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The most beautiful experience we can have is the mysterious.

It is the fundamental emotion which stands at the cradle of true art and true science.

Albert Einstein

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LIST OF ABBREVIATIONS

3-OH-C4: 3-hydroxy-butyrylcarnitine

AA: amino acids

ADFI: average daily feed intake

BC: body condition

BF: back fat thickness

BW_B: birth weight

C4: (iso)butyrylcarnitine

CI: colostrum intake

CY: colostrum yield

DFI: daily feed intake

g: gram

GLUT: glucose transporter

h: hour

Ig: immunoglobulin

IR: interquartile range

kg: kilogram

min: minute

NEFA: non-esterified fatty acids

SD: standard deviation

SEM: standard error of the mean

TG: triglyceride

CHAPTER 1

GENERAL INTRODUCTION

1. MAMMARY GLAND

1.1. Anatomy

The sow's mammary gland exists of 12 to 18 mammary gland packets depending on the breed (Labroue *et al.*, 2001) These are stretched from the anterior to the posterior abdominal wall in 2 parallel rows. Within each packet, the secretory mammary tissue is organized in different lobules with extra-parenchymal tissue in between. Within each lobule, there are numerous alveolar lumens which are the secretory units of the mammary gland. Each alveolar lumen is connected to ducts which end in the small milk ducts to convert eventually in on average 2 teat ducts (1 to 3) with their representative teat opening at the top of the nipple. Different from what is seen in cattle, the sow does not have a teat or udder cistern but only a small teat sinus. The alveolar lumen is demarcated by a single layer of mammary epithelial cells, also called lactocytes, which are oriented with their apical side into the alveolar lumen while on their basal side there is a basal membrane, myo-epithelial cells, capillaries and connective tissue (Hartmann and Holmes, 1989; Farmer *et al.*, 2008). The structure of the mammary gland is represented in **Figure 1**.

The myo-epithelial cells, with oxytocin receptors on the cell surface, surround the lactocytes and contract in response to oxytocin, pushing the lactocyte to secrete into the milk ducts. This is called the milk ejection reflex but the same mechanism stands for colostrum (Ellendorf *et al.*, 1982).

The vasculature of the mammary gland of the sow is complicated and an overview is represented in **Figure 2**. The mammary gland receives blood via several arteries. The external pubic artery ramifies into different branches after leaving the inguinal cavity and together with the arteria epigastrica caudalis and the arteria epigastrica superficialis it supplies the posterior mammary glands. The arteria epigastrica cranialis supplies the anterior 5 mammary glands. All these arteries form anastomoses. Blood leaves the mammary gland in 2 distinct

ways. The blood from the cranial mammary glands drain via 2 subcutaneous abdominal veins into the external thoracic vein while the caudal mammary glands drain via the same subcutaneous veins into the external pubic vein. Typically for pigs, there are venous anastomoses between the left and right mammary gland of each pair of glands (Farmer *et al.* 2008, Trottier et al 1995).

At the level of the secretory mammary tissue, the vasculature ramifies into numerous capillaries which irrigate the lactocytes but also the myo-epithelial cells. A sufficient blood supply is important. Indeed, Trottier *et al.* (1997) estimated that 550 liters of blood is necessary to produce 1 liter of milk. On the other hand, the extraction rate of nutrients from the blood by the lactocytes, measured as the difference between the arterial and the venous concentration, is only 20-40% (Boyd and Kensinger, 1998). It is unclear whether the blood supply or rather the extraction rate is the most limiting factor for colostrum and milk yield.

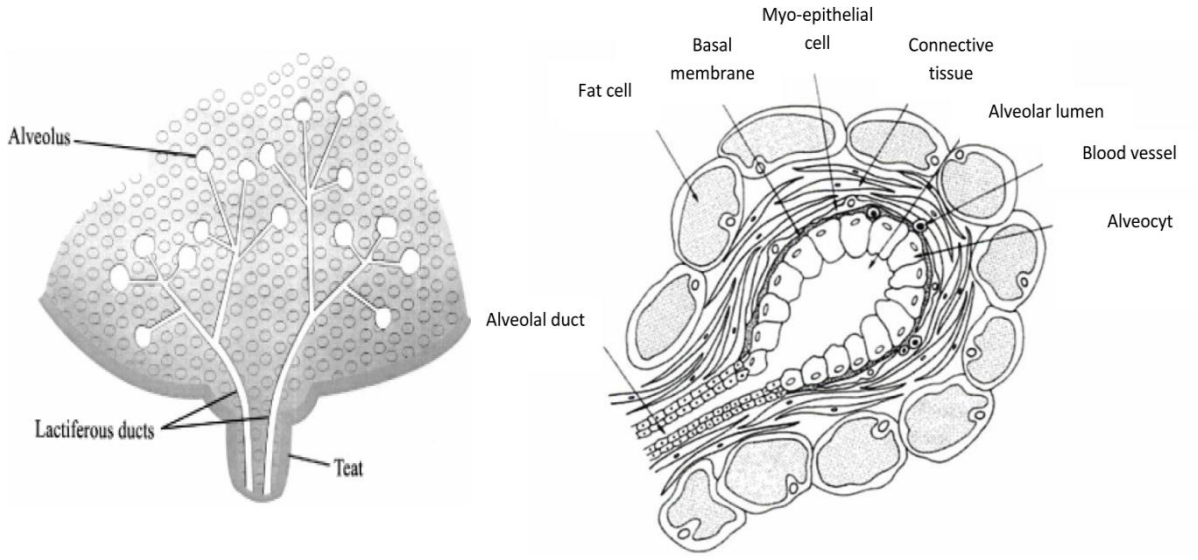

Figure 1. *Gland organization (left) and alveolar lumen organization (right) of the mammary gland in sows. (after Martineau et al., 2010; after Delouis et al., 2001)*

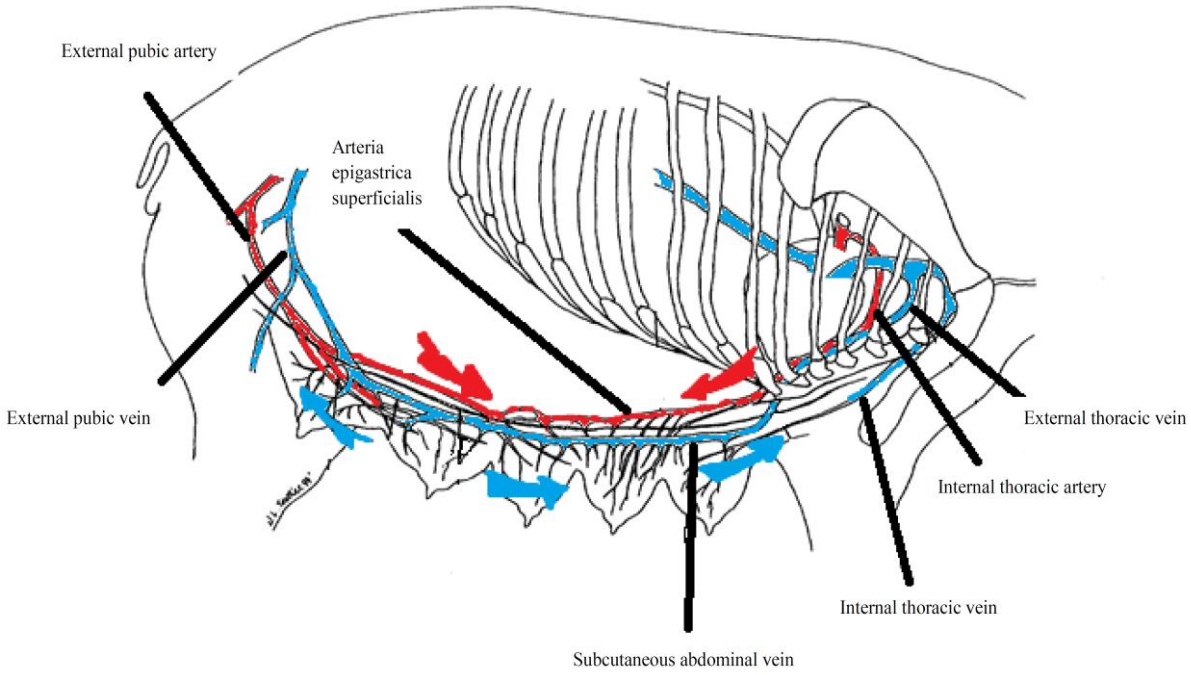

Figure 2. *Schematic presentation of the vasculature of the mammary gland in sows (after Trottier et al., 1995)*

1.2. Ontogeny

A large amount of functional mammary tissue is of great interest to pig production. Functional mammary tissue is critical for milk production and piglets' weight gain (Head and Williams, 1991; Nielsen *et al.*, 2001) and the higher the number of functional mammary secretory cells, the higher the milk production (Head and Williams, 1991). Unfortunately, a correlation between colostrum yield (**CY**) and the amount of functional mammary tissue has not yet been investigated but it can be assumed that the available functional mammary tissue is determinant for its potential production of both colostrum and milk. We distinguish 3 periods during the sow's life in which abundant mammogenesis occurs (Farmer, 2013). At birth, the mammary glands of the female piglet mostly exists of subcutaneous stromal tissue and the duct system is still poorly developed (Delouis *et al.*, 2001). Mammary development is negligible up to 90 days of age but between 3 and 8 months of age, the accumulation rate for mammary tissue and mammary DNA, which is indicative for the cell number, is 4-6-fold higher compared to pigs younger than 3 months of age (Sorensen *et al.*, 2002). At the time of first insemination, the mammary gland is macroscopically still very small but the duct system is well developed (Farmer, 2013).

During gestation, mammary development is low during the first two-thirds of gestation. From approximately d 75 of gestation onwards, mammary development becomes abundant as indicated by a significant increase in dry, fat-free mammary tissue, wet mammary weight, crude protein and mammary DNA (Kensinger *et al.*, 1982; Sorensen *et al.*, 2002; Ji *et al.* 2006). The composition of the mammary gland shows a shift from primarily an adipose tissue in early gestation to an extensive lobuloalveolar tissue in late gestation. This is shown in **Figure 3**. The wet weight of the middle glands was greater than that of posterior glands at d 102 of gestation (Ji *et al.*, 2006). The development of the different mammary gland packets is partially independent from each other because next to a general regulating mechanism, there

are also local regulating mechanisms. Secretions in the alveolar lumens were abundantly present at d 105 of gestation (Kensinger *et al.* 1982), or partially at d 102 and clearly at d 112 of gestation (Ji *et al.*, 2006).

Mammogenesis continues during lactation. Kim *et al.* (1999a) showed a significant increase in mammary tissue wet weight, dry weight, dry-fat free tissue and DNA between d 5 and 21 of lactation. As the amount of DNA per unit of mammary tissue increased, there is a clear indication that mammogenesis during lactation is a result of both hyperplasia and hypertrophy.

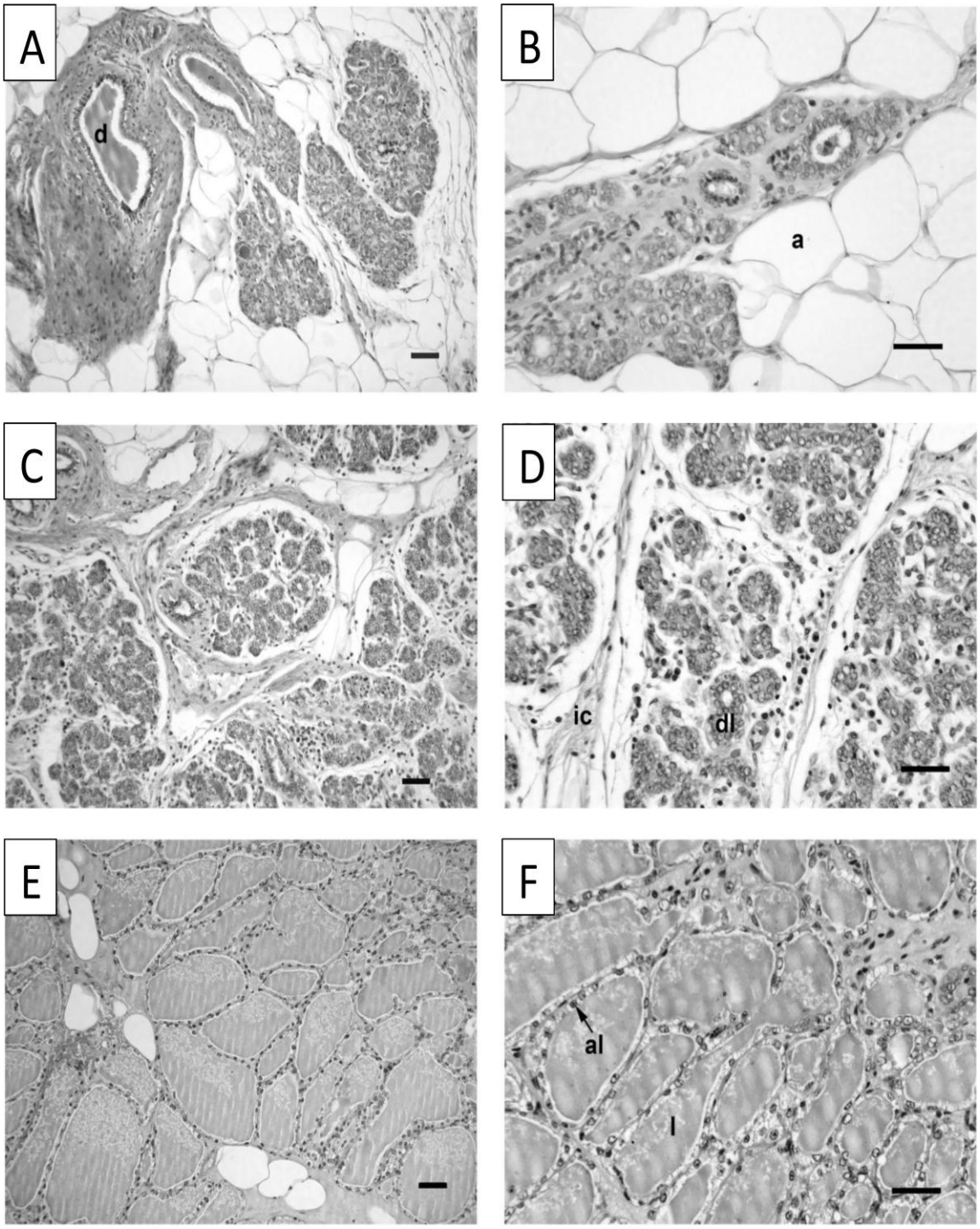

Figure 3. *Development of the mammary gland from fatty tissue to secretory tissue during gestation (A-B: d 45, C-D: d 75, E-F: d 112; a = adipocyte, al = alveocyt, d = duct, dl = ductile in lobule, ic = connective tissue, l = alveolar lumen; after Ji et al., 2006)*

1.3. Factors affecting mammogenesis

1.3.1. Hormones

The prepuberal mammogenesis starts at 90 days of age and this is preceded by a weight gain of the ovaries, the development of antral follicles and oestrogen secretion around 70 days of age. Oestrogen plays a crucial role in prepuberal mammogenesis and the latter can even be stimulated by supplementation of the phyto-oestrogen genistein to gilts between 90 and 183 days of age (Farmer *et al.*, 2010a). Administration of recombinant porcine prolactin for 4 weeks to gilts of 75 kg resulted in a 116% increase in mammary parenchymal tissue and a 160% increase in mammary DNA (Farmer and Palin, 2005). It is very likely that next to oestrogen and prolactin, other hormones or growth factors play their part in prepuberal mammogenesis but this remains quite unknown (Farmer and Sorensen, 2001).

Mammogenesis during gestation is under influence of several hormones. Again, oestrogen plays an important role as Kensinger *et al.* (1986a) showed a correlation between serum oestrogen and mammary DNA at d 110 of gestation. Supplementation during gestation with zearalenone, a mycotoxin with oestrogen-like effects, resulted in squamous metaplasia and ductal hyperplasia of the mammary gland (Chang *et al.*, 1979). Another important hormone for gestational mammogenesis is relaxin. Relaxin is produced by the corpora lutea. Gilts that were ovariectomized at d 80 or 100 of gestation had a detrimental suppression of mammary development that could be prohibited by relaxin injections (Hurley *et al.*, 1991). Winn *et al.* (1994) showed that relaxin alone has only little effect but together with oestrogen it leads to clear mammary development and together with progesterone it reduced the organisation of the extracellular matrix of the mammary gland, which is beneficial for lobuloalveolar development. In contrary to what is seen in cattle (Glimm *et al.*, 1988), growth hormone (DeHoff *et al.*, 1986) and growth hormone releasing factor (Farmer *et al.*, 1997) do not seem to affect gestational mammogenesis in sows. Prolactin has proven to be of major importance

for mammogenesis. Indeed, gilts supplemented with bromocriptine, an antagonists of prolactin, between d 70 and 110 of gestation only had half the amount of parenchymal mammary tissue and mammary DNA at d 110 of gestation (Farmer *et al.*, 2000b). The specific time-window in which prolactin exerts most of its stimulatory effect on the mammary gland was shown to be between d 90 and 110 of gestation (Farmer and Petitclerc, 2003).

Administration of exogenous porcine prolactin to sows during lactation increased serum concentrations of prolactin but did not alter weight of parenchymal and extraparenchymal mammary tissue nor did it alter number of prolactin receptors and their affinity in parenchymal tissue compared to negative control sows which implies that during lactation all mammary prolactin receptors are saturated (Farmer *et al.*, 1999).

1.3.2. Nutrition

A restricted or *ad libitum* feeding strategy to gilts between weaning and 90 days of age did not affect future mammary development, whereas *ad libitum* feed intake after 90 days of age resulted in more mammary tissue, RNA and DNA compared to restricted fed sows (Sorensen *et al.*, 2006). Farmer *et al.* (2004) showed that between 90 and 200 days of age, a low protein intake (0.7% lysine and 14.4% CP compared to 1.0% lysine and 18.8% CP) did not affect mammary gland development but a 20% reduction in feed intake resulted in a decreased mass of parenchymal and extraparenchymal mammary tissue. When a reduced feed intake occurs after 90 days of age, the negative effects on the prepuberal mammary gland development cannot be compensated by subsequent overfeeding (Farmer *et al.*, 2012a), although the overfeeding in this experiment was not sufficient to induce compensatory growth. Some of these gilts were observed during their first 2 parities and the difference in mammary gland development was almost completely compensated by d 110 of the first gestation although the

percentage of protein in mammary parenchymal tissue tended to be lower compared to the control group (Farmer *et al.*, 2012b).

Gestational mammogenesis is also influenced by nutrition. Weldon *et al.* (1991) showed that gilts fed adequate energy between d 75 and 105 of gestation had 27% more parenchymal mammary tissue and 30% more mammary parenchymal DNA at d 105 of gestation compared to gilts fed the double amount of energy whereas they could not find an effect of protein intake during late gestation on mammary development. The latter was also found by Kusina *et al.* (1999) who showed no difference in amount of parenchymal mammary tissue, mammary DNA, RNA and protein at the end of gestation between gilts receiving diets differing in protein levels (measured as 4, 8 or 16 g of lysine daily) between d 25 of gestation and 105 of gestation.

Nutrition can also affect mammary gland development during lactation. Kim *et al.* (1999b) offered sows 4 diets that were combinations of different amounts of energy and protein (50.2 or 73.2 MJ ME per day; 32 or 65 g lysine per day). They showed quadratic effects of both energy and protein intake on amount of parenchymal mammary tissue and mammary DNA.

