Current situation in pig breeding

Since reproductive failure is one of the main reasons for culling in young sows, improving next parity reproductive performance might increase longevity and thereby decrease replacement costs. Suboptimal litter sizes or farrowing rates in the next parity are often related to excessive weight loss during lactation. Since “litter sizes” and “number of piglets weaned” have increased in the last decade, the metabolic demands on sows have also increased, whilst feed intake did not.

Lactating sows are not able to ingest sufficient energy to produce the large amount of milk they are presently capable of. Therefore, sows use a considerable amount of body reserves to maintain their milk production. Addition of fat to the diet is often used to increase energy intake during lactation. However, fat may affect subsequent reproduction in different ways. Fat-rich diets increase milk fat output. Doing so, nullifying the effect of a higher energy intake. But, more important, it depress secretion of insulin and IGF-1, which directly or indirectly affect LH, estradiol and progesterone secretion and follicle development of the next ovulation cycle.

Furthermore, selection on short weaning to estrus interval (WOI) has been successful and most sows come in estrus 4-5 days after weaning. This period however, might not be sufficient for sows to recover from high lactation weight losses. Both the higher weight loss en short WOI can negatively influence follicle and oocyte development and /or embryonic survival and make sows more at risk for reduced litter sizes or farrowing rates in the next parity.

Up to the mid-nineties, negative effects of severe feed and protein restriction during lactation were mainly expressed as a prolonged WOI, while more recent studies mainly show negative effects on ovulation rate an embryonic survival. The shift from prolonged WOI to reduced “embryonic survival” and “ovulation rate” is probably due to genetic selection for a short WOI. When sows with lactation weight loss return to estrus shortly after weaning, follicle and oocyte quality can be compromised since these follicles develop during a period of negative energy balance and are recruited immediately after weaning. Compromised follicle development can lead to lower quality oocytes and less developed corpora lutea, causing increased embryonic losses.

Around 50% of the second parity sows show a lower litter size in second parity compared with first parity. The reduced reproduction decreases the reproductive efficiency of second parity sows but might also lead to early culling. Analyses of relations of second parity litter size with subsequent performance showed that sows with a low litter size in second parity also had lower litter size in parity 3 and up compared with sows with a medium or high litter size in second parity. These data show that

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15 Lucia et al 2000
16 Schenkel et al 2010
17 Bergsma 2011
18 Van den Brand 2006
19 Quesnel 2009
20 Quesnel 2009
21 Zak et al 1997
22 Hoving et al 2011
a large part of the sows with poor reproductive performance in second parity can be expected to have a poor reproductive performance in subsequent parities, also affecting culling rates.

Preweaning piglet mortality is largely attributed to the incidence of low birth weight and birth weight variation within the litter. Therefore, developing strategies to increase within-litter uniformity of piglet birth weight is important. The main strategy to achieve this goal was to change the sows’ diet before insemination to a carbohydrate rich diet. But literature and especially global experiences from the last decade shows this is maybe not sufficient.

**Literature statements about preparation of the sow for insemination through dietary changes.**

It is now widely accepted that changes in dietary intake promote changes in circulating concentrations of both metabolic hormones, such as glucose, insulin, leptin and IGF-1 and reproductive hormones. These affect the developing ovarian follicle and/or the composition of reproductive tract secretions on which early embryos rely for their nutrition.

Adding dextrose to the sows’ diet in the WOI (weaning to estrus interval) is common practice these days to prepare the sow for an optimal insemination period. It is generally believed by breeders it would increase litter size, birth weight and uniformity of the upcoming litter through a beneficial effect on the insulin levels of the sow. The increased insulin level would benefit the developing follicles.

Literature on the other hand is not as unanimous as one might think. On one hand it is concluded that addition of dextrose during the weaning to estrus interval did not increase litter size, but seemed to affect the uniformity in birth weight of the litter. In 2009 it has been concluded that the combination of dextrose and lactose during the WOI seems to enhance litter size but only in sows with low previous litter size. It also seems to have the potential to reduce the within litter variation in birth weight. On the other hand it stated that administering dextrose before insemination had no influence on the number of piglets at birth. In addition they found that supplementing gestation diet with L-arginine during the last third of pregnancy reduced within- litter variation of piglet birth weight. Combining L-arginine dietary supply with a supplementation of dextrose before insemination provided no additional effect.

This disagreement doesn’t mean that there is no truth in the statement that supplementation of dextrose to the sows’ diet, therefore high insulin levels, benefits the next litter. It just shows that it is only part of the story. In order to understand the full story, it is important to understand the physiology of the estrus of the sow.

