility could be due to:

1. Histamine and endotoxins released during the drop in the pH of the rumen due to ruminal acidosis destroy the microvasculature in the corium causing laminitis. Histamine and endotoxins also effect endocrine/ovarian funtion and disrupt the LH surge (Nocek, 1997).
2. Hormones released due to lameness disrupt GnRH/LH (Melendez et al., 2003).
3. Post partum NEB may be greater in cows with lameness as they are less able to feed (Melendez et al., 2003)

5.5. Fertility terms and the vet's role

5.5.1. Record Keeping

- **Basic:** recording by hand in an ad hoc manner by farmer. Wide range of sophistication. No milk recording/computerised records.
- **Standard:** Manual records and milk recorded data.
- **Comprehensive:** Computer based records. Either performed on-farm or by a vet/office service.

5.5.2. Fertility Terms

Confusing arrays of terms have been coined by various fertility professionals to describe fertility performance and demonstrate improvement, so in this paragraph I will introduce the most widely used terms and explain their meanings.

1. *Calving Interval*: Number of days between one calving and the next as an average for the entire herd. It can mask large variations between animals and fails to adjust for culled animals. *Target:* 365-375 days (355-430).

2. *Calving to first service interval:* number of days from the time the cow calves to first service. It's a herd average; it may disguise variations and can't pinpoint problems. *Target:* 60-65 days (40-80).

3. *Voluntary Waiting Period:* time after calving when the cow is left unnerved. Allows for uterine involution/increased fertility as the quality of oocytes increases with each oestrus. It can be difficult to track and implement without computerised records. *Target:* 45-55 days (50-80).

4. *Submission Rate:* percentage of cows inseminated at least once in the first three weeks of the mating period after the voluntary waiting period. *Target:* 70% (40-90%).

5. *Heat Detection Rate:* proportion of cows identified in heat as a percentage of those eligible for heat in a period. It counts missed heats/false positives. An indicator of the extent of oestrus expression/heat detection. *Target:* 70% (40-90%).

6. *Calving to Conception Rate:* number of days from calving to the service at which a cow gets pregnant. It's the average performance of all cows pregnant in the breeding season. It can mask extreme results. *Targets:* 85-95 days (80-150).

7. *Days Open:* average number of days from calving to conception for cows conceiving and from calving to culling for those failing to. It can be low if animals are culled due to decisions based on milk etc. with no relevance to fertility. *Target:* 120 (120-150).

8. *First Service Pregnancy Rate:* percentage of cows that have a pregnancy diagnosis following first insemination. If there's a delayed interval to first service it's possible to have high pregnancy rates but see a slip in calving pattern. *Target:* 55% (35-75%).

9. *Overall Pregnancy Rate:* the number of services given to a herd, over a period, resulting in a diagnosed pregnancy as a percentage of the total services. It's too historical and can't pinpoint problems. *Target:* 55%+ (35-75%).

10. *Assumed Pregnancy Rate:* Any pregnancy rate not calculated from a diagnosis. Usually based on a lack of service 60 days after the first. Can over-estimate the true occurrence. *Target:* 65%+ (35-85%).

11. *Non-return Rate:* calculated by AI services on the assumption that a cow not being re-served is pregnant. It ignores animals sold not in calf and cows later served by a bull. It can over estimate pregnancy rate. *Target:* 75% (55-75%).

12. *Conception Rate:* measures the number of cows actually conceiving distinct from maintaining a pregnancy. This only measures the ability to conceive. Typically 30-40% that conceive are later not in calf.

13. *Culling Rate:* the number of cows, that are sold, die or are transferred out of the herd before starting another lactation. It's too historical and cannot catch problems before they develop. A high culling rate may not indicate a fertility issue. *Target:* 12-18% (12-35%).

14. *Failure to Conceive Culling Rate:* all the cows, transferred out of a herd for failure to conceive. It's a percentage of the number of cows calving. It's too historical and does not pinpoint causes. *Target :*< 6% (1-20%).

15. *100 Day In-calf Rate:* percentage of cows in the herd diagnosed in-calf again to a service within 100 days of calving. *Target:* 90%+ (60-95%).