Nutrition of sows during gestation can also influence future mammary development of their progeny. Linseed is a rich source of the lignin precursor secoisolariciresinol diglucoside and when offered to sows from d 63 of gestation until the end of lactation, their progeny had a higher amount of parenchymal mammary tissue per kg body weight at 220 days of age (Farmer and Palin, 2008).

1.3.3. Other factors

Teats that were not suckled for 24 h had a lower production during the remainder of lactation while teats not being suckled for 72 h regressed and could not be used anymore during that lactation (Theil *et al.*, 2005). This raises the question whether non-use of a teat during

lactation could have repercussions on teat development in the next lactation. Fraser *et al.* (1992) showed that piglets suckling teats that were not suckled during the previous lactation had a lower weight gain compared to litter mates suckling teats that were suckled during the previous lactation but the use or non-use of teats was confounded with teat location. Farmer *et al.* (2012c) clearly demonstrated that the use of a teat is crucial for its amount of functional mammary tissue in the next lactation. By taping half of the teats in the first lactation and letting the non-taped or the taped teats being suckled in the next lactation, they clearly demonstrated that teats that were not suckled in the previous lactation had a lower amount of parenchymal mammary tissue, a lower amount of mammary DNA and tended to have a lower amount of mRNA from the prolactin receptor gene.

Gilts from the Upton-Meishan breed had a lower amount of parenchymal mammary tissue and less mammary DNA and RNA at d 110 of gestation compared to Large White gilts. The explanation for this breed effect on mammogenesis probably lies in the lower number of prolactin receptors observed in the Upton-Meishan breed (Farmer *et al.*, 2000a). Therefore, the prolactin-regulating genes (STAT5a and STAT5b) were sequenced (Palin *et al.*, 2002; Farmer *et al.*, 2010b) which showed correlations between mammary development and STAT5b especially in Large White gilts but the levels of STAT5b did not differ between breeds. The prolactin-regulating genes thus are related to mammary development but could not clearly explain the observed difference in mammary development between breeds.

Parenchymal mammary tissue was higher in litters with 12 piglets compared to litters with 6 piglets although the weight of the individual suckled glands was lower in litters with 12 piglets (Kim *et al.*, 1999c).

2. COLOSTRUM COMPOSITION

Colostrum is the first secretion of the mammary gland and it can be obtained already a few hours before parturition. Compared to milk, it is characterized by a higher percentage of dry matter and proteins, especially immunoglobulins (**Ig**), but the concentrations of lactose and fat are lower. Colostrum is gradually replaced by milk during the first 24-36 h after parturition (Klobasa *et al.*, 1987). A strong decrease in Ig and an increase in lactose and fat concentration are the main indicators of the switch from colostrum into milk (Gallagher *et al.*, 1997). An overview of the composition of the major constituents of sow colostrum and milk during the first 3 days of lactation is given in **Figure 4**.

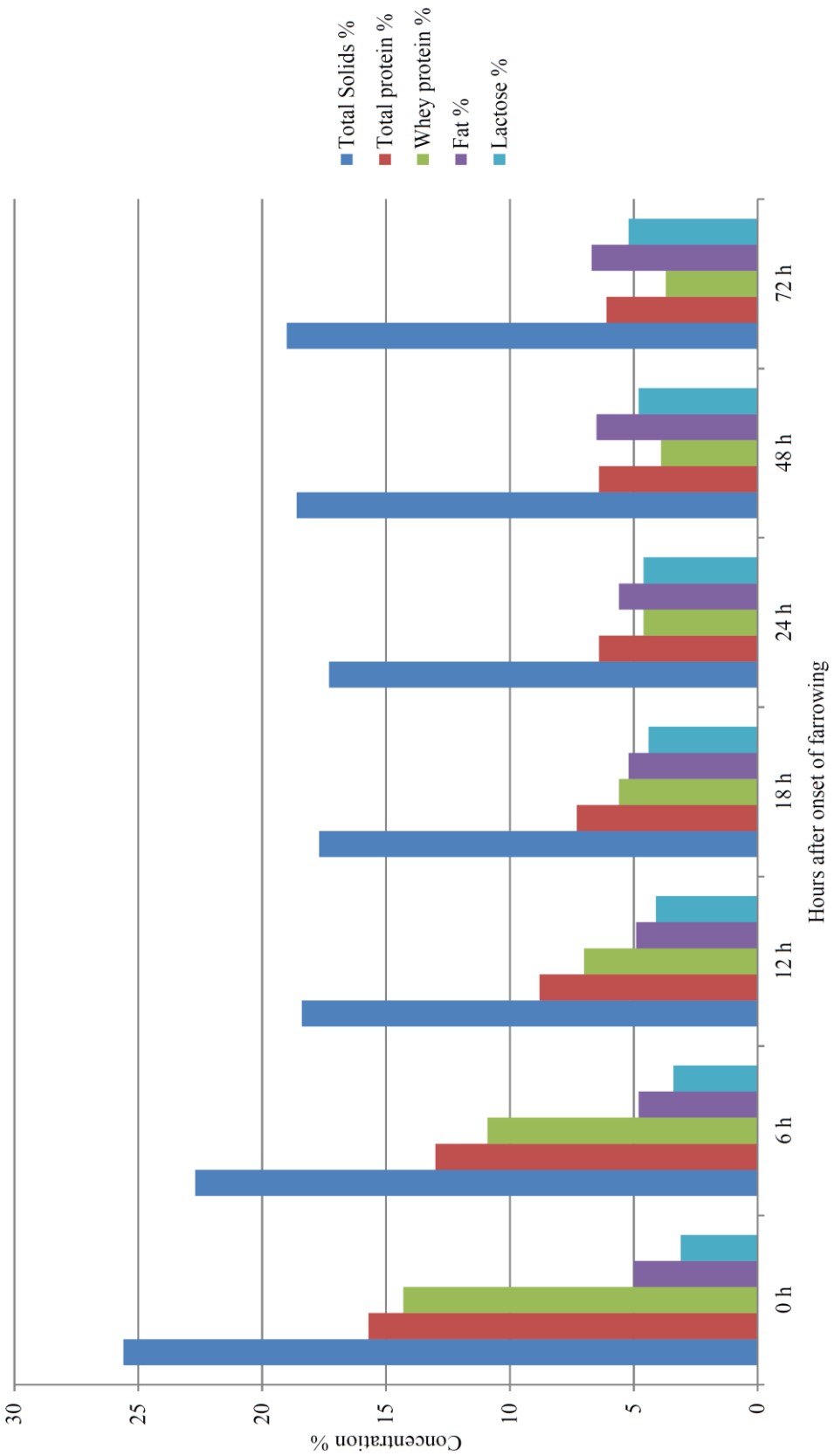

Figure 4. *Average composition (%) of the major constituents of sow colostrum during the first 3 days of lactation (after Klobasa et al., 1987).*

2.1. Carbohydrates

Lactose is the predominant carbohydrate in colostrum and milk. At parturition, the concentration of lactose averages around 3.0% and increases to 4.5% after 24 h and over 5.0% after 3 days of lactation (Klobasa *et al.*, 1987). Lactose is the major osmotic component that determines milk yield (Leong *et al.*, 1990). Foisnet *et al.* (2010a) also found indications that a reduced lactose synthesis by a reduced uptake of glucose by the mammary gland might be a reason for a ower CY. Lactose synthesis in the alveocyt depends on the availability of its main precursor glucose (Shennan and Peaker, 2000). Factors affecting the flow of glucose towards the mammary gland are discussed later (capital 3.3. of the general introduction).

Meishan breeds had lower lactose content in colostrum compared to Yorkshire (Zou *et al.*, 1992), whereas no difference was observed between Meishan and crossbred sows (Alston-Mills *et al.*, 2000). Farmer *et al.* (2007) also showed differences in colostral lactose content between lean breeds.

Farrowing induction at d 112 of gestation did not alter colostral lactose content (Jackson *et al.*, 1995) but Foisnet *et al.* (2011) did observe higher colostral lactose content at onset of farrowing when farrowing was induced at d 113 of gestation compared to sows with natural onset of farrowing although gestation length did not differ between groups.

2.2. Fat

The concentration of fat in colostrum averages 5.0% at farrowing, reaches its maximum concentration around 24-72 h after parturition and decreases slowly during the rest of lactation (Klobasa *et al.*, 1987, Jackson *et al.*, 1995, Csapo *et al.*, 1996). Colostral fat mainly comprises triglycerides (**TG**) (97-98%) but also diglycerides, monoglycerides, phospholipids, glycolipids, cholesterol, cholesterol esters and free fatty acids (Hartmann and Holmes, 1989). There are very few short chain fatty acids and the predominant fatty acids are oleic, palmitic,

linoleic and stearic acid which account for 90% of all fatty acids (Csapo *et al.*, 1996). The fat in colostrum and milk originates from 3 sources namely *de novo* synthesis in the mammary gland, the body fat reserves and the dietary fat.

A first method to alter colostral fat content is via the feed of the sow. The fatty acid profile of the colostrum is a reflection of the fatty acid profile of the serum (Witter *et al.*, 1970b) which is a reflection of the fatty acid profile of the sow's diet (Witter and Rook, 1970a). The fat source of the sow's diet is reflected in the fatty acid profile of the sow's milk (Bontempo *et al.*, 2004; Lauridsen and Danielsen, 2004; de Quelen *et al.*, 2010). Sows in a negative energy balance have more C18 fatty acids, reflecting the increased use of body fat reserves (Darragh and Moughan, 1998). Moreover, the fat source of the sow's gestation diet affects the fatty acid profile of the milk as the fatty acids from the diet are stored in the body fat of the sow and mobilized during lactation for milk synthesis (Amusquivar *et al.*, 2010). Supplementing the sow's diet with fat resulted in a higher fat content in the milk (Coffey *et al.*, 1982; Christon et al, 1999; Jackson *et al.*, 1995) but the percentage of crude protein in a sow's diet (5-10-15%) did not alter fat content or fatty acid composition of colostrum (Elliot *et al.*, 1971). Feeding sows a diet with high fibre content (23%) resulted in a higher fat percentage in colostrum 24 h after onset of farrowing (11% vs. 8%) compared to sows fed a diet with lower fibre content (13%) (Loisel *et al.*, 2013a) but differences in peripartal concentrations of the main hormones involved in lactogenesis were not observed. A reduction of feed intake (1.0 vs. 3.4 kg/d) during the last 2 weeks of gestation resulted in an increased colostral fat content (Göransson, 1990).

Meishan breed had higher fat concentrations in colostrum and milk compared to Yorkshire (Zou *et al.*, 1992), in colostrum compared to Large White (Le Dividich *et al.*, 1991) and in milk compared to crossbred (Alston-Mills *et al.*, 2000). Klaver *et al.* (1981) indicated that milk fat was lower in sows with a thin condition compared to sows in a normal condition

when feed intake was high but no difference was observed when feed intake was low. Unfortunately, condition and feed intake were not defined. Nonetheless, Meishan is known to be a fat breed and thus the observed breed differences might be partially caused by differences in body condition (**BC**). Mahan *et al.* (1998) reported a linear decrease in colostral fat content when parity increased with the largest decline between parity 1 and 2, but this was confounded by the higher back fat thickness (**BF**) in first and second parity sows. Also, Farmer *et al.* (2007) compared the composition of colostrum and milk between 4 lean breeds and observed no differences in fat content.

Farrowing induction at d 112 of gestation resulted in a decreased concentration of colostrum and milk fat probably because of a functionally immature mammary gland at that moment (Jackson *et al.*, 1995). Colostral fat tended to be lower ($P = 0.05$) immediately after farrowing when sows were induced at d 113 at gestation although gestation length did not differ from the negative control group. The difference in fat concentration was not present anymore after 24 h (Foisnet *et al.*, 2011).

The method of milk collection might influence the fat content. The last milk contains more fat (Atwood and Hartmann, 1992) but confounding with teat location was present in this study. Nonetheless, whether a teat is partially or totally milked might affect the fat content of the collected milk (Csapo *et al.* 1996).

2.3. Protein

At the time of parturition, the concentration of total protein averages around 15.5 - 16.5% and decreases during the first 24 h to 6.5 – 11.5% (Klobasa *et al.*, 1987; Csapo *et al.*, 1996). The essential amino acids (**AA**) cover 45% of colostral protein at farrowing and 24 h later. Glutamic acid and leucine are the 2 main AA of colostrum (Wu and Knabe, 1994; Csapo *et al.*, 1996).

Colostral proteins can be divided into caseins and whey proteins. The caseins contain several subtypes (α, β, κ); the whey proteins consist of blood serum albumin, α-lactalbumin, β-lactoglobulin, IgG, IgA, IgM, lactoferrin, and other minor proteins (Gallagher *et al.*, 1997). Colostrum also contains non-protein nitrogen (Darragh and Moughan, 1998). Whey protein represents over 90% of colostral total protein at farrowing and decreases to about 53% mainly during the first 24 h whereas casein represents 9% of colostral total protein at farrowing and increases to 47% mainly during the first 24 h (Csapo *et al.*, 1996; Xu *et al.*, 2003). Casein mainly serves as a source of dietary AA for the neonatal piglet but also serves as a carrier of calcium and may result in various types of bioactive compounds after digestion (Xu *et al.*, 2003). The whey fraction of the colostral protein mainly consists of Ig and because of their importance, these will be described separately. The relative distribution of different proteins within colostral protein is presented in **Figure 5**.

It can be discussed whether the AA composition of milk and protein represents the AA requirements for piglet's growth and development. A large part of the colostral protein, namely the Ig, is not hydrolysed as they serve an immunological rather than a nutritional purpose. Also, piglets' growth is below their potential during lactation (Pluske *et al.*, 1995) which is not desirable in intensive pig production. The AA requirement for maximal growth may differ from the requirements for maintenance and development (Xu *et al.*, 2003) which is an important fact when developing milk replacers. It was hypothesized that the AA composition of colostrum and milk might be an evolutionary balance between the needs of the sow and the piglets (Darragh and Moughan, 1998) but still, colostral protein is highly digestible (apparent digestibility of 95 - 98%) and available to the piglets (Lin *et al.*, 2009). Potential daily weight gain during lactation when piglets are fed *ad libitum* with a milk replacer was estimated to be 450 g/d and this reduced time to gain slaughter weight (110 kg) by 10 days (Harrell *et al.*, 1993).

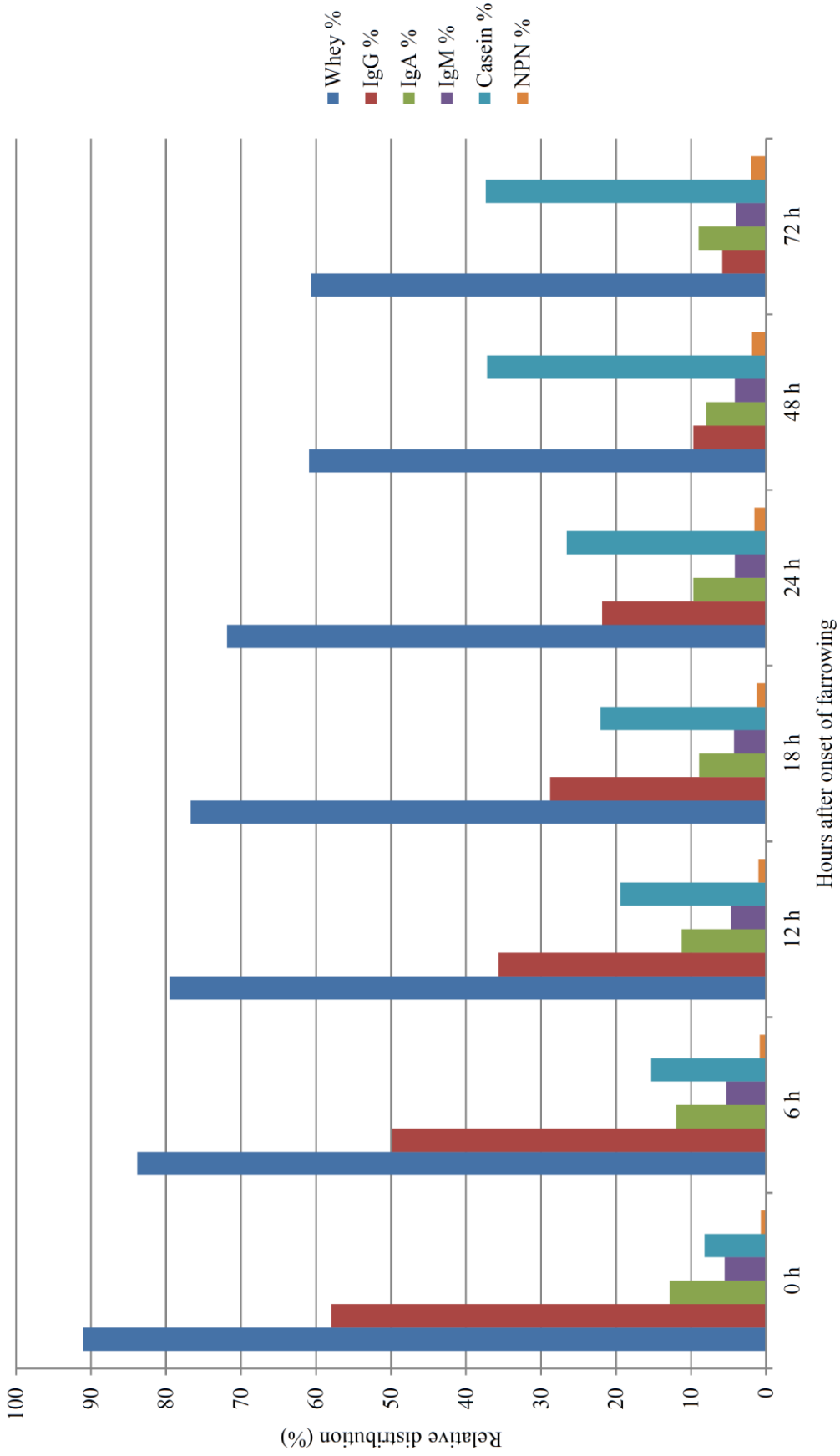

Figure 5. *Components of colostral/milk protein during the first 3 days of lactation (expressed relative to total protein; after Klobasa et al., 1987).*

2.4. Immunoglobulins

At farrowing, Ig represent most of the whey and total protein and approximately 50% of the dry matter in colostrum. After 24 h of lactation, the Ig only represent 50% of whey protein, 35% of total protein and 15% of dry matter (Klobasa *et al.*, 1987). There are 3 types of Ig in colostrum: IgG, IgA and IgM and all of them decline during this period but the most remarkable drop is seen in IgG (Klobasa and Butler, 1987). An overview of the change of protein components during the first 3 days of lactation is shown in **Figure 5**. The relative distribution of Ig differs between species. In swine, cattle, horse and sheep the IgG is predominant during the colostral phase whereas in humans, IgA is predominant during the colostral phase (Hurley and Theil, 2011).

The IgG is a monomeric antibody and the best represented in colostrum at the beginning of parturition. By 48 - 72 h of lactation, this predominant position is taken over by IgA, which is mostly found in a dimeric form with a typical secretory component which protects the sIgA from hydrolysis by proteases. The secretory component is the extracellular fraction of the poly-Ig receptor. A minor part of the IgA is also present in a monomeric form and a dimeric form without the secretory component. The IgM is a pentameric antibody and the Ig with the lowest concentration in colostrum.

