Institution: University of Nottingham

Unit of Assessment: 6; Agriculture, Veterinary and Food Science

Title of case study: Developing tools to restore fertility in dairy cows

1. Summary of the impact

Fertility of dairy cows has been in decline since the 1970's and this has threatened sustainability of the dairy industry worldwide. Research led by Nottingham University (UoN) identified key drivers of fertility and provided genetic and nutritional tools for the industry, to help combat the decline. The genetic tool was the UK Fertility Index, which is used universally by breeders for national and international bull selection. The nutritional tool, which is widely applied by international feed companies, used the concept that nutritional manipulation of insulin enhances fertility. Evidence shows that use of these tools between 2008 and 2013 has reversed the decline, and fertility is being restored. This has brought commercial benefits for breeding companies, cattle food producers and farmers and had a positive impact upon animal welfare.

2. Underpinning research

Key researchers:

Professor Tony Flint, Prof of Animal Physiology (UoN 1993-2009), PI for genetic research.
Professor Phil Garnsworthy, Prof of Dairy Science (UoN 1980-present), PI for nutritional research.
Professor Bob Webb, Prof of Animal Science (UoN 1997-2012), PI for reproductive physiology research.
Professor Kevin Sinclair, Prof of Developmental Biology (UoN 2003-present), reproductive physiology.
Dr George Mann, Associate Prof (UoN 2003-present), reproductive physiology.
In collaboration with the Roslin Institute (D. Armstrong, J. Gong, J Woolliams), Scottish Agricultural College (SAC) Aberdeen (K. Sinclair until 2003, then J. Rooke) and SAC Edinburgh (E. Wall, M. Coffey).

Nottingham has a long history of world-leading research in bovine reproduction and pioneered the use of milk progesterone to monitor fertility of dairy cows. By comparing progesterone data in the 1990s and 1970s **[a]** UoN revealed a significant decline in fertility among UK dairy cows, which was negatively associated with genetic merit for milk yield **[1]**. Similar trends have since been identified in most countries with well-developed dairy industries. Cows exhibited delayed ovulation and conception rate was declining by 1% per annum. Poor fertility was estimated to cost the UK dairy industry £350 million per annum, mostly through premature culling of healthy cows that failed to conceive. With strategic funding from Defra and industry, a collaborative research programme, led by Nottingham, was started in 2000 to find ways to restore fertility through genetics and nutrition, the two main drivers of poor fertility.

In the genetic work **[b]**, UoN established genetic characteristics of dairy cow fertility traits derived from milk progesterone data, which were combined with heritability of management measures of fertility obtained at SAC **[1]**. In a Nottingham-led follow-up programme **[c]** approximately 1.4 million daughter records from 18,000 sires were used to generate a Fertility Index for bulls. The Index was based on daughters' calving interval, insemination data, pregnancy rate, milk yield and body condition score. An Index value was calculated for each bull so that bulls could be ranked for selection purposes **[2]**.

In the nutrition work **[d-g]**, it was noted that, cows with high genetic merit for milk yield had lower plasma insulin concentrations than average cows and hypothesised that nutritional manipulation of insulin might enhance fertility. A pilot study demonstrated that, a diet that stimulated insulin secretion increased the proportion of cows ovulating in the first 50 days postpartum **[3]**. In subsequent studies with 23 dietary treatments, equations were developed to predict effects of nutrition on insulin and fertility **[4]**. Parallel studies explored physiological mechanisms at the ovarian and systemic levels to explain whole-animal responses. The novel observation was made that although diets that induced higher insulin concentrations stimulated ovarian follicles **[4]**, high insulin was detrimental to oocyte quality **[5]**. A key insight was that reproductive performance of dairy cows might be improved by differential nutrition at different phases of the reproductive cycle. It was demonstrated that feeding a diet designed to stimulate insulin during the early postpartum

period and then a diet designed to lower insulin during the mating period increased the proportion of cows pregnant at 120 days of lactation from 27% in control treatments to 60% in the optimum treatment. Crucially, fertility was improved without compromising milk yield or cow health **[6]**.

3. References to the research

Evidence of the international quality of the research is indicated by publication in intermediate-to-high impact peer-reviewed journals. J Dairy Science is ranked highest and Animal 8th in the category 'Agriculture, Dairy and Animal Science'; Biology of Reproduction is ranked 4th and Reproduction 8th in the category 'Reproductive Biology'.