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25 Quesnel et al (2014)
Insulin, Growth hormone and Insulin-like growth factor I (IGF-1) concentrations and their role during lactation.

Growth hormone (GH) and insulin-like growth factor-1 (IGF-1) control growth and lactation in swine and this is controlled by the somatotropic axis. Also insulin participates in the endocrinology of growth and lactation because insulin and GH are opponents in their actions.

Growth hormone (GH) is a pituitary hormone that controls growth and lactation. IGF-1 is released from the liver in response to GH binding to its receptors on the liver cells and it controls growth and lactation as well. IGF-1 can be seen as a mediator of GH. In addition to causing IGF-1 release, GH antagonizes insulin action. Antagonizing the actions of insulin has a nutrient partitioning effect through which the development of lean tissue and the production of milk are favored. Insulin causes the shift of glucose from the bloodstream to the body cells. GH counteracts this effects and ensures that glucose stays in the bloodstream and can be used in the mammary gland for milk production.

During lactation both GH and IGF-1 concentrations are elevated in sows (compared with dairy cows). Nonetheless, sows that become catabolic (negative energy balance) during the last week of lactation will have reduced IGF-1 concentrations. This imbalance will occur when feed intake cannot match requirements for maintenance and milk production which will result in an extended weaning to mating interval and subsequently a possible delay of “in heat behaviour”, a lower fertility and a drop in reproductive performances. Sows that are nutritionally compromised during the last week of lactation have low concentrations of insulin and IGF-1 in their blood and this theoretically reduces ovarian responsiveness to LH and FSH.

Although sows are inseminated after weaning, there appear to be carry-over effects of the previous lactation on the ovarian follicular population that develop after the sow is weaned. Understanding the mechanisms through which metabolic hormones control ovarian function may lead to improved reproductive management in sows. This mechanism will be explained in the next chapter.

Obesity in sows creates farrowing difficulties and metabolic problems and also antagonizes postpartum milk production. Sows, therefore are fed a maintenance ration during gestation and their body condition is managed carefully. After farrowing and during lactation, ad libitum feeding is practiced. Sow milk production is lowest immediately after farrowing. Greatest levels of milk production are achieved near the time of weaning.

26 Renaville et al 2002
27 Etherton and Bauman 1998
28 MC lucy 2008
29 Aherne and Williams 1992
30 Noblet and Etienne 1989
After farrowing there is an increase in blood GH concentrations\textsuperscript{31}. The increase in blood GH is associated with an increase in blood NEFA concentrations during lactation. This implies that GH is mediating lipid catabolism during lactation. This is because body cells have to find another energy source than glucose. The increase in GH during lactation is caused partly by the suckling stimulus from the piglets\textsuperscript{32}. The suckling-induced GH release explains why a relatively high blood GH concentration is sustained throughout lactation even in well-fed sows. Post-partum sows have elevated IGF-1 after farrowing\textsuperscript{33} and this endocrine state suggests that the increase in GH after farrowing can stimulate the liver to synthesize and secrete IGF-1. (This is in contrast with post-partum dairy cows)

With respect to insulin concentrations in lactating sows there are some discrepancies. Some studies report greater insulin concentrations \textsuperscript{34} whereas other report lower concentrations\textsuperscript{35}. Sows may become insulin-resistant during lactation\textsuperscript{36}. Sows fed more energy have greater blood IGF-1 post-partum.\textsuperscript{37} The increase in IGF-1 after farrowing may be partly explained by the fact that gestating sows are fed maintenance diets during late pregnancy. In the gestating sows, therefore, feeding level may limit liver IGF-1 production.

The combination of elevated GH and ad libitum feeding after farrowing drives the somatotropic axis and increases liver IGF-1 production. During lactation IGF-1 concentration may remain high in well-fed sows or may decrease over time.\textsuperscript{38} This is the result that in underfed sows the IGF-1 concentrations decrease during lactation because the somatotropic axis becomes uncoupled (The liver becomes insensible to the large amounts of GH and stops to produce IGF-1). This may occur in the second and third week of lactation when litter milk consumption and sow milk production are greater and finally the sow will end up with a negative energy balance.

Weaning is associated with changes in GH, insulin, glucose and IGF-1 but these changes may be confounded by the lower feed level after weaning and other management considerations. Weaning is stressful for sows and the combination of stress and the discomfort of a fully engorged mammary gland may depress appetite. Loss of appetite and decreased feed intake reduce blood insulin and IGF-1. Growth hormone concentrations typically decrease after weaning\textsuperscript{39} because suckling stimulates GH releases in pigs.