All IgG, approximately 85% of IgM and 40% of IgA in colostrum is derived directly from the plasma of the sow which indicates that colostrum is not just a secretion but also a transudate (Bourne and Curtis, 1973). The non-secretory IgA mostly originates from the plasma after transudation (Porter, 1969) whereas the sIgA is secreted via the poly-Ig receptor (Le Jan, 1993). The 60% of IgA not being a result of transudation may originate from selective transport of IgA from the induction site to the blood stream to the mammary gland but more importantly from IgA plasma cells present in the mammary gland which originate from lymphocytes of the gut-associated lymphoid tissue (Salmon *et al.*, 2009). The different

pathways to transport IgG from the plasma to the colostrum will be discussed later (capital 3.2. of the general introduction).

The concentration of IgG in colostrum varies widely and is affected by many factors such as parity, season, genotype, and teat location (Inoue at al., 1980; Klobasa and Butler, 1987; Rooke and Bland, 2002; Tuchscherer *et al.*, 2006; Quesnel, 2011) but it is not influenced by farrowing induction (Milon *et al.*, 1983; Jackson *et al.*, 1995; Foisnet *et al.*, 2011). Total colostral IgG was not changed due to vaccination (Arey *et al.*, 2000), but Le Dividich *et al.* (2005a) stated that titres of specific antibodies in colostrum might increase after vaccination without altering total colostral IgG. On the other hand, Klobasa and Butler (1987) did observe an increase in total IgG after vaccination. Still, the majority of the variation of IgG concentration in colostrum is due to individual sow variation (Klobasa and Butler, 1987) and might partially be explained by the individual variation of IgG concentration in the serum of the sow (Quesnel, 2011). The IgG and IgA concentration of colostrum increases with parity in sows (higher in parity 4 sows compared to primiparous sows; Carney-Hinkle et al., 2013) but the same principle was seen in other species such as dairy cattle (Kehoe et al, 2011). The concentration of IgG was negatively correlated with the concentration of lactose and positively to the concentration of IGF-I in colostrum (Foisnet *et al.*, 2010a). An increase in colostral IgG was seen when the diet of the sow was supplemented with active components with probably an immunomodulating effect a week to a month prior to farrowing: conjugated linoleic acid (Bontempo *et al.*, 2004), non-specific immunostimulating products (Krakowski *et al.*, 2002), shark liver oil (Mitre *et al.*, 2005), source of essential oils (Wang *et al.*, 2008), fermented liquid feed (Demeckova *et al.*, 2003), and mannan oligosaccharides (O'Quinn *et al.*, 2001). On the other hand, supplementation with vitamin E from mid-gestation had no effect (Nemec *et al.*, 1994) and prenatal stress decreases colostral IgG concentrations (Tuchscherer *et al.*, 2002). Parity and genotype could partially explain the large variation in

colostral IgA concentrations but similar to IgG, most variation in colostral IgA was due to individual sow variation (Inoue *et al.*, 1981, Klobasa and Butler, 1987).

2.5. Cells

Colostrum contains abundant amounts of viable cells (range 10^6 - 10^7) including epithelial cells, polymorphonuclear cells, macrophages, and lymphocytes (Salmon *et al.*, 2009). *In vitro* studies indicated that epithelial cells, representing about 20% which is rather high compared to other species, can act as antigen-presenting cells and produce cytokines (Le Jan *et al.*, 1996). Polymorphonuclear cells, mostly neutrophils, and macrophages are capable of phagocytosis of bacteria and subsequent killing but with much lower efficiency compared to blood polymorphonuclear cells and alveolar macrophages (Wagstrom *et al.*, 2000). Colostral lymphocytes consist of 70% T-lymphocytes and 30% B-lymphocytes (Le Jan *et al.*, 1996).

2.6. Hormones, growth factors and other minor components

Hormones involved in parturition and lactogenesis like progesterone, oestradiol, cortisol, and prolactin (Devillers *et al.*, 2004a), relaxin (Frankshun *et al.*, 2011), oestrone (Farmer *et al.*, 1987), and somatotropin (Farmer *et al.*, 1992) were identified in sow colostrum as were hormones involved in the gastrointestinal metabolism like insulin, neurotensin, bombesin (Weström *et al.*, 1987), and leptin (Estienne *et al.*, 2000).

Colostrum also contains several growth factors like epidermal growth factor (Jaeger *et al.*, 1987), insulin-like growth factor I and II (Simmen *et al.*, 1988; Donovan *et al.*, 1994), and transforming growth factor β (Xu *et al.*, 1999).

To support the digestive tract of the neonatal piglet, colostrum and milk contain several digestive enzymes such as lipase, α-amylase, esterase, protease and alkaline phosphatase (Darragh and Moughan, 1998). More typical for colostrum is the presence of protease

inhibitors (Weström *et al.*, 1982; Zhou *et al.*, 2003) to protect Ig and growth factors from hydrolysis.

Colostrum also contains several substances with non-specific antimicrobial or immunomodulating effects. Lactoferrin and transferrin have an iron-binding function and lower the iron available to iron-dependent bacteria (Wagstrom *et al.*, 2000). Lactoferrin also stimulates the cytotoxic function of natural and lymphokine-activated killer cells *in vitro* (Shau *et al.*, 1992). Lysozyme is an enzyme with an antimicrobial activity but its main property is that secretory IgA only binds complement in the presence of lysozyme (Hill and Porter, 1974). The lactoperoxidase-thiocyanate-hydrogen peroxide system oxidizes thiocyanate which results in a bacteriostatic effect. *Streptococcus* spp. which produce peroxide are especially sensitive to this tripartite system (Reiter, 1978a, b). Several interleukins, TNF-α and IFN-γ were identified in colostrum and have a potential role in supporting and stimulating the piglet's immune system (Nguyen *et al.*, 2007).

2.7. Vitamins and minerals

Vitamins play a key role in many important biochemical systems. Vitamin C and E also have a function as antioxidant. Passage of vitamin E through the placental barrier is minimal meaning that colostrum is the main source of vitamin E for the piglets (Pharazyn *et al.*, 1990; Mahan and Vallet, 1997). Colostral vitamin E can be increased by supplementation of vitamin E to the sow's diet (Pinelli-Saavedra *et al.*, 2008) or by giving the sows 2 injections of vitamin E the week before farrowing (Chung and Mahan, 1995). On the other hand, vitamin C does not seem to change when the sow's diet is supplemented during late gestation (Mahan and Vallet, 1997). Injecting the sow intramuscularly with vitamin D before parturition increased its concentration in the milk (Xu, 2003). Supplementing the sow's diet with vitamin A during late gestation increased the content of vitamin A in colostrum (Bland *et al.*, 2001).

Colostrum also contains a lot of macro- and microminerals. Potassium and sodium contribute to the osmolarity of milk. Concentrations of calcium and phosphorus are high in colostrum but their concentration is independent of the dietary supply of these minerals (Mahan and Vallet, 1997) which also accounts for zinc, copper and iron (Xu *et al.*, 2003). Iron and copper are low in sow's colostrum and milk and this might result in deficiencies in the piglets (Csapo *et al.*, 1996). Selenium is a mineral with an antioxidant function and transplacental transport is good (Mahan, 1990). The concentration of selenium in colostrum can be increased by supplementing the sow's diet with organic selenium (Quesnel *et al.*, 2008b). There was a difference between breeds selected for high or low serum cholesterol in milk concentrations of boron, aluminium, cupper, and mangane (Park *et al.*, 1994).

3. LACTOGENESIS

Lactogenesis is the period characterized by the production of colostrum, the transfer of IgG from sow serum to the mammary gland, and morphological changes in the mammary gland. It can be subdivided in lactogenesis I and lactogenesis II (Hartmann *et al.*, 1997; Devillers *et al.*, 2006). Lactogenesis I is characterized by an active secretion of milk constituents by the lactocytes, resulting in an accumulation of small amounts of pre-colostrum in the alveolar lumen, and by structural and metabolic differentiation in the mammary gland. Lactogenesis II is characterized by an abundant secretion of the lactocytes, is closely related to farrowing (Hartmann *et al.*, 1997; Neville *et al.*, 2001) and switches to galactopoiesis during the first 24-48 h of lactation. Galactopoiesis is the phase following lactogenesis and is characterized by abundant milk secretion which is being sustained by the suckling stimulus (Farmer *et al.*, 2006).

Colostrum is mainly produced during lactogenesis I and this mainly occurs before farrowing. Starting from d 85 of gestation, an increase in the ratio RNA/DNA, which indicates active protein synthesis by the lactocytes, and an accumulation of proteins and lipid drops in the lactocytes were observed (Kensinger *et al.*, 1982; Kensinger *et al.*, 1986b). Another indication for the active production of colostrum constituents from d 85 of gestation is the presence of β-lactoglobulin in the serum of the sow (Lee *et al.*, 1993; Dodd *et al.*, 1994). Nonetheless, the secretory activity of the lactocytes remains rather low until the last days before farrowing which is indicated by the raise of β-lactoglobulin and the appearance of α-lactalbumin and lactose in the plasma of the sow (Devillers *et al.*, 2006).

3.1. Hormonal control

The peripartal period is characterized by major alterations in prolactin, progesterone, estrogen, relaxin, cortisol, and prostaglandin F2α. An optimal organization of these hormonal

changes is needed to assure copious lactation (DeHoff *et al.*, 1986; Farmer and Quesnel, 2009). These hormones can regulate colostrum production in 3 ways. First, gestational mammogenesis is under hormonal control. Second, they control the delivery and synthesis of different colostral constitution. Third, hormones play a role in the closure of the mammary gland barrier.

3.1.1. Importance for mammogenesis

This was extensively discussed elsewhere in this thesis (capital 1.3.1. of the general introduction).

3.1.2. Importance for the delivery and synthesis of colostral constituents

Prolactin is the most important hormone for establishing successful lactogenesis. Administering bromocriptine, an inhibitor of prolactin synthesis, at the end of gestation suppressed lactation (Whitacre and Trelfall, 1981; Taverne *et al.*, 1982; Farmer *et al.*, 1998). Sows with impaired lactation had lower serum concentrations of prolactin (Trelfall *et al.*, 1974) which could be countered by administration of prolactin (Dusza *et al.*, 1991) but administering prolactin to sows without impaired lactation did not increase milk production (Farmer *et al.*, 1999). It seems that a cut-off concentration of prolactin needs to be reached above which extra prolactin has no additional benefit. Prolactin stimulates protein synthesis in the mammary gland by increasing transcription of α-lactalbumin and caseins (Rosen *et al.*, 1999; Houdebine, 2000; Tucker, 2000), by increasing uptake of AA by the mammary gland (Farmer *et al.*, 2008), by stimulating the transport of secretory vesicles towards the apical membrane of the alveocyt and stimulating exocytosis of caseins (Truchet and Ollivier-Bousquet, 2009), and by increasing the half-life of mRNA coding for proteins *in vitro* (Guyette *et al.*, 1979). Prolactin also stimulated *de novo* synthesis of lipids in porcine

mammary gland *in vitro* (Plaut *et al.*, 1989). Foisnet *et al.* (2010a) observed lower colostral lactose concentration in sows with a delayed increase in prolactin and a delayed decrease in progesterone.

Progesterone is detrimental for lactogenesis and a strong decrease at the end of gestation is an important and strong trigger to initiate lactogenesis. Plasma progesterone concentrations were negatively correlated with CY and colostral lactose content (Martin *et al.*, 1978; Willcox *et al.*, 1983; Devillers *et al.*, 2004a) and administering progesterone to the sow at the end of gestation slows down the increase in lactose content of colostrum (Gooneratne *et al.*, 1979; Whitely *et al.*, 1990). Piglets born to sows with a higher plasma progesterone level after farrowing have a lower weight gain the first 3 days of lactation compared to sows with lower progesterone concentrations (de Passillé *et al.*, 1993). Progesterone reduces the numbers of mammary prolactin receptors in rabbits and rodents (Nishikawa *et al.*, 1994; Mizoguchi *et al.*, 1996), reduces the production of prolactin in the rat (Pétridou *et al.*, 2001), competes with cortisol for binding onto the glucocorticoid receptor, diminishing the positive effects of cortisol on lactogenesis in cows (Collier and Tucker, 1978), and suppresses the transcription of proteins in the genome of the alveocyt of the mouse (Buser *et al.*, 2007).

Estrogen increases the number of mammary prolactin and oxytocin receptors in the rat (Tucker, 1981; Delouis *et al.*, 1980) and glucocorticoids increase and potentiate prolactin receptors in the mammary gland of the cow (Delouis *et al.*, 1980; Tucker, 1981; Houdebine *et al.*, 1985). The increase in plasma estrogen concentrations at the end of gestation were concomitant to the appearance of mRNA coding for β-lactoglobulin in sows (Lee *et al.*, 1993). A positive correlation was found between the plasma concentration of cortisol at farrowing and the colostral lactose concentration (Willcox *et al.*, 1983) but this was not confirmed by other studies (Martin *et al.*, 1978; Whitely *et al.*, 1990).

Relaxin partially controls the secretion of prolactin in sows (Li *et al.*, 1991; Li *et al.*, 1993). It increases basal concentrations of oxytocin in the rat (Parry *et al.*, 1994; Summerlee *et al.*, 1998) but the effect of relaxin on oxytocin in the sow seems absent, probably because concentration of oxytocin is constantly high in sows at farrowing (Lewis and Hurnik, 1985; Devillers *et al.*, 2006).

Oxytocin results in milk ejection by stimulating contraction of the myo-epithelial cells and might stimulate secretory activity of lactocytes (Ollivier-Bousquet and Devinoy, 2005) but the mechanism remains unclear.

Insulin stimulates the transcription of proteins in the mammary gland of the mouse by itself (Menzies *et al.*, 2009) or in combination with prolactin where their effect is synergetic (Choi *et al.*, 2004). In the sow, little is known about the effect of insulin on the synthetic activity of the mammary alveocyt but insulin, next to prolactin and cortisol, is necessary to induce lactogenic effects in porcine mammary tissue *in vitro* (Jerry *et al.*, 1989).

3.1.3. Importance for the closure of the mammary gland barrier

Leaky tight junctions between the mammary lactocytes are characteristic for the period of colostrum production. The closure of these tight junctions, also called the mammary gland barrier, indicates the transition from colostrum to milk production (Neville *et al.*, 2001) and it prevents the loss of milk components from the lumen of the mammary gland into the blood circulation of the sow (Itoh and Bissell, 2003). The leaky mammary epithelium is present at the end of gestation but not during lactation (Linzell and Peaker, 1974; Pitelka *et al.*, 1973). The concentration of lacteal components secreted by the alveocyt such as β-lactoglobulin, α-lactalbumin and lactose in the sow's plasma is high before farrowing but drops sharply during the first 24-48 h after farrowing which indicates the closure of the mammary gland barrier (Dodd *et al.*, 1994; Devillers *et al.*, 2006). This is also supported by the changes in

concentrations of IgG in the sow's plasma and colostrum (Huang *et al.*, 1992). This is shown in **Figure 6**. Nonetheless, still much remains unclear considering the regulating mechanisms of the closure of the mammary gland barrier in the sow.

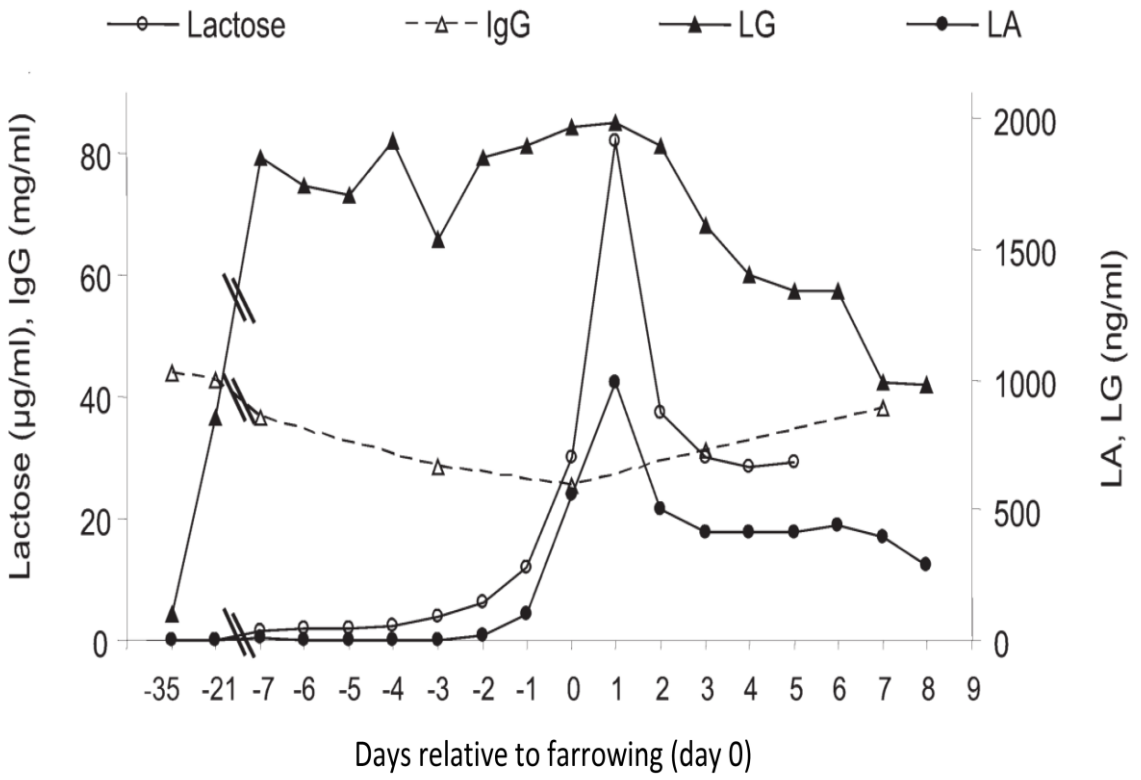

Figure 6. *Concentration of lactose, IgG, β-lactoglobulin (LG) and α-lactalbumin (LA) in the sow's plasma around farrowing. (after Hartmann et al., 1984; Dodd et al., 1994; Huang et al., 1994, Devillers et al., 2006).*

Hormonal control is important. Preventing the production of prolactin in mice and rat *in vivo* resulted in a reduced closure of the mammary gland barrier (Flint and Gardner, 1994; Nguyen *et al.*, 2001) and prolactin promoted tight junctions *in vitro* by increasing production of occludines (Stelwagen *et al.*, 1999). In sows, the concentration of prolactin was negatively correlated with colostral IgG concentrations (Devillers *et al.*, 2004a), which could indicate a reduced paracellular transport of IgG due to closure of the mammary gland barrier (explained in detail in capital 3.2. of the general introduction). Blocking the production of progesterone in mice at the end of gestation accelerated the formation of tight junctions in the mammary

gland *in vivo* (Nguyen and Neville, 1998). Recently, this promoting effect of prolactin and prohibiting effect of progesterone on the formation of tight junctions in the mammary gland was shown in sows (Foisnet *et al.*, 2010a). Indeed, sows with a low CY had a slower increase in plasma prolactin and slower decrease in plasma progesterone and this was accompanied by a leaky mammary epithelium which was indicated by a higher Na:K ratio in colostrum. This is presented in **Figure 7**.