Selected references to key outputs from the research described in the previous section are:

1. Royal, M.D., Flint, A.P.F. and Woolliams, J.A. (2002) Genetic and phenotypic relationships among endocrine and traditional fertility traits and production traits in Holstein-Friesian dairy cows. *Journal of Dairy Science* 85, 958-967. doi:10.3168/jds.S0022-0302(02)74155-6
2. Wall, E., Coffey, M., Simm, G., Brotherstone, S., Stott, A.W., Santarossa, J., Flint, A.P.F., Royal, M.D. and Woolliams, J.A. (2002) Introducing a UK fertility index. *Cattle Practice* 10, 373-378. Available on request.
3. Gong, J.G., Lee, W.J., Garnsworthy, P.C. and Webb, R. (2002) Effect of dietary-induced increases in circulating insulin concentrations during the early postpartum period on reproductive function in dairy cows. *Reproduction*, 123, 419-427. Doi:10.1530/rep.0.1230419
4. Garnsworthy, P.C., Lock, A., Mann, G.E., Sinclair, K.D. and Webb, R. (2008) Nutrition, Metabolism and Fertility in Dairy Cows: 1. Dietary Energy Source and Ovarian Function. *Journal of Dairy Science*, 91, 3814-3823. Doi: 10.3168/jds.2008-1031.
5. Fouladi-Nashta, A. A., Gutierrez, C. G., Gong, J.G., Garnsworthy, P. C. and Webb, R. (2007) Impact of dietary fatty acids on oocyte quality and development in lactating dairy cows. *Biology of Reproduction*, 77, 9-17. Doi: 10.1095/biolreprod.106.058578
6. Garnsworthy, P.C., Fouladi-Nashta, A.A., Mann, G.E., Sinclair, K.D. and Webb, R. (2009) Effect of dietary-induced changes in plasma insulin concentrations during the early postpartum period on pregnancy rate in dairy cows. *Reproduction*, 137, 759-768. Doi: 10.1530/REP-08-0488

Underpinning research projects:

a. 1995-1998: MAFF: Postgraduate Studentship "Quantitative analysis of genetics of pregnancy failure in cattle". Awarded to A.P.F. Flint (Nottingham) vice M Royal, £28k.
b. 1999-2000: Improvement of reproductive efficiency in cattle. A.P.F. Flint (PI) (Nottingham led plus Roslin Institute) MAFF/MDC/SOAEFD, **99/R4/02**, £390k
c. 2001-2005: Developing a Fertility Index. A.P.F. Flint (PI) and R.Webb (Nottingham led plus Roslin Institute and SAC Edinburgh). LINK (Defra, Holstein UK, Genus ABS, National Milk Records, Livestock Services UK, Cogent Breeding, Dartington Cattle Breeding Centre), **LK0639**, £1.39m.
d. 1999-2000: Improvement in the reproductive efficiency of cattle through the short-term manipulation of nutrition. R. Webb (PI) and P.C. Garnsworthy (Nottingham led plus Roslin Institute). DEFRA **LS0204** – Bridge LINK, £567k.
e. 2001-2005: Nutrition and fertility in dairy cows. R. Webb (PI) and P.C. Garnsworthy. (Nottingham led plus Roslin Institute and SAC Aberdeen). LINK (SEERAD, ABNA Ltd, BOCM PAULS Ltd, Provimi Ltd **LK0646,** £382k.
f. 2001-2006: Nutrition and fertility in dairy cows. R. Webb (PI) and P.C. Garnsworthy. (Nottingham led plus Roslin Institute and SAC Aberdeen). DEFRA Strategic grant **LS3306**, £2.02m.
g. 2006-2007: Improvement of dairy cow fertility through studies of liver metabolism, molecular markers and oestrous expression. P.C. Garnsworthy (PI), R. Webb and A.P.F. Flint (University Of Nottingham). DEFRA **AC0205,** £206k.

4. Details of the impact

This research arose out of the urgent need to address the worldwide decline in fertility of dairy cows, as outlined in Section 2, which was attributed to a combination of genetic and nutrition-related factors. Fertility had been in decline for 40 years, so a quick fix was not expected.