**Insulin, Growth hormone and Insulin-like growth factor I (IGF-1) concentrations and their role in reproduction**

Before being born, the ovaries of the female piglet contain a pool of primordial follicles. These will be continuously recruited to develop into an antral follicle. This development takes 80-100 days and results into an antral follicle pool with follicles from 2 up to 5 mm. Antral follicles who don’t receive the right hormonal stimuli will degenerate\textsuperscript{40}.

\textsuperscript{31} Schams et al 1994; Govoni et al 2007
\textsuperscript{32} Rushen et al 1993
\textsuperscript{33} Schams et al 1994; Govoni et al 2007
\textsuperscript{34} Guedes et al 2001
\textsuperscript{35} Revell et al 1998
\textsuperscript{36} Quesnel et al 2007
\textsuperscript{37} Van den Brand et al 2001
\textsuperscript{38} Van den Brand et al 2001
\textsuperscript{39} Mejia-Guadarrama et al 2002; Govoni et al 2007
\textsuperscript{40} Suls L, Vandenbosch A. 2010
Follicular development is controlled by a combination of LH and FSH, both hormones produced by the pituitary gland in the brain. The inhibition of LH secretion caused by the NEB of the sow and the suckling stimulus of the piglets prevents pre-ovulatory follicular development in sows before weaning. In sows, suckling inhibits LH pulsatility and the lack of LH pulsatility leads to anestrus. This is the reason sows don’t come in to estrus during lactation (unlike dairy cows). Sows that are underfed during the last week of lactation have low blood IGF-1 concentrations. The stress of weaning can cause underfeeding in sows and will suppress IGF-1 further, compromise follicular development (prolonged WOI and reduced ovulation rate) and reduce embryonic survival.

After weaning GnRH secretion rises and basal LH concentrations and numbers of LH peaks increase. There’s also an elevation of FSH concentration in the bloodstream leading to the development from an antral follicle into a Graafian follicle. These follicles start to produce estrogen and inhibin, causing a decline in GnRH production. This is the reason why only a few antral follicles will develop into a Graafian follicle. These dominant follicles have also more LH receptors on their surface, allowing them to continue their development despite dropping GnRH production. The mechanism prevents a superovulation, making sure that the number of embryos that will mature doesn’t exceed the capacity of the uterus or the metabolic state of the sow. Through the continuously development of the dominant follicles, the estrogen concentration keeps on rising.

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41 Varley and Foxcroft 1990
42 William and Griffith 1995
43 Zac et al. 1997
Also, according to the GH hypothesis, nutritionally induced changes in liver IGF-1 secretion have a direct effect on the ovary through the endocrine actions of IGF-1. Sows that are nutritionally compromised have low concentrations of insulin and IGF-1 in their blood. In the pig, granulosa and theca cells of the follicle have insulin as well as IGF-1 receptors. Follicular growth in sows depends on LH and FSH, insulin and IGF-1.

Insulin and IGF-1 can act at the level of the hypothalamus to stimulate gonadotrophin releasing hormone secretion and therefore control the release of LH and FSH. The duo-localization of IGF and gonadotropin receptor genes suggests a coordination of gonadotropin an IGF action within the ovary. The synergism is caused by the ability of IGF’s and insulin to increase gonadotropin receptor numbers and increase the activity of gonadotropin receptor second messenger systems. At the same time, gonadotropins increase IGF-1 receptor expression and may increase IGF-1 synthesis in granulosa cells of the follicle.

Thus insulin and IGF-1 can act directly on ovarian cells in pigs. The lower levels reduce ovarian responsiveness to FSH and LH. At the same time, weaned sows have already low LH concentrations.

Lucy 2003; Daftary and Gore 2005
Overcoming one limitation (for example insulin by administering dextrose) will not necessarily recover ovarian function. Responses to metabolic hormones and gonadotropins typically follow a plateau model where improvement in reproductive function is not seen unless a critical threshold of hormone concentrations is achieved.

![Hormone diagram]

**Fig 6: The hormones needed for the reproductive cycle**

It has been proven that GH and IGF-1 have a positive influence on the proliferation of porcine granulosa cells and its steroidogenesis.\(^45\) GH also stimulates follicular development through FSH and LH. It has also been proven that IGF-1, independent from GH, stimulates the proliferation of theca cells.\(^46\) GH on the other hand stimulates the estrogen secretion by these theca cells. Lin et al. showed that IGF-1 increases significantly the number of LH receptors on the granulosa cells.\(^47\)

The development of the embryo before implantation in the uterus is also influenced by IGF-1 concentrations. In vitro trials showed that mitosis in embryos is geared up by administering exogenous IGF-1.\(^48\)\(^49\) An elevated IGF-1 in sows results in an improved development of the placenta and improved intra uterine nutrition of the embryos. This can have an influence on the piglets’ weight.\(^50\)\(^51\) (See chapter: Literature statements about intrauterine growth restriction (IUGS), fetal growth and IGF-1)