On the other hand, administering altrenogest, a progesterone-like product, at the end of lactation did not prevent closure of the mammary gland barrier. In fact, sows treated until d 113 of gestation had a better closure of the mammary gland at farrowing which was hypothesized to be due to affinity differences between progesterone receptors for altrenogest and endogenous progesterone (Foisnet *et al.*, 2010b). Preventing the production of maternal cortisol prohibited closure of the mammary gland barrier which could be neutralized by administering dexamethasone (Nguyen *et al.*, 2001) and administering hydrocortisone to 1 side of the udder of goats, resulted in more tight junctions in the treated side (Thompson, 1996). Cortisol increases the expression of proteins that are important for tight junctions' formation (Balda and Mater, 2009) and is counteracted by progesterone, probably because of competition for the receptor (Ganguley *et al.*, 1982). Supraphysiological levels of oxytocin negatively affected the tight junctions in the rabbit and the cow (Linzell *et al.*, 1975; Allen, 1990), probably because the contraction of the myo-epithelial cells interferes with the structure of the mammary epithelium but it would also reduce expression of proteins important for the tight junctions (Werner-Misof *et al.*, 2007). Farrowing induction at d 113 of gestation did not alter hormonal profiles around farrowing and as such had no effect on closure of the mammary gland barrier (Foisnet *et al.*, 2011) but gestation length did not differ from sows naturally farrowing in this study.

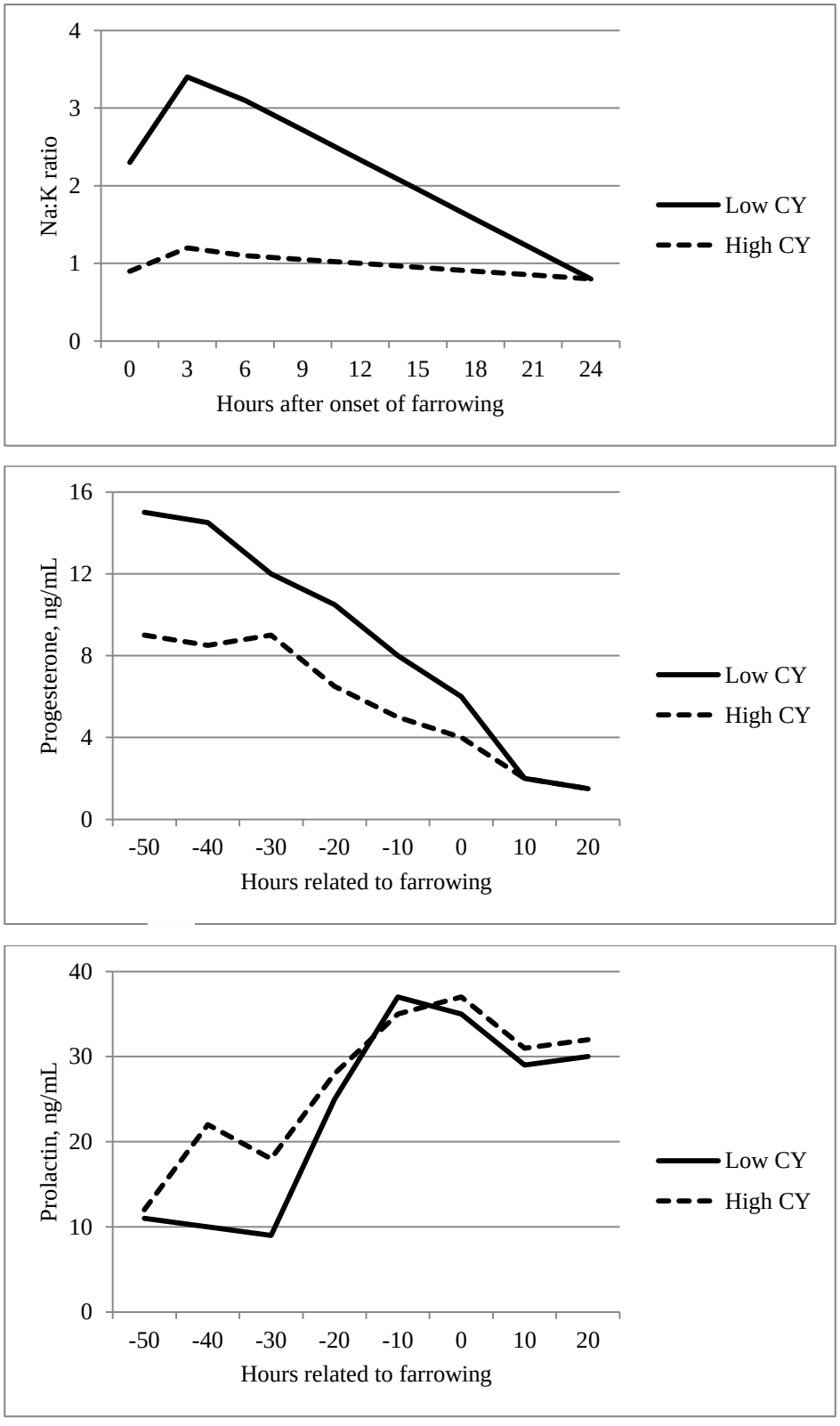

Figure 7. *Plasma concentrations of Na:K ratio, progesterone and prolactin in sows with low (< 1.4kg) and high (>2.8kg) CY around farrowing (after Foisnet et al., 2010a).*

3.2. Transportation of nutrients in the mammary gland

The colostral components are transported to the alveolar lumen by 4 different routes. They are presented in **Figure 8**.

3.2.1. Exocytosis

Proteins and lactose are produced via the endoplasmatic reticulum and the Golgi-apparatus and transported in vesicles towards the apical membrane of the alveocyt where the content of the vesicle is secreted while the vesicle membrane fuses with the apical membrane of the alveocyt. These vesicles also contain electrolytes (Na^+, K^+, Cl^-, Ca^{2+}) and citrate (Shennan and Peaker, 2000; Devillers *et al.*, 2006).

3.2.2. Secretion of lipid drops

Lipid drops inside the lactocyte merge and migrate to the apical membrane and are surrounded by membrane of the alveocyt during and after secretion (Keenan, 2001). These lipid drops also contain lipid soluble hormones, vitamins, leptin, and some growth factors (Shennan and Peaker, 2000).

3.2.3. Transcellular transport

Some components are surrounded by membrane of the alveocyt when they enter the alveocyt at the basal side and then they are transported in these vesicles towards the apical membrane of the alveocyt where the content of the vesicle is secreted while the vesicle membrane fuses with the apical membrane of the alveocyt. Various organelles are involved and sometimes this route is combined with exocytosis (Shennan and Peaker, 2000). Immunoglobulins, growth factors and several hormones are transported this way (Devillers *et al.*, 2006).

3.2.4. Paracellular transport

Paracellular transport includes transport between cells via leaky tight junctions which is characteristic for the period of colostrum production. It is observed for immune cells, Ig and electrolytes (Shennan and Peaker, 2000; Devillers *et al.*, 2006).

3.2.5. Transport of immunoglobulins

A drop in the plasma concentration of IgG accompanied by an increase in the colostral concentration of IgG was observed before closure of the mammary gland barrier while the inverse changes were observed after closure of the mammary gland barrier (Huang *et al.*, 1992). This indicates paracellular transport of Ig in the mammary gland. Nonetheless, colostral concentrations of Ig were several folds higher than serum concentrations (Porter, 1969; Devillers *et al.*, 2004a; Voisin *et al.*, 2006; Foisnet *et al.*, 2010a). Huang *et al.* (1992) showed that the difference in IgG concentrations between colostrum and serum differed between IgG subtypes. These observations indicate that transport of Ig is not just via the passive paracellular way but a major part originates from selective and active transport. In accordance to other mammals, Schnulle and Hurley (2003) showed the presence in sows of the neonatal Fc-receptor which is believed to be responsible for massive transcellular transport of Ig in the mammary gland, in accordance to observations in cattle (Kemler et al., 1975).

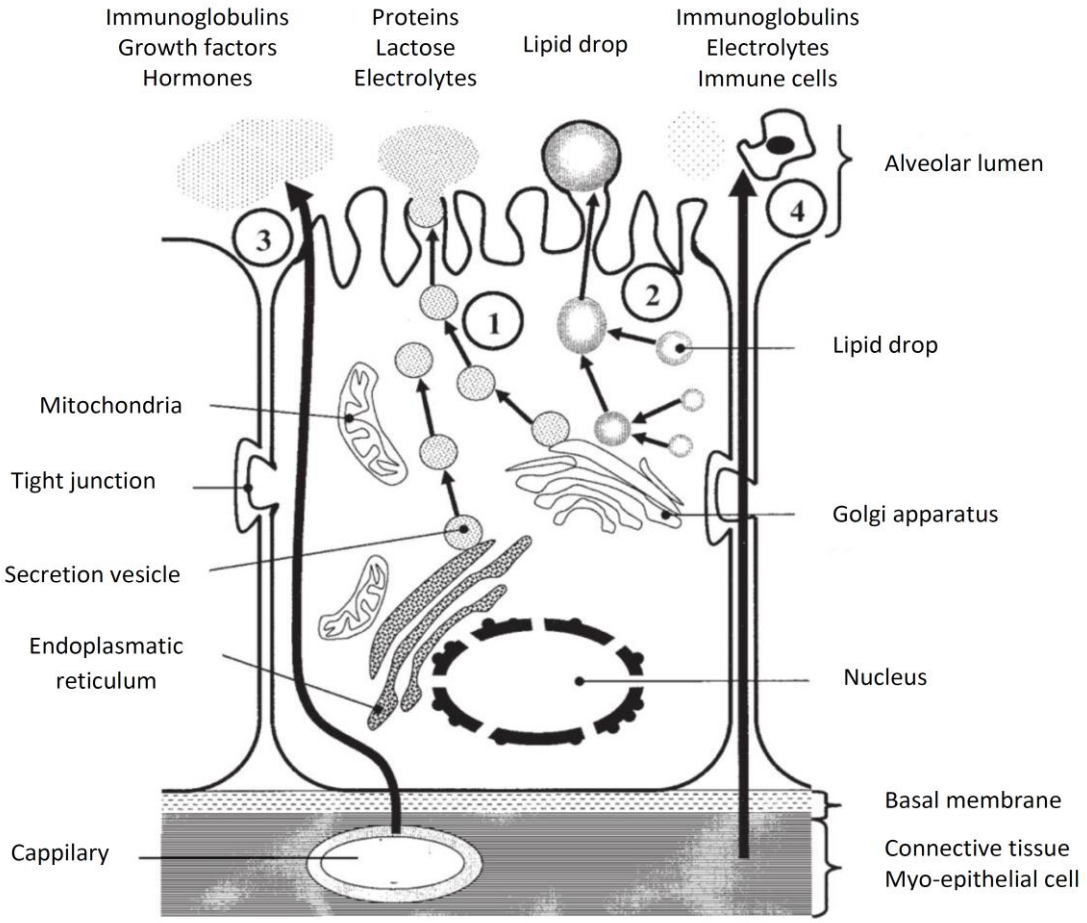

Figure 8. *Schematic overview of the 4 different transport routes of nutrients in the mammary gland. 1: exocytosis, 2: secretion of lipid drops, 3: transcellular transport, 4: paracellular transport (after Devillers et al., 2006).*

3.3. Uptake of nutrients by the mammary gland

The uptake of nutrients by the mammary gland is mainly based on studies measuring the difference of the arterial input and the venous output of nutrients in the mammary gland (Trottier *et al.*, 1997; Nielsen *et al.*, 2002a; Hurley *et al.*, 1996). It is important to realize that not all nutrients taken up by the mammary gland are used for the synthesis of milk components but also for mammogenesis and maintenance of the mammary gland. A simplified overview of the partition of absorbed glucose, fat and AA is shown in **Figure 9.**

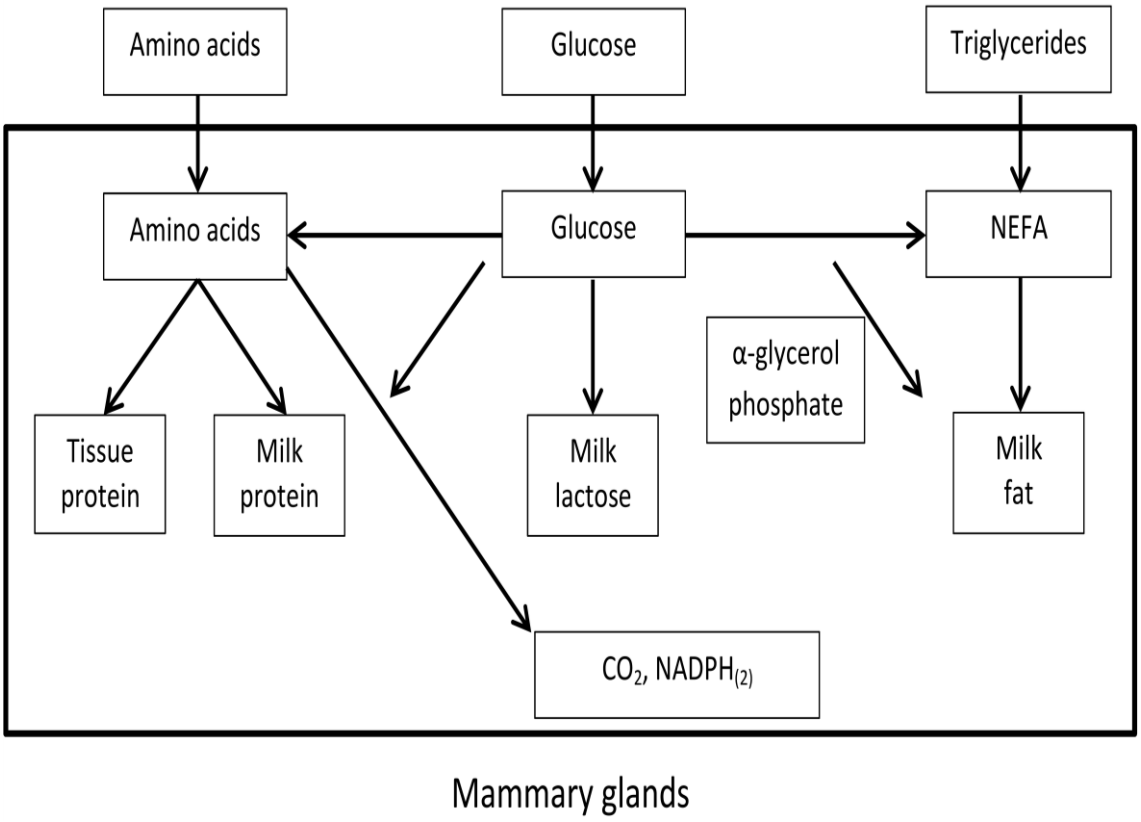

Figure 9. *Partitioning of glucose, TG and AA after uptake by the mammary gland for milk production. Probably, the same principles apply to colostrum production. Amino acids can be used to synthesize milk protein but also for mammary growth and energy source for the mammary gland. Glucose can be used for lactose synthesis, to deliver energy for synthesis of AA, via α-glycerol phosphate for de novo fatty acid synthesis, and as energy source for the mammary gland. Triglycerides are metabolized to NEFA and used for the synthesis of fat. (after Boyd and Kensinger, 1998).*

3.3.1. Glucose

The transport of glucose is facilitated by glucose transporters (**GLUT**). The GLUT-1 is the main transporter molecule in porcine mammary tissue. Therefore, uptake of glucose by the mammary gland is insulin independent. Indeed, insulin infusion does not enhance glucose use by the mammary gland (Reynolds and Rook, 1977; Holmes *et al.*, 1988). Uptake of glucose by the mammary gland is also independent of the arterial concentration of glucose (Dourmad *et al.*, 2000; Farmer *et al.*, 2008). The GLUT-1 gene is up regulated from 5 days before

farrowing to d 2 of lactation and even more until d 14 of lactation (Boyd and Kensinger, 1998). These data indicate that the glucose uptake is regulated by intra-mammary demand and it is also suggested that glucose uptake is affected by the presence of other blood nutrients (Farmer *et al.*, 2008). Insulin sensitivity in sows changes towards the end of gestation (Père *et al.*, 2000) which reorganises the distribution of glucose between different tissues.

The extraction rate of arterial glucose by the mammary gland is 20-30% (Spincer *et al.*, 1969; Linzell *et al.*, 1969; Trottier *et al.*, 1995; Dourmad *et al.*, 2000; Renaudeau *et al.*, 2003). Linzell *et al.* (1969) used labelled glucose carbon and estimated that 53% of glucose was used for lactose synthesis, 34% was oxidized to CO_2 and the remaining 13% was used for the synthesis of glycerol, fatty acids or AA. The proportion of glucose used for lactose synthesis may, however, vary (Farmer *et al.*, 2008).

3.3.2. Lipids

The main precursors for colostral lipids are circulating TG (Linzell *et al.*, 1969; Spincer *et al.*, 1969; Dourmad *et al.*, 2000). Lipoprotein lipase present in the capillaries of the mammary gland liberates the fatty acids which are then transported as non-esterified fatty acids (**NEFA**) (Barry *et al.*, 1963).

The extraction rate of arterial TG is 16-23% (Boyd and Kensinger, 1998). According to Boyd and Kensinger (1998), approximately 50% of fatty acids in milk are taken up from the blood while the remaining 50% originate from *de novo* synthesis.

3.3.3. Amino acids

There are 5 AA transporters present in the mammary gland (Baumrucker, 1985) but also blood peptides could be absorbed by the mammary gland and serve as a source of AA (Bequette and Backwell, 1997). Cysteine can be derived from mechanism involving glutamyl

transpeptidase, glutathione and red blood cells (Baumrucker, 1985). Competition of AA for the AA transporters might affect the uptake by the mammary gland as shown for valine (Jackson *et al.*, 2000) and lysine (Hurley *et al.*, 2000).

The extraction rate of arterial AA is 20-40% (Boyd and Kensinger, 1998). The AA uptake exceeds the amount secreted for all essential AA (Trottier *et al.*, 1997). This indicates that AA are not only used for colostrum and milk components but also for other processes within the mammary gland such as mammogenesis, synthesis of non-essential AA, synthesis of functional proteins and energy source for the production of lactose and fatty acids, but probably not for gluconeogenesis (Boyd and Kensinger, 1998). Especially considering the branched-chain AA and arginine, the ratio to lysine for mammary uptake is higher compared to the ratio to lysine in milk composition (Boyd and Kensinger, 1998).

3.3.4. Vitamins and minerals

The extraction of arterial calcium and phosphorus was 4% and 3% respectively but there was relatively low or no uptake observed for riboflavin, vitamin B12 or folic acid (Dourmad *et al.*, 2000; Nielsen *et al.*, 2002b).

4. FUNCTIONS OF COLOSTRUM

Based on the complex composition of colostrum, many functions can be ascribed to colostrum. Colostrum mainly serves as a source of energy and maternal immunity and it also stimulates gastrointestinal development in the piglets.

4.1. Energy resource

4.1.1. Piglets' energy requirements

A newborn piglet uses energy for maintenance, physical activity, thermoregulation, and weight gain. Under thermoneutral conditions and when physical activity is limited (bottle-feeding), the energy requirement for maintenance during the first 24 h after birth is 275 kJ/kg birth weight (**BW_B**). Under field conditions, we should add the requirement for thermoregulation (2 kJ/kg BW_B/h/°C), a minimum of 105 kJ/kg BW_B for physical activity, and 300 kJ/kg BW_B to achieve a weight gain of 70 g/kg BW_B (Le Dividich *et al.*, 1994; Le Dividich *et al.*, 2005a). The thermoneutral temperature of piglets is 32-34 °C but the room temperature at farrowing ranges between 20-25 °C (Berthon *et al.*, 1994; Vanderhaeghe *et al.*, 2010). With a room temperature of 25 °C, we can estimate that piglets need approximately 700 kJ/kg BW_B during the first 24 h of life without achieving weight gain and approximately 1000kJ/kg BW_B to achieve moderate weight gain.