Dissemination and uptake of any innovation takes time and it can be many years before benefits can be quantified. In the dairy industry, reproductive performance is measured only once per year, the generation interval is 5 years and cows stay in the herd for up to 10 years. Nevertheless, the latest statistics indicate that fertility is improving, both genetically and phenotypically, and will continue to improve for generations to come.

Bull proofs for fertility were first made available to the breeding companies involved in the project in December 2003. Although originally made publicly available through the Milk Development Council website in 2005, the Fertility Index has become firmly established and increasingly important in the 2008-2013 period **(Sources 1-3)**. The Index provided producers, for the first time, with the facility to select bulls on the basis of daughter fertility. The production of the Fertility Index is managed through DairyCo (DairyCo is the levy board which utilises dairy farmer levy payments in Great Britain), with a spin-out company based at Scottish Rural College (eGenes) established to collect and analyse the relevant data from the industry.

Analysis of national artificial insemination records shows fertility trends in bulls and cows **(Figure 1; Source 1)**. Genetic merit of AI bulls for calving interval flattened off after release of the Index to breeding companies, indicating an early effect upon fertility trends. When farmers started using the Fertility Index to select bulls, the fertility trend was reversed. The rate of reduction from 2008 to 2012 was 20% faster than the rate of increase from 1990 to 2000, showing an accelerated rate of improvement in fertility. In cows there was a slowing in the rate of increase genetic merit for calving interval and a reversal from 2008 onwards, showing that choices of bulls were feeding through into their daughters' performance. Daughter performance is reported by year of birth; hence the latest data are for cows born in 2010.

Figure 1: *The increasing Calving Interval from 1990-2007 indicates declining fertility. The Fertility Index and use of new dietary formulations has contributed to the rapid improvement in calving interval since 2008.*

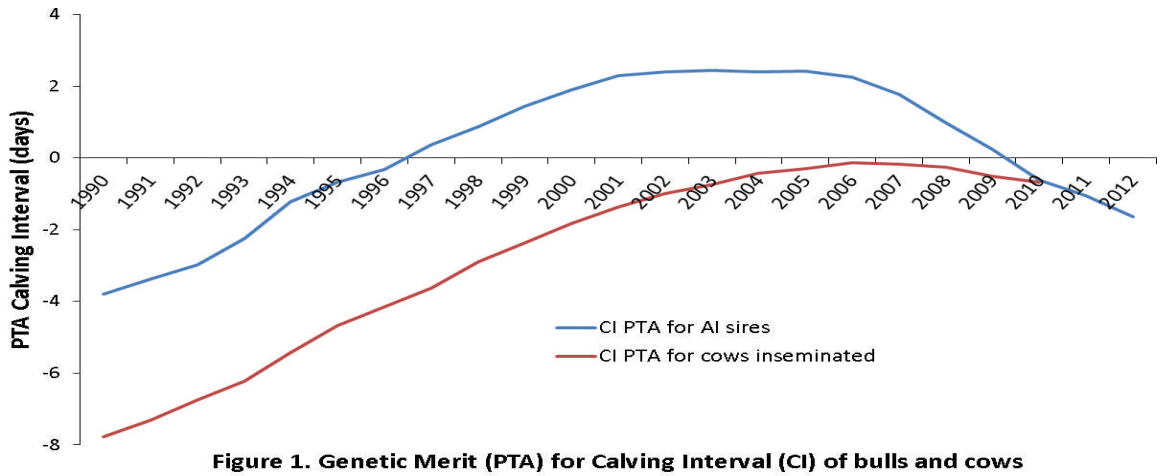

Figure 1. Genetic Merit (PTA) for Calving Interval (CI) of bulls and cows

The Fertility Index has become firmly incorporated into international genetic evaluations through Interbull (a subcommittee of the International Committee for Animal Recording) **(Source 1)** - see Interbull (2012) (**Source 2**). It is also widely used by international breeding companies to promote superior bulls (e.g. WorldWide Sires **[Source 3]**).