To conclude, sows are weaned approximately 1 week before insemination. Weaning has an enormous effect on the sow’s metabolism and her serum concentrations of insulin and IGF-1. The sow is nutritionally compromised and is having a compromised state of ovarian follicular development. This
developed already during previous lactation and can potentially influence follicular growth and the time of estrus after weaning.\(^5\)

Adaptive feeding increases the responsiveness of the ovary to LH and improves the quality of the embryos through its effects on insulin and IGF-1. IGF-1 secretion by the liver cells of the sow can not only be affected by a NEB but by a variety of factors. Immune system activation due to infections, inflammation or viruses and heat stress are also recognised to reduce GH receptor sensitivity leading to reduced levels of IGF-1.

All these data suggest that IGF-1 plays a significant role in fertility and reproduction. Administration of Lianol around weaning reverts the lactating sow towards an anabolic state by increasing serum IGF-1 through dietary AhR-activation. (See chapter: Lianol bioactivity: a triple mode of action)

### Supplementing your sows with the right additives after weaning.

#### Trial 1: Walloon agricultural research centre

*The use of 10 gram Lianol Ferti bolus per day per sow during five days in the period around weaning increases the IGF-1 levels and the litter size.*

#### Material & Method:
- Thirty F1 sows (Belgian Landrace x French Landrace) x Pietrain boar, equally divided over the control and the Lianol Ferti group.
- The parity was 3,5 for the control and 3,7 for the Lianol Ferti group.
- The Lianol Ferti group received 10 grams of Lianol Ferti per sow per day, during five days (starting Monday before weaning till Friday after weaning, weaning was on Thursday). The control group had no treatment.
- IGF-1 serum levels were measured on the Monday at the start of treatment and the next Monday, at insemination.
- Number of piglets born and weaned in the next litters where registered.

#### Results:

<table>
<thead>
<tr>
<th>IGF-1 levels</th>
<th>Control group</th>
<th>Lianol group</th>
</tr>
</thead>
<tbody>
<tr>
<td>on Monday before weaning:</td>
<td>53,3 ng / ml</td>
<td>46,3 ng / ml</td>
</tr>
<tr>
<td>on Monday after weaning:</td>
<td>57,7 ng / ml</td>
<td>60,3 ng / ml</td>
</tr>
<tr>
<td>increase:</td>
<td>4,4 ng/ml</td>
<td>14 ng/ml</td>
</tr>
<tr>
<td>increase in %:</td>
<td>8,25 %</td>
<td>30,2 %</td>
</tr>
</tbody>
</table>

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\(^5\) Lucy et al 2001
IGF-1 levels in ng/ml

Litter size:

<table>
<thead>
<tr>
<th></th>
<th>Control group</th>
<th>Lianol group</th>
</tr>
</thead>
<tbody>
<tr>
<td>- live born: 11,36 per litter</td>
<td>- live born: 12,02</td>
<td></td>
</tr>
<tr>
<td>- weaned: 9,95</td>
<td>- weaned: 10,80</td>
<td></td>
</tr>
<tr>
<td>- % mortality: 12,55 %</td>
<td>- % mortality: 10,1 %</td>
<td></td>
</tr>
</tbody>
</table>

Number live born - weaned - mortality %

Conclusion:
The use of 10 gram Lianol Ferti per day per sow during five days in the period around weaning increases the IGF-1 levels and the litter size. The Lianol Ferti gives 0,66 piglet more at birth and 0,85 piglet more at weaning.
Trial 2: University of Leuven

*Master’s thesis - effects of stimulation of the somatotropic axis with Lianol Ferti on fertility in sows*

**Material & Method:**

- 896 gilts and 896 primi- and multiparous sows. Both groups contained 2 genetic lines; (Topigs-20 x York) x (Hungarian landrace x Pietrain).
- During 5 days 10 g Lianol Ferti from 3 days before weaning until 1 day after weaning.
- IGF-1 serum levels were measured.
- Number of piglets born and weaned in the next litters were registered.

**Results:**

![Graph showing IGF-1 conc. (ng/ml) in sows after administering Lianol Ferti®](chart1)

![Graph showing total number of piglets born/litter without and with use of Lianol Ferti®](chart2)
Conclusion:

The treatment with Lianol Ferti in multiparous sows gives a significant rise in the number of total born piglets / litter with 1.9 piglet (P<0.05). In primiparous sows it gives a significant rise with 1.2 piglet in the number of total born piglets (P<0.05).