4.1.2. Piglet's energy resources: body reserves and colostrum

Piglets' energy reserves at birth are stored in body glycogen, fat and protein. The glycogen reserve at birth is approximately 30-38 g/kg BW_B. Liver glycogen is used to maintain the glucose balance and muscle glycogen is used for shivering and physical activity (Herpin *et al.*, 2002). Under conventional conditions, approximately 75% of liver glycogen and 40% of muscle glycogen are spent 12 h postpartum under conventional conditions (Elliot and Lodge,

1977). The fat reserve at birth is approximately 10-20g/kg BW_B, most of it being structural fat (Herpin *et al.*, 2002). Brown adipose tissue is lacking (Trayhurn *et al.*, 1989). The use of body protein reserves for thermoregulation is very low in neonatal pigs (Le Dividich *et al.*, 1994). The body glycogen and fat reserves at birth can provide about 420 kJ/kg BW_B which is not even half of what is needed. Attempts to increase the body energy reserves of piglets at birth via the feed of the sow were unsuccessful. Indeed, increasing sow's blood concentrations of glucose, free fatty acids and gluconeogenic substrates via the sow's diet or fasting did not increase glycogen and lipid reserves of the neonatal piglet (Anderson and Wahlstrom, 1970; Ruwe *et al.*, 1991; Père, 2003; Metges *et al.*, 2012). Feeding a fat-rich diet to the sow improved the neonatal piglet's ability to metabolize fat and use ketogenic substrates (Coffey *et al.*, 1982; Kasser *et al.*, 1982; Ruwe *et al.*, 1991; Corson *et al.*, 2008) but did not increase triacylglycerol and glycogen storage in the neonatal pig (Campion *et al.*, 1984). Also, genetic selection for leaner carcasses has resulted in leaner pigs at birth (Herpin *et al.* 1993) with lighter livers and less liver glycogen (Canario *et al.*, 2007). The difference between available energy reserves and energy requirements during the first 24 h are presented in **Figure 10**.

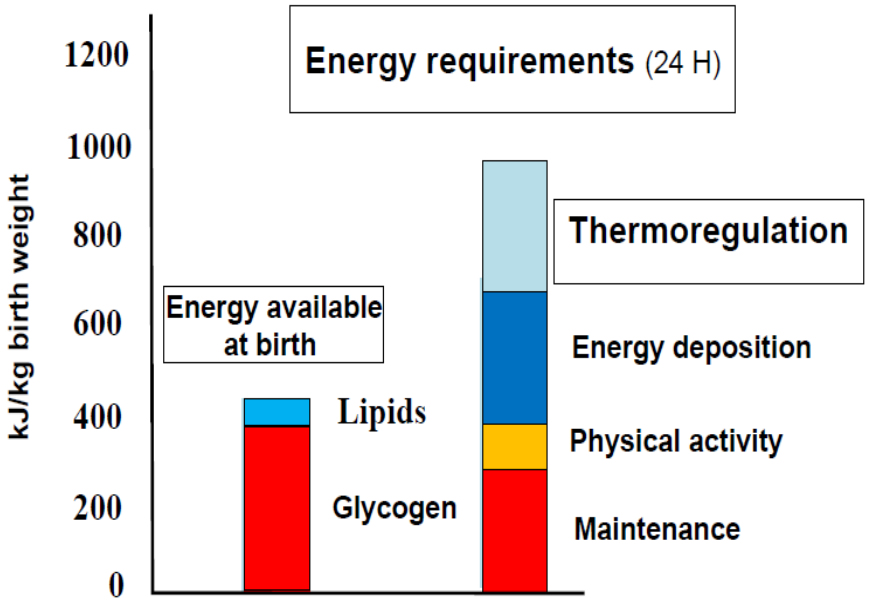

Figure 10. *The available energy reserves hardly cover half of the energy requirements during the first 24 h after birth in piglets (after Le Dividich et al., 2005a).*

The significant gap between the energy requirements (1000 kJ/kg BW_B) and the energy reserves (420 kJ/kg BW_B) needs to be eliminated by the intake of colostrum. Colostral lactose is an important energy source as it is hydrolysed to glucose and galactose, the latter being an important precursor of hepatic gluconeogenesis (Duée *et al.*, 1986). Lipids, however, are the most important energy source of colostrum representing 35% of colostral energy at onset of farrowing and 50% after 24 h (Huo et al, 2003). As discussed before, the fat content of colostrum can be altered via the feed of the sow but it is the ratio protein/fat that determines body weight gain. When the colostral fat content increases without a concomitant increase in protein, piglets will deposit more fat tissue but this will not result in a higher weight gain (Le Dividich *et al.*, 1997). The piglet, however, has remarkable capacities to deposit fat soon after birth as under experimental conditions, the fat content of the piglet can increase with 25-100% during the first day of lactation. The piglet also has remarkable capacities to consume fat as, under experimental conditions, increasing colostral fat content to 10.0% did not reduce voluntary colostrum intake (**CI**) (Le Dividich *et al.*, 1997).

Colostrum intake is positively correlated with heat production, maintaining the rectal temperature, and plasma glucose concentration in neonatal piglets (Noblet and Le Dividich, 1981; Devillers *et al.*, 2011). This is important as hypothermia and hypoglycemia are major causes of pre-weaning mortality, in most cases as underlying cause of crushing (Edwards, 2002; Farmer *et al.*, 2006). Indeed, 50% of pre-weaning mortality occurs during the first 3 days of lactation (Tuchscherer *et al.*, 2000) and insufficient CI has been identified as 1 of the major causes of neonatal mortality (de Passillé and Rushen, 1989a; Edwards *et al.*, 2002; Milligan *et al.*, 2002) but also of mortality during the entire lactation period (Devillers *et al.*, 2011). This is presented in **Figure 11**. Most piglets not suckling within 2 h after birth die (Bünger *et al.*, 1984), piglets dying within the first 3 days mostly lost body weight indicating no or low colostrum and milk intake (Devillers *et al.*, 2004b), 72% of piglets dying within the

first 4 days of lactation have not consumed any colostrum (Damm *et al.*, 2005), and there is a significant difference in mortality rate between piglets that consumed less or more than 200 g colostrum (> 50% vs.; < 10%) (Quesnel *et al.*, 2011).

For each gram weight gain, a piglet needs approximately 2.5 g of colostrum or 4.5 g of milk. Colostral energy and nitrogen are used very efficiently after absorption, with a value of 89% for the conversion of absorbed into retained nitrogen, and 91% for the utilization of metabolisable energy (Le Dividich *et al.*, 1994; Le Dividich *et al.*, 1997). More importantly, CI during the first 24 h of lactation affects daily weight gain up to 6 weeks of age. Piglets consuming less than 290 g of colostrum weighed on average 10.5 kg at 42 days of age whereas piglets consuming more than 290 g of colostrum weighed on average 12.3 kg (Devillers *et al.*, 2011). This is presented in **Figure 12**.

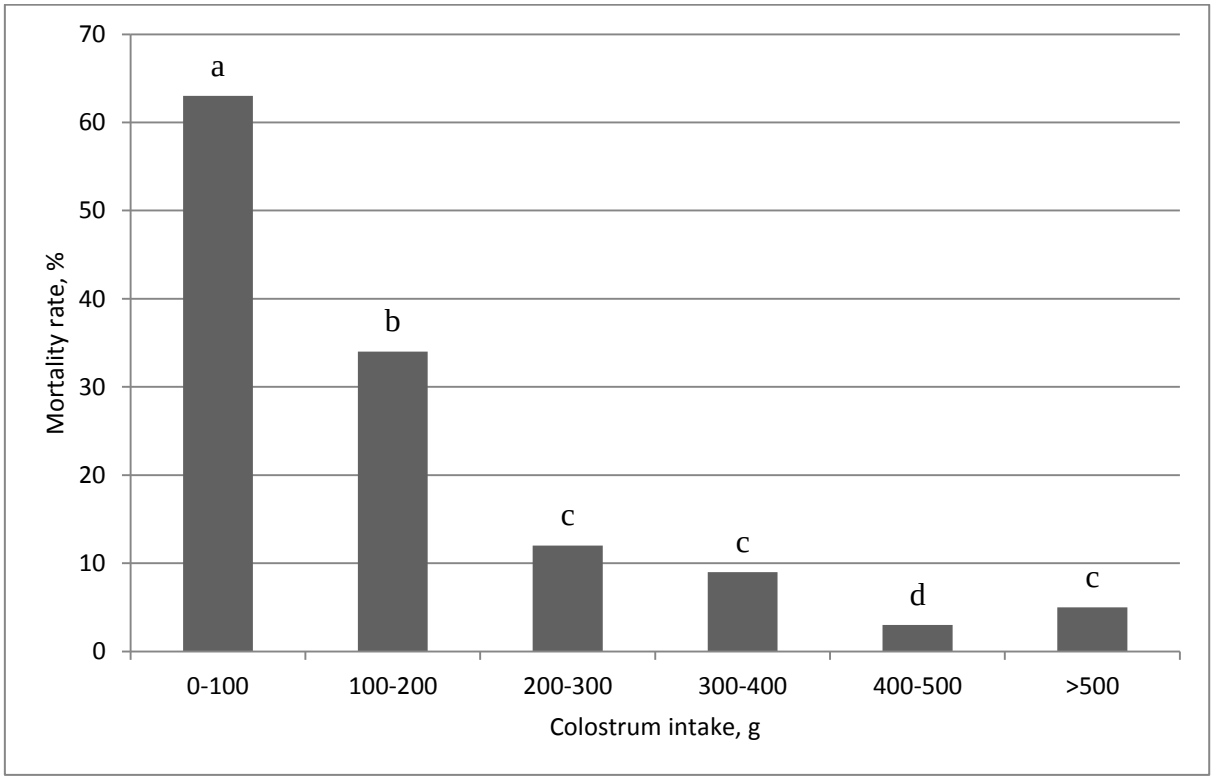

Figure 11. *Effect of CI on pre-weaning mortality rate (after Quesnel et al., 2012).*

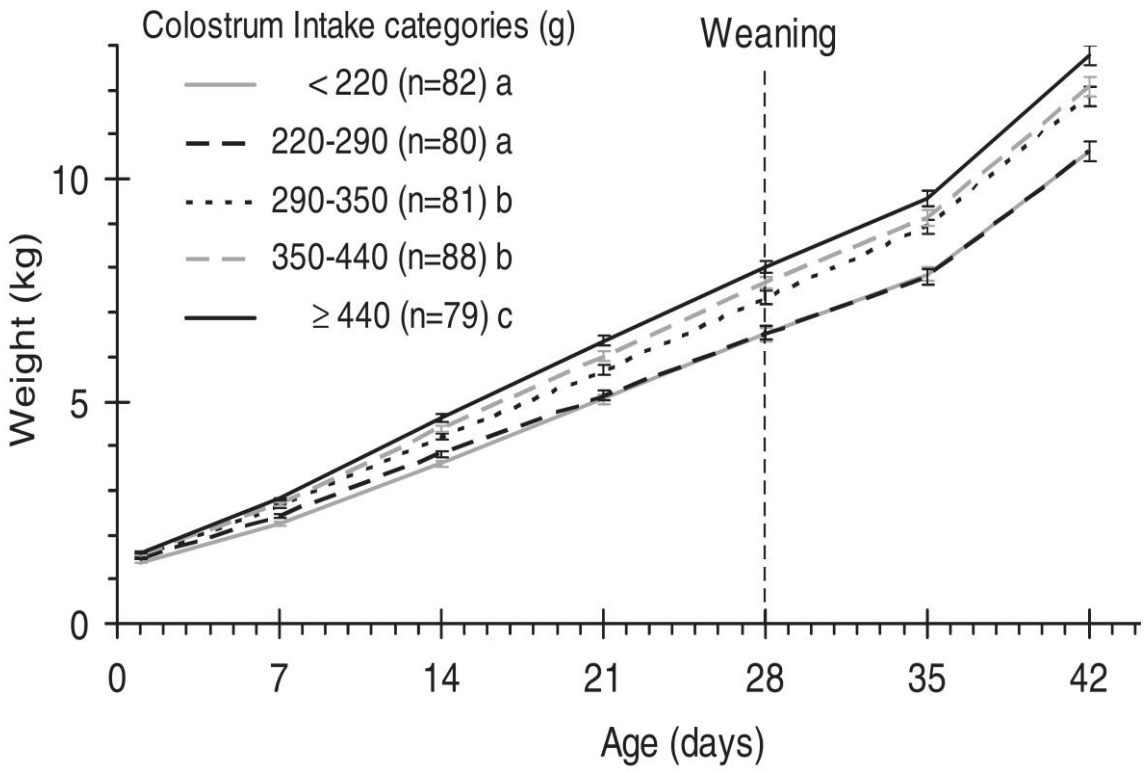

Figure 12. *Amount of CI during the first 24 h of lactation affects weight gain in piglets at least until 6 weeks of age (after Devillers et al., 2011).*

4.2. Resource of immunity

4.2.1. Piglets' immune system at birth

Most components of the immune system are present at birth in pigs but they are functionally underdeveloped. Neonatal piglets have T-cells in the lamina propria of the intestine but they are low in numbers and the response to mitogens is marginal, the number of antigen-presenting cells is low (Gaskins, 1998), blood mononuclear cells show a low response against a T-cell dependent antigen (Hammerbergh, 1989), and Ig-secreting cells in spleen and bone marrow are lower at 1 week of age compared to 4 weeks of age (Bianchi et al, 1999). The epitheliochorial placenta in pigs as well as in cattle and horses consists of 6 layers. It separates the blood tract from sow and fetus, and is almost impermeable for Ig. Small amounts of Ig might pass the placental barrier (Diponkor *et al.*, 2014) and this could probably be due to the

presence of the FcRn receptor in placental tissues (Butler *et al.*, 2002). The fetal piglet is able to synthesize *de novo* antibodies after contact with an antigen or mitogen from d 70-80 of gestation onwards (Redman, 1978; Tlaskalova-Hogenova *et al.*, 1994, Cukrowska *et al.*, 1996). Nonetheless, the Ig concentration that can be achieved before birth is approximately 1000-fold lower than in suckling piglets (Le Dividich *et al.*, 2005a), the IgG concentration does not increase until 6 days after birth in colostrum-deprived piglets (Klobasa *et al.*, 1981; Drew and Owens, 1988), and the immune response of piglets remains immature until approximately 4 weeks of age (Hammerbergh, 1989; Bianchi *et al.*, 1999). Dogs have an endotheliochorial placenta in which the endothelium of the bitch is in direct contact with the chorion of the fetal membranes and this allows limited passage of IgG before parturition. Nonetheless, the majority of IgG transfer also occurs via colostrum intake (Snoeck et al., 2006).

4.2.2. Acquisition of maternal passive immunity

Neonates are continuously exposed to microbes, a part of them being pathogens. They depend completely on CI for immunological protection as it provides the piglet with maternal, passive immunity consisting of Ig, immunological cells, and bioactive peptides.

Absorption of intact cells in the blood of the neonatal piglet is only possible for colostral lymphocytes from the piglet's own mother (Tuboly *et al.*, 1988) and this mainly occurs in the duodenum (Williams, 1993; Le Jan *et al.*, 1996). The compartment-specific adhesion molecules on the lymphocytes have yet to be determined (Salmon *et al.*, 2009). Colostral lymphocytes could be identified in piglet's liver, lung, lymph nodes, spleen, and gastrointestinal tissues 24 h after first CI (Williams, 1993). They exert an immunostimulating effect on piglet immune response to non-specific mitogen (Williams, 1993), play a direct role in the active immunity response (Cepica and Derbyshire, 1984; Bianchi *et al.*, 1999; Bandrick

et al., 2008) and stimulate the cell-mediated immunity of the young pig (Wagstrom *et al.*, 2000). These positive effects of passive cellular maternal immunity has been studied more into detail in cattle (Riedel-Caspari, 1993; Reber et al., 2008a, b). Feeding sows a diet with reduced levels of vitamin E and selenium (0.29 mg vitamin E/kg feed, 0.089 mg selenium/kg feed) during gestation leads to reduced mitogenic responses of colostral lymphocytes and reduced phagocytic and microbicidal activity of colostral polymorphonuclear cells compared to sows fed the same diet supplemented with 60 mg vitamin E/kg feed and 0.3 mg selenium / kg feed (Wuryastuti *et al.*, 1993), whereas supplementation with 250 mg oregano oil/kg feed compared to no supplementation during gestation had no effect on T-lymphocytes (Ariza-Nieto *et al.*, 2011). It is not clear whether milk lymphocytes can pass the neonatal intestinal epithelium and be transported to distant sites but at least factors produced by the lymphocytes might be transferred to the neonate (Salmon *et al.*, 1999).

Maternal, passive immunity can be divided into 2 major parts based on time during lactation. The first part is characterized by a transfer of intact Ig to the serum of the piglet and is situated during the colostral phase. IgA is not retained in the serum but is relocated to the mucosal surfaces, especially the respiratory tract (Bradley *et al.*, 1976a, b). Nonetheless, most of the IgA, and all of the secretory IgA, is not transferred to the serum but stays in the gut. After gut closure (explained in detail in capital 4.2.2.2. of the general introduction), there is no transfer of intact Ig from the gastrointestinal tract to the serum. This is the start of the second part of maternal immunity which lasts until the end of lactation. This is characterized by local immunity in the gut, IgA being the predominant actor. IgA adheres to pathogens and in the gut and prevents them from penetrating the mucus layer (Magnussen and Stjernstrom, 1982). It is important to realize that passive, maternal immunity only protects the piglets against pathogens for which the respective Ig are present in colostrum and milk, meaning that the sow should have been in previous contact with the antigen, by infection or vaccination.

The latter is widely practiced in livestock e.g. immunization of the cow, ewe or sow against enterotoxigenic *Escherichia coli* to protect the neonate via immunoglobulins in the colostrum and milk. This principle can also be used to create heterologuous immune milk in which colostrum or milk from one species (mostly cattle) is used to immunize other species (e.g. human, swine) (Hurley and Theil, 2011).

4.2.2.1. Immunoglobulins in the gut: hydrolysis or not?

Immunoglobulins are proteins and 3 factors protect these proteins from being hydrolysed in the gut of the neonatal piglet. First, not pepsin but chymosin is the most important protease in the stomach which results in clotting of the milk and as such protects the Ig (Sangild *et al.*, 2000). Second, the proteolytic activity in the gastrointestinal tract is low in neonatal piglets. Third, colostrum contains protease inhibitors (Zhou *et al.*, 2003). Removing (Carlsson *et al.*, 1980) or adding (Weström *et al.*, 1985) trypsin inhibitors to colostrum resulted in a decreased or increased IgG transfer to the serum of the piglet, respectively. These 3 factors are mainly present during the colostral phase. After this phase, the main Ig is secretory IgA (Klobasa *et al.*, 1987) which is protected against hydrolysis via the secretory component (Porter, 1973).

4.2.2.2. Gut closure

Immunoglobulins are rapidly taken up by the enterocytes by non-specific pinocytosis. They are localized in vesicles (Clarke and Hardy, 1971; Sangild *et al.*, 1997; Sangild *et al.*, 1999, Danielsen *et al.*, 2006) that form vacuoles and progress towards the basolateral membrane (Weström *et al.*, 1997). This feature is only present in fetal enterocytes, not in postnatally developed enterocytes (Smith and Jarvis, 1978; Smith and Peacock, 1980). Complete replacement of fetal enterocytes takes up to 19 days (Smith and Jarvis, 1978), but the transfer of Ig to the piglet's serum is only possible during the first 24 h of life (Speer *et al.*, 1957).