The main deliverable of the UoN nutritional research was a new way of thinking when evaluating dairy cow nutrition in relation to milk yield and fertility – the industry now considers not only nutrient supply, but also the effect of diet on metabolic hormones, and their influence on the reproductive system. The three commercial partners in UoN LINK programmes (LK0646 **[e]**) are well known for their innovative approaches to dairy cow nutrition. BOCM PAULS is market leader in UK dairy compound feed; AB Agri is the leading UK supplier of blended feeds for dairy cattle; Provimi is a world leader in animal nutrition with plants in 27 countries. BOCM PAULS and Provimi incorporated UoN predictive equations into their ration formulation programmes to provide nutritional indexes for insulin and progesterone as aids to fertility.

The Head of Ruminant Development at BOCM PAULS stated: *"Our goal is to improve fertility and longevity by focusing on extending the productive life of the cow and reducing the costs associated with infertility and high replacement rates. The Nottingham fertility research provides a central feature of our approach, by predicting the likely influence of nutrition on metabolic hormones, particularly insulin, and consequences for fertility. To this end, we incorporated fertility indexes for insulin and progesterone into our ration formulation packages. Every dairy cow ration that we have designed since 2008 incorporates an assessment of potential effects on fertility. Using this approach, we have seen significant improvements in fertility on many dairy farms. In 2012, BOCM PAULS became part of the ForFarmers Group, the largest feed company in Europe with a turnover of € 6.6 billion. As part of the integration process, we have shared technical information and ideas with partner companies in the Group. Thus, the concepts generated by the Nottingham fertility research are being implemented in dairy nutrition programmes throughout Northern Europe"* **(Source 4)**. Feed companies not associated with the project have also incorporated concepts generated by UoN into marketing material, e.g. Volac **(Source 5)**. The findings are incorporated into advice to farmers from DairyCo on feeding for fertility **(Source 6)**.

Data confirm that practical application of genetic, nutritional and management tools reversed the decline in fertility among cows. Between 2000 and 2008, average calving interval of UK Holstein cows *increased* at the rate of 4 days per year; between 2009 and 2010, the interval *decreased* by 4 days **(Source 7)**. This rapid trend reversal is highly significant. If maintained, rate of restoration of fertility will be 5 times the rate of genetic progress. As the genetic gain in fertility occurs year on year, it is therefore cumulative over time.

In 2012 DairyCo estimated that the typical UK herd was losing £250/cow/year through poor fertility. A shorter calving interval would save £2/cow per day of interval reduction. On this basis the savings associated with improving fertility amounted to £16m nationally in 2009-2010. Genetic trends suggest that improvement will continue so, by 2020, annual savings will approach £100m. Approximately half of this can be attributed to the Fertility Index and half to better nutrition and management **(Source 8)**.

5. Sources to corroborate the impact

1. Head of Genetics DairyCo. *Will provide corroboration for incorporation of research information into UK Fertility Index leading to significant improvement in genetic merit for fertility of UK dairy animals*
2. Interbull (2012) http://www-interbull.slu.se/Female_fert/framesida-fert.htm. *Corroboration for use of UK Fertility Index in International genetic evaluations*
3. World Wide Sires (2012) Addressing dairy cow fertility through better breeding (http://www.ukcows.com/theCDI/Article.aspx?nid=2082). *Corroboration for use of Fertility Index information in promoting genetic merit of dairy bulls on the international market*
4. Head of Ruminant Development BOCM PAULS LTD. *Corroboration for the incorporation of nutrition equations for insulin, progesterone and fertility into their ration formulation packages.* 2013
5. Volac (2009) http://www.volac.com/news/agriculture-news/news156/fertility-remains-among-the-major-issues-in-dairy-herds. *Corroboration for use of nutrition research by companies outside the LINK partnership*.
6. DairyCo (2013) http://www.dairyco.org.uk/technical-information/feeding/planning-your-nutrition/nutrition-and-fertility/. *Provides corroboration for incorporation of nutrition research into independent advice on fertility given to dairy farmers.*
7. Centre for Dairy Information (2013) Breed Performance Statistics 1999-2010. http://ukcows.com/theCDI/Docs/Statistics/2010/Full/CDIStatsBook2010.pdf. *Provides corroboration for phenotypic (genetic plus nutrition and management) improvement in fertility of dairy cows from 2009 to 2010.*
8. DairyCo (2012) PD+ Fertility Improvement Programme. http://www.dairyco.org.uk/resources-library/technical-information/fertility/pdplus-section-5-establishing-your-starting-point/ *Corroboration for cost of poor fertility and value of improvements through genetics and nutrition.*