16. *6-Week In-calf Rate:* the proportion of cows intended for re-breeding diagnosed in-calf six weeks after the start of the breeding season. *Target:* 75%+ (25-85%).

17. *200-Day Not In-calf Rate:* number of cows that are diagnosed not in calf 200 days post calving. *Target:*<6% (1-20%).

18. *Percent Conceiving Of Calved:* percentage of calved animals that conceive again. *Target: 87-89% (70-90%).*

19. *Percent Conceiving of Served:* proportion of the number of animals served that conceive. *Target: 95% (75-95%).*

5.5.3. Role of vets in modern fertility management

The role of the veterinarian has evolved over the years. In the fifties and sixties infectious causes of infertility were the main concern (Brucella abortus, Campylobacter fetus and Trichomonas fetus) along with imbalances in mineral concentration. During the seventies innovations led to hormonal manipulation. Vets could synchronise oestrus, induce parturition, treat cystic ovaries, endometritis and repeat breeders. The eighties brought a shift to herd fertility aided by computers. New infectious diseases (such as leptospirosis and BVD) were discovered as well as non-infectious conditions (lameness, increased milk yield, periparturient problems and heat stress)(Mee, 2007a).

As veterinarians became aware of the declining fertility causes were proposed, genetic selection policies and management policies (Mee, 2004). It has been said that vets fail to turn their theoretical knowledge of the pathophysiology of infertility into practical solutions (Opsomer et al, 2006.).

The focus must shift from concentrating on individuals, problems and diseases to a herd based approach. Herd management, suboptimal performance metrics and non-infectious production disorders are becoming important. Vets must also compete with paraprofessionals in the fertility business. AI technicians, US technicians and farmers themselves (Mee, 2007a) are bypassing vets and performing checks on uterine health, energy balance and quality of estrus (Roelofs and Hamoen., 2006).

Many vets are reluctant to change their methodologies due to five main reasons identified by Mee:

1. **Clients do not demand it.** Especially older farmers/small herds. They call the vet for emergency cases.
2. **Vets cannot justify the cost-benefit ratio.** Many vets will need to up skill and invest in the new services. Clients are unwilling to shift from old systems.
3. **Lack of training and confidence needed to provide a specialised fertility management service.** Especially in vets who are qualified over fifteen years.
4. **Challenging perceived wisdom.** Vets are used to being the sole expert on farms. This is opposite to the team based approach of modern fertility management.
5. **Lack of financial incentives.** Many vets make substantial financial gains through meat inspection and government eradication schemes making labour intensive fertility work unappealing. Farmers see no need to invest in fertility when milk prices are high.

6. CONCLUSIONS

I believe that a concerted approach is required to manage fertility in Ireland. The upcoming removal of the quota system will drastically change the Irish dairy landscape. Larger more professional dairy farmers will be encouraged whereas the smaller less efficient herds will be put under more strain. Vets must change with the times and switch from individual interventions to educating the farmer about management and prevention, and working with other fertility specialists. A herd level preventative programme that will minimise risks and maximise productivity should be the goal. Every potential hindrance to productivity must be recognised and planned for. The aspects of nutrition, mating management and disease control are hugely important to this strategy.

A balanced breeding approach should be adopted in the future that recognises not only milk producing ability but also fertility and health sub-traits. Farmers must move away from cows narrowly focused on milk production to a more rounded, healthier and more fertile cow. The Economic Breeding Index is a great asset in this regard. This will reduce losses associated with repeated services, more days open, scattered calving dates, vet interventions and culling. Furthermore more fertile cows will have longer lactation periods and better grass utilization. These factors are critical to the Irish seasonal system where synchrony between grass demand and grass availability is of critical importance.

In-depth and current record keeping should be encouraged and studied to improve the understanding of the fertility picture and allow for corrective measures to be taken. Milk recording and computer data bases should become a part of every serious dairy farmer's arsenal. Farmers and vets must work together to anticipate and negate potential fertility problems before they develop and cause serious economic impacts.

These steps will increase the value of the average dairy cow, improve her health, her fertility and maximise her productive life span, therefore resulting in a sustainable, competitive and economically viable dairy industry for Ireland.

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