Therefore, the intact uptake of Ig is limited in time. This is not due to a decrease in uptake of Ig by the enterocytes but to cessation of transfer across the basolateral membrane: so called gut closure (Rooke and Bland, 2002; Le Dividich *et al.*, 2005a). Despite the presence of FcRn-receptors in the neonatal gut (Stirling *et al.*, 2005), absorption of Ig does not seem to occur selectively as similar ratios of IgG, IgA and IgM can be found in colostrum and serum of the piglet (Salmon *et al.*, 2009). On the other hand, the preferred absorption site of IgG is the villi while for IgA and IgM this is the crypts (Butler *et al.*, 1981). Selective absorption between whey proteins was shown (Carlsson *et al.*, 1980; Kiriyama, 1992; Harada *et al.*, 1999; Rooke and Bland, 2002).

Gut closure is not only induced by CI as fasting (Klobasa *et al.*, 1990) or feeding intravenously (Mehrazar *et al.*, 1993) delayed but did not prohibit gut closure. Several studies with fractionated colostrum showed that the intake of nutrients, rather than the intake of IgG, accelerates gut closure (Lecce *et al.*, 1966; Werhahn *et al.*, 1981, Bikker *et al.*, 2010). Gut closure is completed after 24 h when only 70 g of colostrum/kg BW_B / 24 h is ingested. This amount of colostrum is insufficient to meet the nutrient requirements and the obtained serum concentrations of IgG remain far below the maximal potential serum level of 26 mg/mL achieved when at least 110 g of colostrum/kg BW_B is ingested before gut closure (Le Dividich *et al.*, 2005b). This is presented in **Figure 13**.

The fact that gut closure is initiated by nutrient rather than IgG intake has implications for piglets that can only start suckling a few h after onset of farrowing e.g. last born piglets, hypoxic piglets, weak piglets failing to compete with litter mates, as colostral concentration of IgG declines rapidly (Klobasa and Butler, 1987). Indeed, 2 groups of piglets that were allowed the same amount of CI, 1 group immediately at onset of farrowing, the other after 8-12 h, showed differences in plasma IgG concentrations that resulted from differences in colostral IgG concentrations (Klobasa *et al.*, 1981; Bland *et al.*, 2000). Also, Le Dividich *et*

al. (2004) showed differences in plasma IgG concentrations between piglets born first or last within a litter.

Several hormones were proposed as regulators of gut closure. Administering insulin accelerates gut closure (Svendsen *et al.*, 1986) but the part directly derived from colostrum is marginal compared to the insulin produced by the piglet following nutrient intake (Burrin *et al.*, 1995). Serum IgG concentration of the piglet was positively correlated with maternal serum concentration of cortisol (Bate and Hacker, 1985), piglet serum concentrations of cortisol at birth (Sangild *et al.*, 1997), and negatively correlated with the use of metapyrone, an inhibitor of adrenal cortisol synthesis (Sangild *et al.*, 1993). Cortisol has a stimulatory effect on gut maturation (Sangild *et al.*, 2000), which indicates that the increased uptake of IgG with increased concentration of cortisol is due to enhanced efficiency of uptake rather than delayed gut closure (Rooke and Bland, 2002). Cold stress in sows before farrowing reduced IgG concentrations in serum of the piglet, probably by increasing maternal cortisol concentrations before farrowing leading to prepartum gut maturation and gut closure (Bate and Hacker, 1985). Also, bio-active factors present in sow colostrum but not (as much) in milk, plasma or bovine colostrum, may enhance Ig uptake (Jensen *et al.*, 2001). Supplementation of the sow's diet with vitamin A, C or E increases the absorption of IgG by the neonatal piglet probably because the vitamins enhanced the uptake efficiency as the intake of IgG via colostrum and the gut closure did not change (Rooke and Bland, 2002; Pinelli-Saavedra *et al.*, 2008). Cold stress of the piglet reduces plasma IgG concentrations, probably by a reduced CI (Le Dividich and Noblet, 1981; Milon *et al.*, 1983).

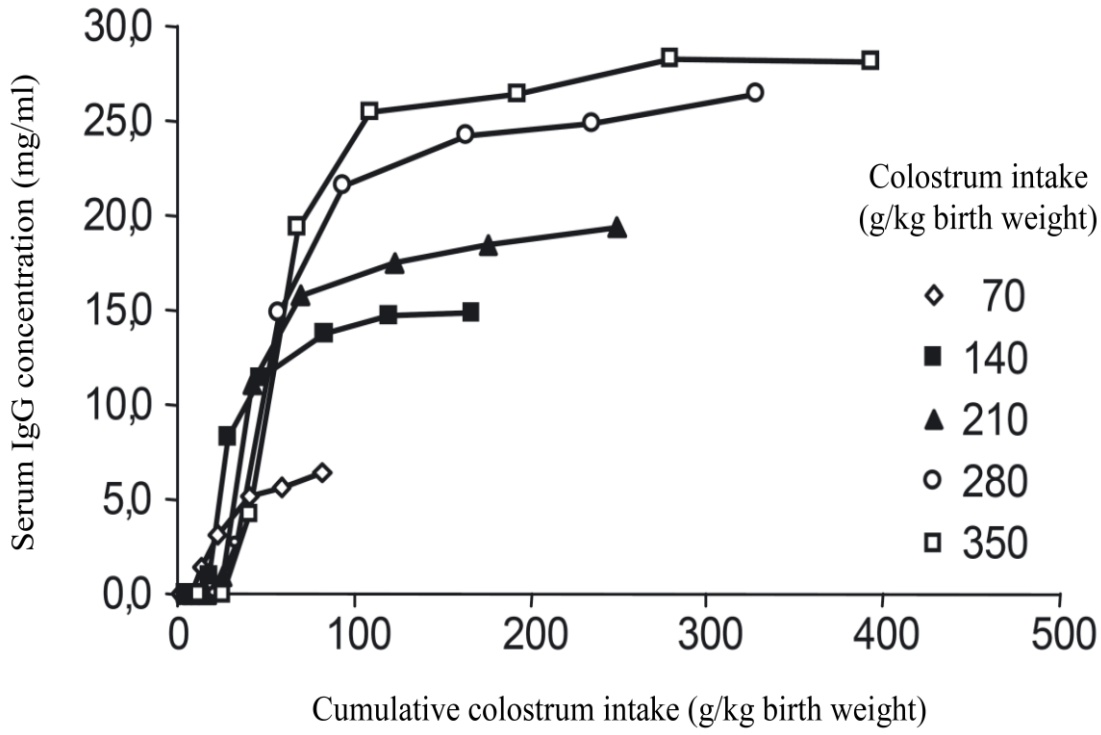

Figure 13. *Piglet serum concentration of IgG following different amounts of CI with known IgG concentration. Serum IgG concentration plateaus when a CI of approximately 110 g/kg* BW_B *was reached which is an indication for gut closure. Below 110 g, CI is linearly related to serum IgG concentration (after Le Dividich et al., 2005b).*

4.2.3. Effect of passive immunity on development of active immunity

The piglets' immune system is functionally immature at birth, mainly because contact with antigen is lacking during the fetal stage (Salmon *et al.*, 2009). The immune response of piglets is not fully matured until approximately 4 weeks of age (Hammerbergh *et al.*, 1989; Bianchi *et al.*, 1999) and in the meantime passive, maternal immunity should offer protection.

This passive, maternal immunity interferes with the contacts between antigens and the piglet's immune system and thus might interfere with the development of active immunity. Klobasa *et al.* (1981) and Drew and Owens (1988) showed that the higher the piglet's serum concentrations of IgG after CI, the longer it took before IgG levels reached a bottom

concentration and then increased again. Therefore, they concluded that maternal derived IgG delays the development of an active immunity because maternally derived IgG diminishes the amount of antigens available for active immune development (Silim *et al.,* 1990). However, the increase in piglet plasma volume during lactation was not taken into account in these studies. On the other hand, it is well known that maternally derived antibodies interfere with active immunity development after vaccination in piglets (Salmon *et al.,* 2009). It was already established that colostrum-deprived piglets started to synthesize IgG from 7 days of age (Klobasa *et al.,* 1981; Drew and Owens, 1988) but Rooke *et al.* (2003) showed that even in presence of maternal antibodies the piglets synthesize IgG as the amount of piglet's plasma IgG which was maternal derived represented less than 70% and less than 60% of total Ig in piglets serum at respectively d 14 and 21 of age. Also, positive curvilinear correlations were observed between levels of plasma IgG at d 7 of age and d 28 of age (Damm *et al.,* 2002; Rooke *et al.*, 2003), between d 2 and 26 of age (Le Dividich *et al.*, 2005b), and between d 2 and 25-31 days of age (Devillers *et al.,* 2011). This implies that a higher level of maternally derived IgG as indicated by levels of IgG up to d 7 of age stimulates active immune development as indicated by levels of IgG at d 28 of age. This is shown in **Figure 14**. It is also important to realize that maternally derived IgG secreting immune cells are present in 1-week old piglets (Bianchi *et al.,* 1999).

Sufficient intake of Ig is essential for the piglets' performance but it is stated that during lactation, sufficient intake of colostral energy is more determinant for survival (Le Dividich *et al.*, 2005a). Intake of Ig is more determinant for performance at weaning. Indeed, piglet performance after weaning is positively correlated with humoral immunity at weaning (Varley *et al.,* 1987; Edwards and Rooke, 1999), which is stimulated by intake of maternal derived IgG via colostrum (Damm *et al.*, 2002; Le Dividich *et al.*, 2005a; Rooke *et al.*, 2003).

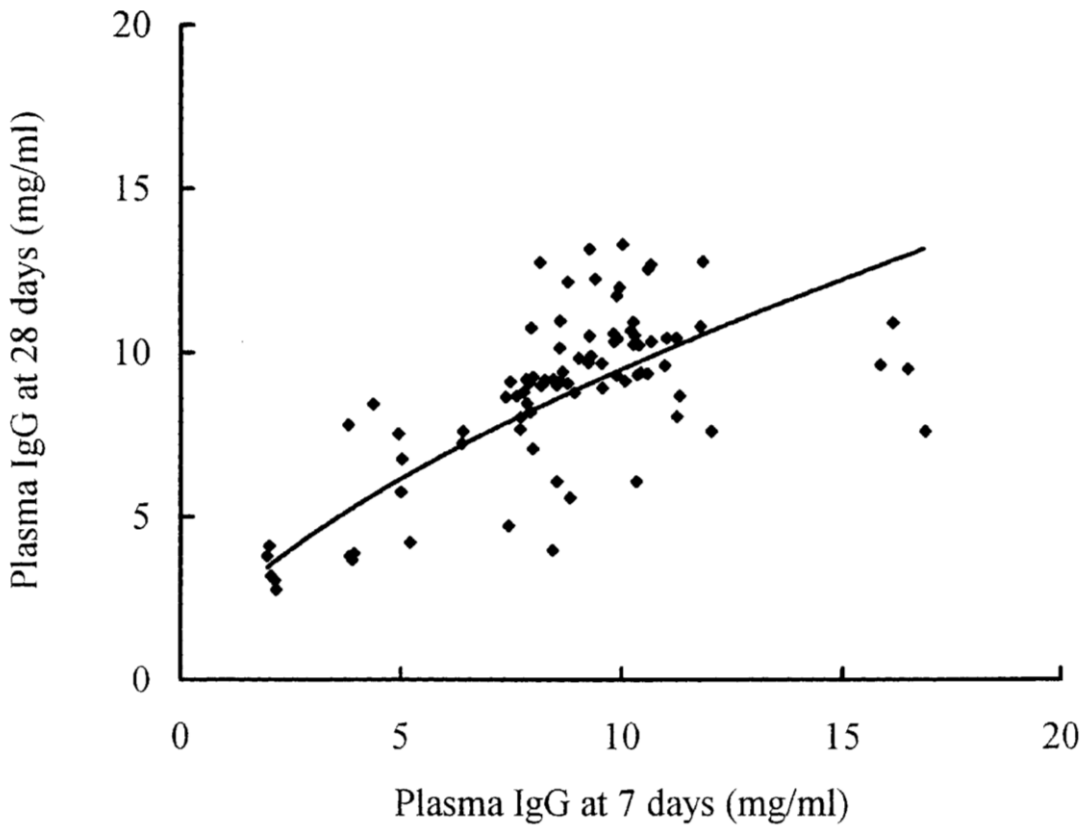

Figure 14. *Piglet plasma IgG concentration at d 7 of age is positively correlated with the plasma IgG concentration at d 28 of age. This indicates that passive, maternal immunity stimulates active immunity development (after Rooke and Bland, 2002).*

4.3. Gastrointestinal development

During the fetal life, piglets receive all nutrients from the maternal circulation via the placenta. At birth, the piglet has to adapt rapidly to oral feeding and digestion of nutrients absorbed via colostrum. During the first days of lactation, the piglet's gastrointestinal tract is characterized by dramatic tissue growth, functional maturation, and increase in various enzymes and brush-border enzymatic activity (Xu *et al.*, 2000). This is shown in **Table 1**. Colostrum intake plays a central role in this remarkable development. Indeed, these changes were not observed in piglets that were prevented from suckling (Widdowson *et al.*, 1976) or were lower in piglets only offered water or electrolyte solution (Burrin *et al.*, 1992; Burrin *et*

al., 1994; Zhang *et al.*, 1998). Thus, it is clear that colostrum has profound effects on gastrointestinal development. This is partially a direct result from the nutrients as they induce gut closure (explained in detail in capital 4.2.2.2. of the general introduction) but various types of growth factors have been identified in colostrum. The latter also play an important role in gastrointestinal development.

Colostrum also favors the development of other organs. Protein synthesis in the liver, spleen, skeletal muscle and brain was higher in piglets fed colostrum compared to piglets fed milk (Burrin *et al.*, 1992; Burrin *et al.*, 1997; Fiorotto *et al.*, 2000). Colostrum deficient in relaxin resulted in a reduced development of reproductive organs in sows and boars (Bartol *et al.*, 2008).

Table 1. *Overview of changes in small intestinal tissue weight, length, and diameter, microscopic features and enzymatic activity during the first days of lactation in neonatal piglets (after Xu et al., 2000).*

Parameter	**Birth**	**d 1**	**d 3**
Intestinal tissue weight, g	35.7	63.4	61.5
Intestinal tissue length, cm	343	426	443
Intestinal tissue diameter, mm	3.85	4.44	4.60
Crypt depth, µm	82	102	115
Villus height, µm	883	1171	1077
Lactase, µmol/min	257	800	-
Sucrase, µmol/min	100	314	-
Maltase, µmol/min	103	223	-
Aminopeptidase, µmol/min	137	251	-

5. MEASUREMENT OF COLOSTRUM YIELD

Several methods to measure CY in sows have been described, each of them with their benefits and disadvantages. Due to the anatomic structure of the mammary gland (no cistern, Farmer *et al.*, 2008) and the physiology of colostrum production (continuously, Illman *et al.*, 2003), it is not possible to milk the sows completely at farrowing to determine CY. Consequently, CY in sows is always measured indirectly through the piglets.

5.1. Isotope dilution method

This technique is based on the water turnover in the piglet corrected for the production of metabolic water (Pettigrew *et al.*, 1987; King *et al.*, 1993; Auldist *et al.*, 1998; Theil *et al.*, 2002). A marker (mostly deuterium oxide) is injected into the blood tract of the piglet before suckling. After a fasting period of 2 h, a blood sample is collected to set the basal value of the marker. The water intake via colostrum or milk dilutes the marker. A second blood sample is obtained when colostrum or milk intake is finished and by determining the dilution of the marker in the blood, the colostrum or milk intake can be calculated. This method is the most precise and considered as the golden standard. Disadvantages are the cost, the precision needed when injecting the isotope, and the precision needed when calculating the dilution. Also, an intravenous injection and 2 blood collections are needed which makes it very intensive (both for researcher and piglets) and only possible under experimental conditions and on small number of piglets.

5.2. Weigh-suckle-weigh method

Piglets are weighed just before and after suckling, the difference in weight representing the milk intake (Salmon-Legagneur, 1956; Lewis *et al.*, 1981; Klaver *et al.*, 1981; Speer and Cox, 1984; Theil *et al.*, 2002). This method seems quite straight forward but has some major

disadvantages. Piglets need to be isolated from the sow for some time, so that when they are allowed to nurse, all milk in the mammary gland is suckled. The imposed nursing bouts, in which the animals are disturbed, result in a 13% reduced milk intake by piglets compared to the isotope dilution technique (Theil *et al.*, 2002). The method is also labour intensive and less suitable for colostrum production as this is ejected continuously rather than in nursing bouts (Illman *et al.*, 2003).

5.3. Weight gain equation model

Devillers *et al.* (2004b) developed an equation model to estimate individual CI in piglets based on BW_B, weight at 24 h of age (BW_{24} spread allowed between 17-25 h), time between birth and first suckling (t_{FS}) and time between first suckling and second weighing (t). The equation model is as follows:

Colostrum intake (g) = $-217.4 + 0.217 \times t + 1861019 \times BW_{24}/t + BW_B \times (54.80 - 1861019/t) \times (0.9985 - 3.7 \times 10^{-4} \times t_{FS} + 6.1 \times 10^{-7} \times t^2_{FS})$

Validation of this method was against the isotope dilution method and bottle-fed piglets and an error of approximately 10% should be kept in mind. Theil *et al.* (2014) also built an equation model, validated against the isotope dilution method which resulted in another equation model. The equation model was as follows:

Colostrum intake (g) = $-106 + (2.26 \times (BW_{24} - BW_B)) + (200 \times BW_B) + (0.111 \times (t - 1414 \times (BW_{24} - BW_B)/t) + (0.0182 \times (BW_{24} - BW_B)/ BW_B)$.

The equation models are easy to apply and a large number of animals can be observed. On the other hand, the difference between both equations show that the experimental conditions should be comparable to the ones in which the model was established and the used model should always be taken into account when interpreting the results of a study. Also, although minimal, there is some manipulation of the piglets during the period of CI.

5.4. Other methods

As piglets are born agammaglobulinemic, an idea was that piglet serum IgG might be a measure for CI. There are reasons at sow and piglet level why this is not a good technique to estimate CI. At sow level, the IgG concentration in colostrum declines sharply after birth (Klobasa and Butler, 1987) and is highly variable between sows (Inoue at al., 1980; Klobasa and Butler, 1987; Rooke and Bland, 2002; Tuchscherer *et al.*, 2006; Quesnel, 2011). At piglet level, it was shown that the piglet serum IgG reaches a plateau when approximately 110 g colostrum/kg BW_B have been ingested, resulting in maximal serum IgG level of approximately 26 mg/mL (Le Dividich *et al.*, 2005b). This is a result of the gut closure being independent of IgG intake. Below this level, there was a linear correlation between piglet serum IgG concentration and CI (Le Dividich *et al.*, 2005b). Colostral IgG concentrations were well-known in this study, whereas this is not the case in practice. The large variation in sow colostral IgG concentration would result in different slopes of correlation for each sow. Also, 110 g colostrum/kg BW_B does not provide sufficient energy to the piglets for survival and serum IgG concentration is not only determined by the amount of IgG uptake but also by blood plasma volume (Rooke and Bland, 2002). As a result, the piglets' serum concentration of IgG cannot serve as an estimator for CI. Jourquin *et al.* (2010a) calculated the coefficient of variation of piglet serum IgG concentration (CV IgG) within litters of 3-day old piglets. The CV IgG and pre-weaning mortality increased with litter size and based on this, they concluded that CV IgG is a measure of the spread of CI within a litter. Mortality in litters with a CV IgG of less or more than 50% was respectively 5.1% and 7.7% (Jourquin *et al.*, 2010b).

Vallet *et al.* (2013) developed an inexpensive and easy method to indicate the transfer of passive immunity to the piglets: the immunocrit method. Especially for low birth piglets, there was some association with preweaning mortality. Whether the immunocrit method gives information on the piglets' individual CI was not established but according to the previous

paragraph, this does not seem likely. Papadopoulos *et al.* (2008) described that the ratio afternoon:morning of urinary levels of K, Na, and Ca were significant predictors of milk production (respectively R^2 0.72, 0.55, 0.42). As there was an important variation between individual sows, predictions could be done at group level, not at the individual sow level. Also, this correlation was only well-established during mid-lactation.

6. COLOSTRUM YIELD

6.1. Assessing the problem: insufficient colostrum yield

Studies on CI and yield in sows are scarce, probably because of the difficult measurements. All studies report large variations in sow CY and piglet CI. Colostrum intake ranges between 0 and 700 g with an average CI of approximately 200-350 g/kg BW_B (Le Dividich and Noblet, 1981; Bland *et al.*, 2003; Devillers *et al.*, 2007; Devillers *et al.*, 2011; Quesnel, 2011), the within-litter coefficient of variation ranges from 15-110% and the between-litter variation averages 30% (Le Dividich *et al.*, 2005a). Colostrum yield ranges between 0.8 and 4.8 kg with an average CY between 3 and 4 kg (Devillers *et al.*, 2007; Foisnet et al, 2010; Quesnel, 2011). The large variation in CY was already expected based on the large variation between litters in litter weight gain during the first days of lactation (Thompson and Fraser, 1988). An overview is given in **Table 2**.

To determine whether insufficient CY and intake is a problem in sows, a first step was to determine the minimal required volumes of colostrum needed per piglet. Quesnel (2011) estimated that a normal BW_B piglet needs to consume 200-250 g of colostrum to ensure survival. Le Dividich *et al.* (1994) showed that bottle-fed piglets kept under thermoneutral conditions needed slightly less than 150 g colostrum per kg BW_B to maintain body weight and in a subsequent study Le Dividich *et al.* (2005b) showed maximal piglet IgG serum concentration when 110 g of colostrum/kg BW_B was consumed. Based on these observations, Le Dividich *et al.* (2005a) proposed that the absolute minimal required CI under conventional conditions was approximately 160-170 g/kg BW_B. When using this cut-off value, approximately 30-45% of sows do not produce sufficient colostrum for their litter (le Dividich *et al.*, 2005a; Foisnet *et al.*, 2010a). This assumes that CY is equally divided between piglets of a litter which is normally not the case in practice (Jourquin *et al.*, 2010b; Theil *et al.*, 2014).

Table 2. *Summary of studies that estimated average piglet CI and sow CY with different methods (WSW = weigh-suckle-weigh, D_2O = deuterium dilution method) (after Farmer et al., 2006).*

Method	Average CI, g	*N*	CY, kg	Reference
WSW	240-328	77	2.86-3.90	Le Dividich and Noblet, 1981
WSW	315	60	2.71	Milon *et al.*, 1983
WSW	405	8	3.24	Varley *et al.*, 1987
D_2O	488	66	-	Chiang *et al.*, 1990
Bottle-fed	585	20	-	Le Dividich *et al.*, 1997
WSW	460-476	67	4.60-4.76	Bland *et al.*, 2003
D_2O	427	12	4.27	Devillers *et al.*, 2004b
Bottle-fed	560	5	-	Devillers *et al.*, 2004b
Equation	297	516	3.57	Devillers *et al.*, 2007
Equation	246	1005	3.32	Quesnel, 2011
Equation	147-333	512	-	Devillers *et al.*, 2011
Equation	434-512	-	-	Flummer and Theil, 2012

6.2. Variation in colostrum yield and intake: what is already known?

6.2.1. Environmental factors

Any environmental change that might affect the nursing behavior might affect CY. Auditory cues between sow and piglets, and between litters stimulate nursing frequency (Nakamura *et al.*, 1995), which increases milk yield (Auldist *et al.*, 2000). Noise disturbs the communication between sow and piglets (Algers and Jensen, 1991). This might result in lower milk or colostrum production (Farmer and Quesnel, 2009).

Feeding sows a diet with a high (23%) or low (13%) fiber content the week before farrowing, did not alter CY (Loisel *et al.*, 2013a). Colostrum yield was positively correlated with serum markers for protein catabolism (Loisel *et al.*, 2014).

Piglets housed at 18-20 °C had a 37% lower CI than piglets housed under thermoneutral conditions (Le Dividich and Noblet, 1981) but effects on CY were not described.

6.2.2. Factors related to the piglet

Characteristics that reduce the piglet's vitality or possibility to reach the teat might lead to reduced CI (Fraser and Lin, 1984) and thus reduced estimated CY. Devillers *et al.* (2007) showed that piglets that were likely hypoxic at birth (indicated by a ruptured umbilical cord or difficulty breathing), or showed splayleg had a significantly reduced CI. This is shown in **Figure 15**. Birth weight was positively correlated with CI (Devillers *et al.*, 2007). We might argue that this correlation is a result of BW_B being a predictor in the equation model used to estimate CI. This, however, cannot explain the correlation completely because 100 g increase in BW_B resulted in a 26-37 g higher CI (Le Dividich *et al.*, 2004; Devillers *et al.*, 2007), whereas purely based on the equation model this increase would be 7 g (Devillers *et al.*, 2004b). Heavier piglets at birth have an advantage over their smaller litter mates to access the nipples and are stronger to successfully extract colostrum from the teats (Pluske and Williams, 1996). Premature piglets consume less colostrum (Milon *et al.*, 1983) possibly due to their lower BW_B and suckle reflex (Silver *et al.*, 1983; Gunvaldsen *et al.*, 2007).

Birth rank does not determine CI when an equation model is used, allowing each piglet a window of 17 - 24 h to consume colostrum (Devillers *et al.*, 2007). We might wonder whether the intake of the last born piglet is colostrum and not milk. This seems rather unlikely as last born piglets, e.g. 6 h after onset of farrowing (normal farrowing lasts 200-300 min (Oliviero et a., 2009)) are weighed the second time at latest 30 h after onset of farrowing, leaving little time to consume milk compared to colostrum when the change is considered to be 24-36 h after onset of farrowing (Klobasa *et al.*, 1987). Also, piglets consume up to 30% of their total CI during the first nursing bouts (Fraser and Rushen, 1992).

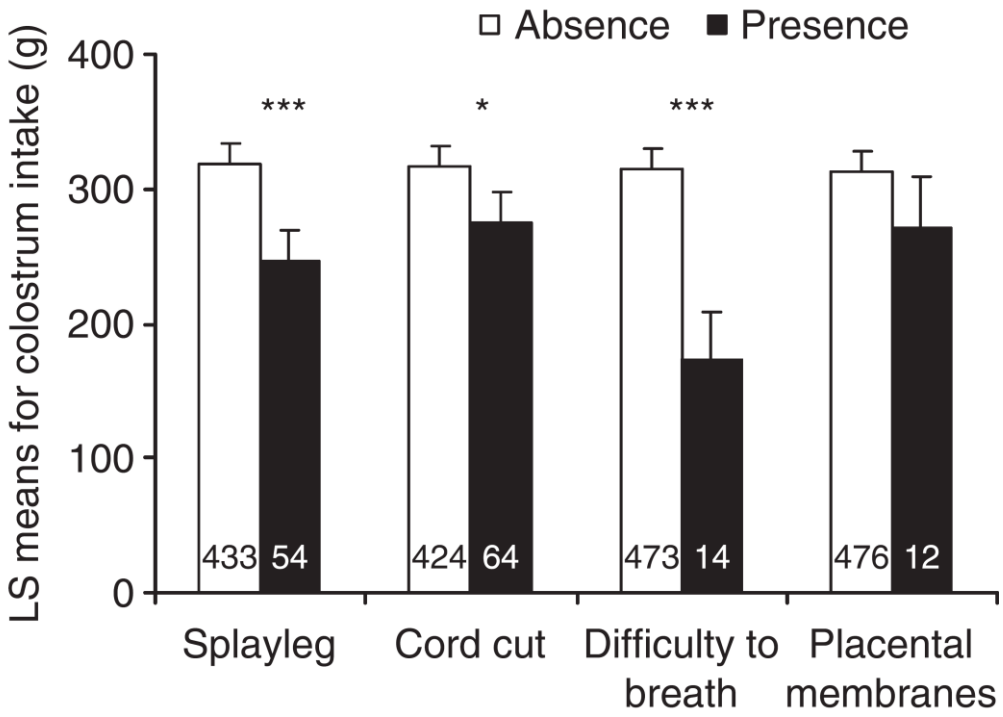

Figure 15. *The effect of some piglet vitality parameters on CI. Number of piglets in each group is at the bottom of the bars (after Devillers et al., 2007).*

6.2.3. Factors related to the sow

Litter size does not affect CY and as a result, mean CI decreases with 22-42 g for each additional liveborn piglet (Le Dividich *et al.*, 2004; Devillers *et al.*, 2007). This is presented in **Figure 16**. Milligan *et al.* (2001) reported already that there was no difference in weight gain during the first 3 days of lactation between litters of 9 and 12 piglets. Parity might affect CY as it tended to be higher in second and third parity sows than in primiparous and older sows (Devillers *et al.*, 2007). The effect of parity on colostrum yield seemed absent in dairy cattle (Kehoe et al., 2011). Le Dividich *et al.* (2004) and Quesnel (2011) found no effect of litter BW_B on CY, whereas Devillers *et al.* (2007) reported a positive correlation. Probably, within-litter BW_B heterogeneity might explain this contradiction as Devillers *et al.* (2007) and Quesnel (2011) showed this to have a negative effect on CY and BW_B heterogeneity was also

correlated with a higher pre-weaning mortality (Milligan *et al.*, 2002; Quiniou *et al.*, 2002). Quesnel *et al.* (2011) reported a negative correlation between CY and the number of stillborn piglets but litter size, parity, and farrowing duration, factors known to affect stillbirth (Fraser *et al.*, 1997; Leenhouwers *et al.*, 1999; Canario *et al.*, 2006b), could not explain the correlation. A decline in colostrum produced by each teat is seen from the most anterior to the most posterior pair of teats (Fraser and Lin, 1984; Fraser and Rushen, 1992).

Body weight, age, duration of parturition, sow's rectal temperature, number of functional teats, and BF 1 week before farrowing did not influence CY (Devillers *et al.*, 2007; Quesnel, 2011). Differences in CY between genotypes were not yet reported.

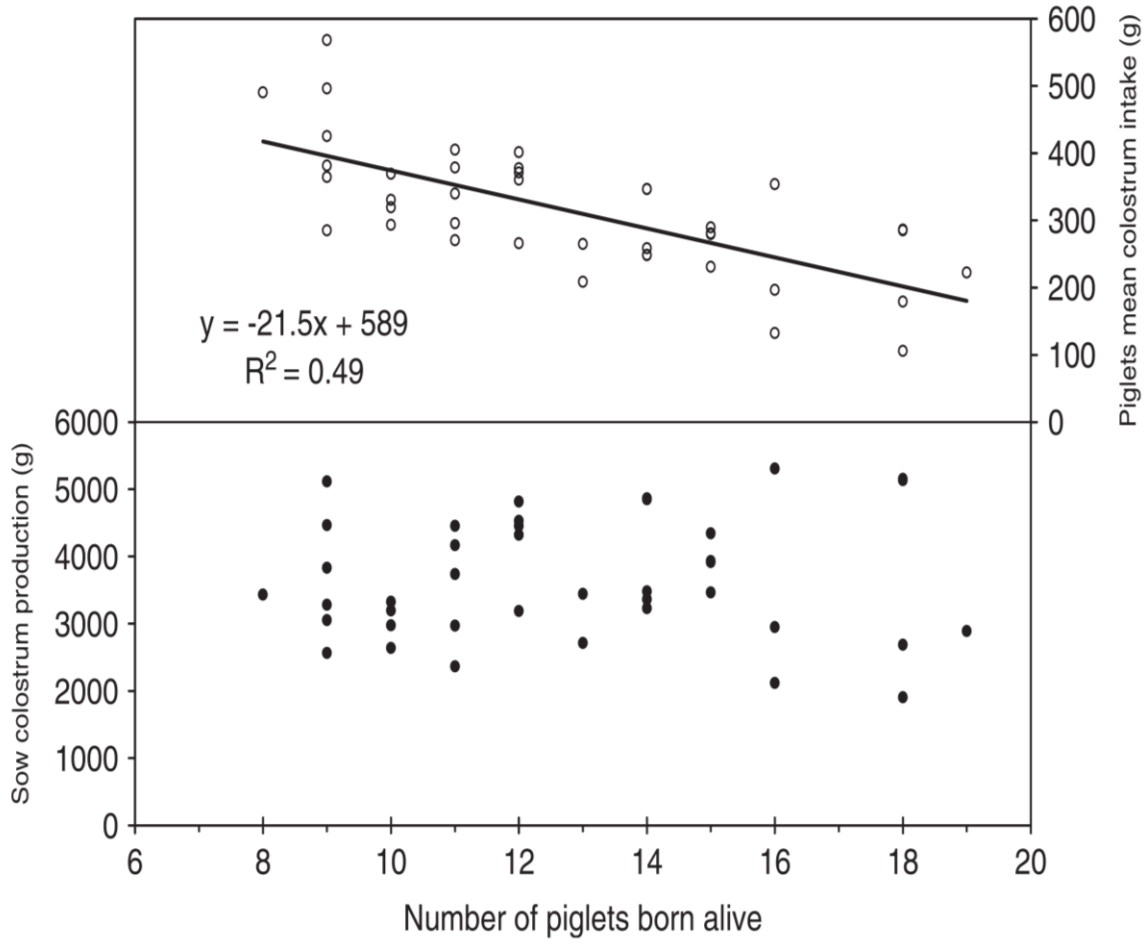

Figure 16. *Colostrum yield is not correlated with litter size (lower chart). As a consequence, colostrum available for each piglet decreases for each extra piglet born (upper chart) (after Devillers et al., 2007)*

7. ENERGY METABOLISM AND COLOSTRUM

Most research on CY in sows focussed on identifying correlations between CY with reproductive parameters or unravelling the influence of the various hormonal changes in the peripartal period and this was extensively discussed in the previous chapters. Very limited information is available on how CY is influenced by the sow's use of energy and protein derived from either the feed or the body reserves. Nonetheless, colostrum production takes place during a period of drastic metabolic changes as the sow evolves from an anabolic gestation homeorhesis to a catabolic lactation homeorhesis (Martineau *et al.*, 2013). In cattle, this period is well-known as a risk period to develop numerous metabolic diseases as a manifestation of the cow's inability to cope with the metabolic demands of high production (Goff and Horst, 1997; Mulligan and Doherty, 2008). As explained before, colostrum in composed of numerous constituents and guiding sufficient precursors/nutrients towards the mammary gland at time of colostrum production might be essential to assure a high CY. The mammary gland needs to be provided with glucose for lactose synthesis, fatty acids for lipid synthesis and AA for synthesis of proteins, and next to synthesis of colostrum constituents, the mammary gland also needs nutrients for her basal metabolism. This large demand for nutrients by the mammary gland has a high priority in sow physiology and when the demands cannot be met by feed intake, they will start mobilizing body reserves (Close *et al.*, 1985; Cools *et al.*, 2013).

7.1. Directing nutrients towards the mammary gland: glucose and the role of insulin

Piglets' growth rate *in utero* increases dramatically during the last third of gestation and concomitant their need for nutrients. Physiological (e.g. blood flow (Père *et al.*, 1996; Trottier *et al.*, 1997)) and metabolic adaptations (change of several blood substrates during gestation (Père *et al.*, 1997)) take place to address this metabolic shift in nutrient priority. One of the

most important changes involves the redirection of glucose by altering the insulin sensitivity in favour of the foetuses for which glucose is the main energetic precursor (Ford *et al.*, 1984; Reynolds *et al.*, 1985; Duée *et al.*, 1987; Père *et al.*, 1995), and in favour of the mammary gland for which glucose is the main precursor of lactose (Shennan and Peaker, 2000) which is a major determinant of CY due to its osmotic characteristics (Leong *et al.*, 1990).

Glucose uptake by cells from the circulation occurs via GLUTs and 14 different types are known so far (Mueckler and Thorens, 2013). They are characterized by differences in tissue distribution (Bell *et al.*, 1990). Liver tissue is predominated by GLUT-2, muscle and adipose cells by GLUT-4, and the mammary gland and placenta by GLUT-1 (Hocquette and Abe, 2000; Zhao and Keating, 2007; Aschenbach *et al.*, 2009). The GLUTs are also characterized by their sensitivity to insulin (Bell *et al.*, 1990). The GLUT-4 is under control of insulin whereas GLUT-1 is not. When insulin binds to the insulin receptor, this leads to a cascade of reactions resulting in the transcription of e.g. GLUT-2 and 4 (Saltiel and Kahn, 2001). The result is that transfer of glucose from the circulation to the cell through these receptors is only possible after insulin binding to its insulin receptor. The difference in tissue distribution and insulin dependency provides the sow with a tool to redirect glucose between different tissues by altering the sensitivity of insulin receptors to insulin. Thus, when the insulin sensitivity decreases by a decline in receptor density or receptor affinity, the response to a certain serum concentration of insulin will decrease e.g. a lower expression of insulin-dependent GLUTs. Therefore, under such conditions, the glucose influx into insulin-independent tissues (mammary gland, placenta) is favoured over glucose influx into insulin-dependent tissues (liver, muscle, fat). Moreover, during late gestation, the expression of GLUT-1 is increased in the placenta (Hahn and Desoye, 1996; Hay, 2006) and the mammary gland (Miller, 1996).

From d 85 of gestation, all sows develop a decreased insulin sensitivity, which is more pronounced in primiparous sows than in older sows (Père *et al.*, 2000; Père *et al.*, 2007). This

is shown in **Figure 17**. Up to date, it is still unknown whether decreased insulin sensitivity is important to assure maximal CY. Foisnet *et al.* (2010a) showed that sows with a low CY had higher serum concentrations of glucose 1 week before farrowing compared to sows with a normal CY. Kemp *et al.* (1996) showed that sows with a decreased glucose tolerance at d 104 of gestation had a greater piglet mortality during the first week of lactation, which is an indicator of reduced CI (Devillers *et al.*, 2011). Also, weight gain of the liveborn piglets during the colostral phase was negatively correlated with sow plasma glucose concentration at d 112 of gestation (Hansen *et al.*, 2012). On the other hand, acute glucose infusion did not alter glucose uptake by the mammary gland (Holmes *et al.*, 1988) and it seems that glucose uptake by the mammary gland is not regulated by the arterial glucose concentration but by intra-mammary demand (Bell and Bauman, 1997). In this way, once the maximal amount of glucose that can be processed by the mammary gland is achieved, the uptake will reach a plateau.

7.2. The citric acid cycle: importance of balance at farrowing

When glucose is available, this is the preferred energy source for the cell. Glucose is converted via glycolysis to pyruvate, which is a precursor for acetyl-CoA that can be used in the Krebs cycle. These steps provide the cell with energy in the form of NADH, $FADH_2$, and ATP. When insufficient glucose is available to the cell, *e.g.* in liver and muscle by decreased insulin sensitivity or a high demand by the mammary gland in late gestation, these cells are forced to use alternative energy precursor which are mostly fatty acids that are broken down to acetyl-CoA via β-oxidation. Acetyl-CoA only can enter the citric acid cycle when combined with oxalo-acetate. Acetyl-CoA can be derived from glucose, AA and fatty acids. In cases of a negative energy balance, the main precursor of acetyl-CoA is fatty acids. Oxalo-acetate can be synthesized from glucose and some AA, especially the branched-chain AA.

When the amount of acetyl-CoA is higher than the amount of oxalo-acetate, the excess amount of acetyl-CoA will be turned into ketone bodies by the hepatocytes. A schematic overview is shown in **Figure 18**. The principle of the energy balance and the ketosis-fatty liver complex is best known in dairy cattle (Goff and Horst, 1997) where it was shown that these ketone bodies can lead to clinical ketosis with suppressed production most apparent from 10 days to 3 weeks after parturition (Larsen and Kristensen, 2010). Clinical ketosis in sows has so far not been described. Ketone bodies clearly increase from d 10 of lactation onwards showing that subclinical ketosis in sows occurs when lactational performance increases but not in the peripartal period (Theil *et al.*, 2013). Nonetheless, restricted feeding in the peripartal period is often applied (Cools *et al.*, 2014) and this might lead to a negative energy balance (Close and Cole, 1986), more use of ketogenic energy substrates resulting in more acetyl-CoA, or a relative shortage of oxalo-acetate. Oxalo-acetate can also be used as a precursor for gluconeogenesis which could even aggravate the imbalance between acetyl-CoA and oxalo-acetate at the citric acid cycle. Limiting the cow's feed intake the day before farrowing increased the risk of fatty liver and ketosis (Goff and Horst, 1997) and supplementing ewes the last week of gestation with 0.75kg cracked maize resulted in a double colostrum yield of superior quality compared to non-supplemented ewes (Banchero et al., 2004).

This increased pressure on the maternal metabolism during the fragile and critical change from gestational homeorhesis to lactational homeorhesis (Martineau et al., 2013) might result in subclinical, suboptimal performance of the sow e.g. a suppressed CY. Up to date, the effect of an unbalance at level of the citric acid cycle on CY in sows was not investigated.

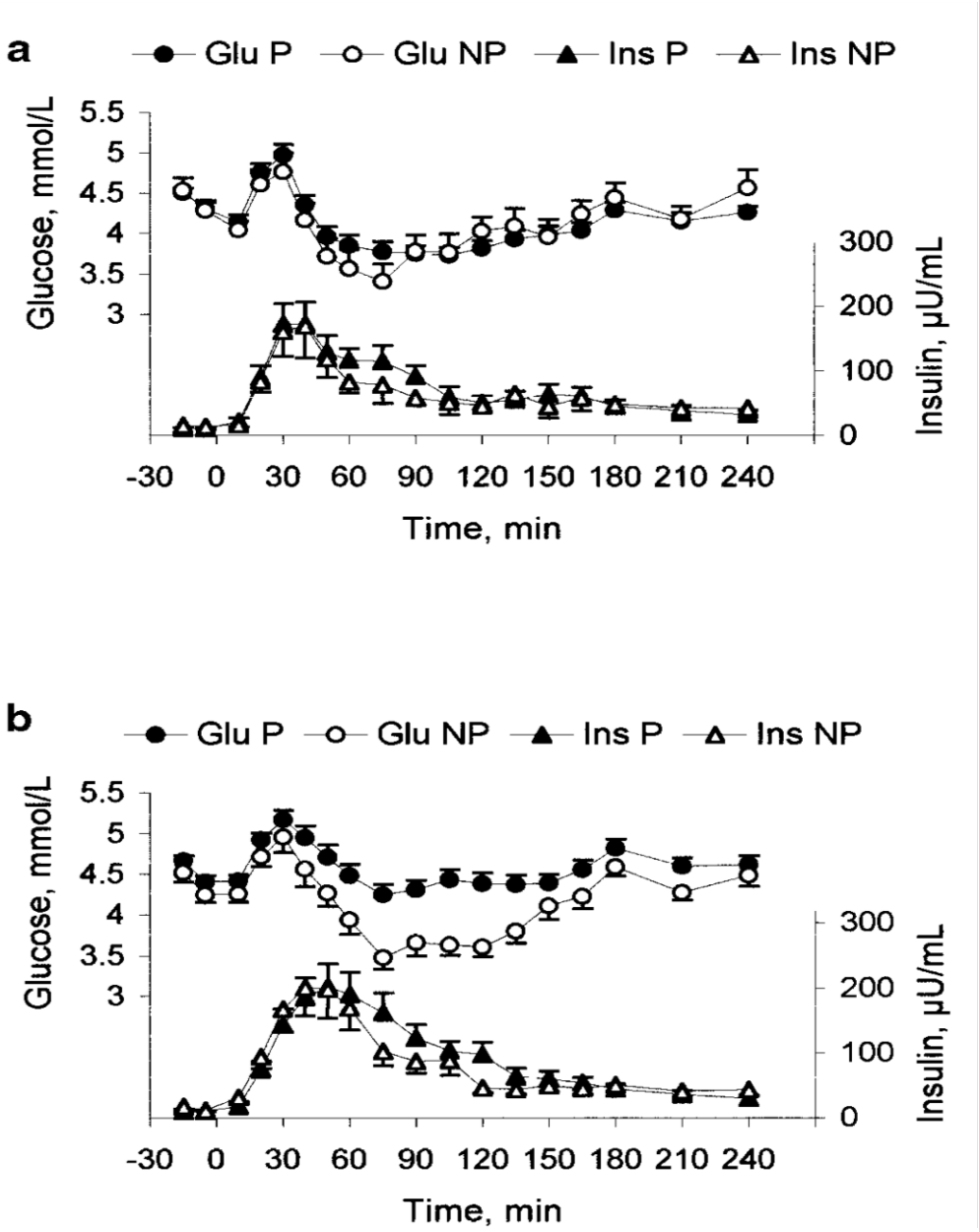

Figure 17. *The glucose (Glu) and insulin (Ins) profiles before (< 0min) and after the morning meal in pregnant (P) and non-pregnant (NP) sows up to 59 days after insemination (a) and 101 days after insemination (b). In (a), the glucose and insulin profile is similar between pregnant and non-pregnant sows. In (b), the insulin response after the morning meal is similar but the glucose concentration takes longer to decrease after the morning meal indicating decreased insulin sensitivity (after Père et al., 2000).*

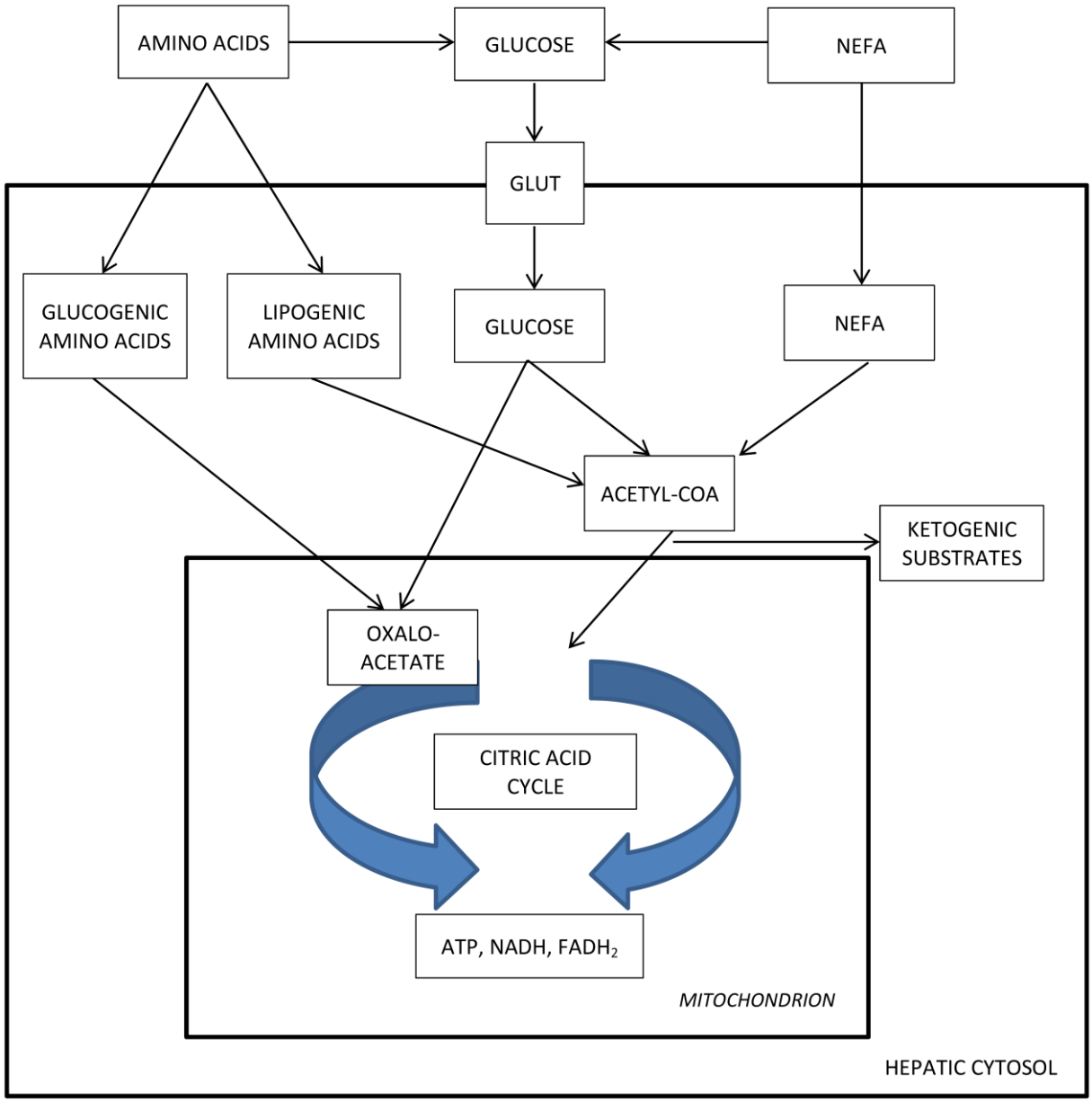

Figure 18. *Simplified overview of the key precursors for the citric acid cycle. In case of a negative energy balance, the use of NEFA as a precursor for acetyl-CoA will increase holding a threat for the supply of sufficient oxaloacetate (after Cools, 2013).*

CHAPTER 2

AIMS

Approximately one third of the sows do not produce sufficient colostrum for their litter (Le Dividich et al., 2005). In contrast to what is seen for milk yield, CY is not correlated with litter size and, therefore, the available colostrum per piglet decreases with each extra piglet born alive (Devillers et al., 2007). This means that a sufficient CY is a critical factor in optimizing piglet performance and thus in better achieving the performance potential of the litter, even more so in the modern high-prolific sows.

To date, most research on CY in sows focussed on identifying correlations between CY with reproductive parameters or unravelling the influence of the various hormonal changes in the peripartal period. Very limited information is available on how CY is determined by the sow's use of energy and protein derived from either the feed or the body reserves.

The general aim of this study was to investigate whether the use of energy and protein from feed or body reserves during gestation could affect CY in sows.

- The first aim was to identify the periods during gestation in which the use of body reserves was related to CY (**Chapter 3.1.**).
- The second aim was to investigate the effect of different peripartal feeding strategies on the CY and composition in sows (**Chapter 3.2.**).
- The third aim was to investigate the effect of the use of body energy reserves during the last month of gestation on CY and composition in sows (**Chapter 3.3.**).
- The influence of CI on piglet's glucose and fat metabolism is well studied but the effect on protein use as an energy source was not yet described. This, together with the importance of CI on long-term performance effects under commercial conditions, was investigated in experiment 4 (**Chapter 3.4.**).

CHAPTER 3

EXPERIMENTAL STUDIES

3.1.

Changes in back fat thickness during late gestation predict colostrum yield in sows

Adapted from

Decaluwé, R., D. Maes, I. Declerck, A. Cools, B. Wuyts, S. De Smet, and G.P.J. Janssens

2013

Animal 7 (12): 1999-2007

ABSTRACT

Directing protein and energy sources towards lactation is crucial for optimizing milk production in sows but how this influences CY remains unknown. The aim of this study was to identify associations between CY and the sow's use of nutrient resources.

We included 37 sows in the study that were all housed, fed and managed similarly. Parity, BF change (**ΔBF**), CY, and performance parameters were measured. We obtained sow serum samples 3-4 days before farrowing and at d 1 of lactation following overnight fasting. These were analysed for NEFA, urea, creatinine, (iso)butyrylcarnitine (**C4**), IgG and IgA. The colostrum samples collected 3, 6 and 24 h after birth of the first piglet were analysed for nutrient and Ig content.

The technical parameters associated with CY were parity group (a; parity 1-3 = value 0 versus parity 4-7 = value 1) and ΔBF d 85-d 109 of gestation (mm) (b) according the following model: CY (g) = 4290 – 842a -113b. (R^2 = 0.41, P < 0.001). The gestation length (P < 0.001) and the ΔBF between d 109 of gestation and d 1 of lactation (P = 0.050) were identified as factors that could explain the observed difference in CY between parity groups. The metabolic parameters associated with CY were C4 at 3 to 4 days before farrowing (a), and 10logC4 (b) and 10logNEFA (c) at d 1 of lactation: CY (g) = 3582 – 1604a + 1007b – 922c (R^2 = 0.39, P = 0.001). The colostrum composition was independent of CY.

The negative association between CY and ΔBF d 85 - d 109 of gestation could not be further explained based on our data. Sows that were catabolic 1 week prior to farrowing seemed unable to produce colostrum to their full potential. This was especially the case for sows with parity 4 to 7 although they had a similar feed intake, litter BW_B and colostrum composition compared to parity 1 to 3 sows.

In conclusion, this study showed that parity and the use of body reserves during late gestation were associated with CY, indicating that proper management of the sow's BC during late gestation could optimize the intrinsic capacity of the sow's CY.

Key words: Colostrum – Sow – Condition - Parity

IMPLICATIONS

Pre-weaning piglet mortality is mainly due to an energy deficit. As colostrum is the piglets' main source of energy, improving CY has economical and ethical benefits. Throughout gestation, changes in body's reserves have to be closely monitored, due to their association with nutrient partitioning in the sow and CY. As CY is vital to sustain piglet performance, evaluating the management measures in order to modulate BF changes in late gestating sows is, therefore, recommended.

INTRODUCTION

The 2 principal functions of colostrum are to deliver energy and passive maternal immunity to the piglet (Rooke and Bland, 2002; Le Dividich et al., 2005a). The piglets' energy reserves at birth can provide about 420 kJ/kg BW_B. This hardly exceeds half of the amount of energy a newborn piglet needs under thermo neutral conditions (Noblet et al., 1997; Le Dividich et al., 2005a). The additional energy needed to maintain a constant body temperature and for weight gain must be supplied through CI. Furthermore, the piglets depend entirely on colostrum in order to obtain passive maternal immunity because the epitheliochorial type of placenta disables its prenatal delivery (Rooke and Bland, 2002; Salmon et al., 2009). Le Dividich et al. (2005a) stated that the piglet needs to consume at least 160 g colostrum per kg BW_B.

Pre-weaning mortality ranges between 10-13% in the main pig-breeding countries (Edwards, 2002; Kilbride et al., 2012; Hales et al., 2014) and piglet mortality usually occurs during the first 3 days after birth (Le Dividich et al., 2005a). Inadequate CI by the piglet is a major direct and subjacent cause of mortality during the first days after birth mainly due to hypothermia

and hypoglycaemia (Le Dividich et al., 2005a). In addition, insufficient intake of maternally derived Ig will have a negative effect on the piglets' health status, thus weight gain and survival, at later stages in life (Rooke and Bland, 2002; Le Dividich et al., 2005a).

Previous studies have shown that the total CY per sow is 3.4 kg on average, but varies largely among sows (Devillers et al., 2007; Foisnet et al., 2010a). This variation can be attributed to environmental related factors, the piglet's and the sow's characteristics (Devillers et al., 2007; Farmer and Quesnel, 2009; Quesnel 2011). The litter size was not correlated with total CY (Devillers et al., 2007) and the CI with bottle-fed piglets rendered twice as much CI compared to sow-reared piglets (Le Dividich et al., 1997), which indicates that the total CY is the major limiting factor for the CI. In general, there is insufficient information available to thoroughly understand how CY can be increased in sows. It is well established that the optimal availability of energy and protein is central in maximizing the intrinsic capacity of the sow's milk production (Boyd et al., 1995). Foisnet et al. (2010a) suggested that sow's peripartal hormonal changes, its insulin sensitivity and the availability of glucose might play an important role in the total CY.

According to our knowledge, studies investigating the partitioning of nutrients in relation to CY are scarce and the association with the sow's BC has never been described. Therefore, the aim of this study is to identify associations between the changes in energy stores and the nutrient metabolism in late gestating sows and CY.

MATERIAL AND METHODS

Description of study population

The experiment was performed during the months of April and May 2011 at a commercial farm in Flanders with 1700 PIC sows in a 2-week batch system. Thirty-seven sows of different parities (1 to 7), equally divided over 2 week-groups, were observed from d 85 of

gestation until d 3 of lactation. The day of first insemination was defined as d 0 of gestation, and the day of parturition as the last day of gestation and d 0 of lactation.

From d 29 until d 107 of gestation, the sows were housed in a group housing system with 15 animals per pen. On d 108 of gestation, the sows were moved to the farrowing unit where they were housed individually in conventional farrowing crates until weaning at 3 weeks of lactation. Floor heating and an infra-red lamp were used to create a microclimate for the piglets.

Between d 85 and d 107 of gestation, the gestation diet (pellets) was provided by 2 feeders per pen that dropped a small amount of feed at regular intervals throughout the day at an average level of 2.2 kg per sow per day. In the farrowing unit, the sows were manually fed a transition diet (meal) once a day, until d 1 or 2 after farrowing. When a sow had not finished the meal of the previous day, the trough was emptied and a smaller amount of fresh feed was given. Starting from d 2 or 3 of lactation, the sows received a lactation diet (meal) 4 times a day. Average ± standard error of the mean (**SEM**) feed intake (kg) 6, 5, 4, 3, 2, 1 days before parturition, at day of parturition and 1, 2, 3 days after parturition was 2.0 ± 0.0, 1.9 ± 0.1, 1.8 ± 0.01, 1.8 ± 0.01, 1.9 ± 0.01, 1.9 ± 0.01, 1.7 ± 0.1, 1.8 ± 0.1, 3.7 ± 0.3, 4.9 ± 0.2, respectively. During the entire experiment, the sows had free access to fresh drinking water (drinking nipple – flow 1.5 to 2 L/min).

The induction of parturition was not applied, and farrowing intervention was kept to a minimum. When the birth interval between 2 piglets exceeded 1 h, manual extraction was performed. Oxytocin was not administered during parturition, as this interferes with mammary secretion (Ellendorf et al., 1982). No additional help or care was given to the piglets unless there was a risk of them getting crushed.

On d 2 of lactation, the litters were standardized to 11 ± 1 piglet by cross-fostering within the observed group of sows or to non-observed sows when too many piglets were present.

Measurements

All the measurements of BF were performed by the same person on standing sows at the P2-position (Maes et al., 2004) after hair removal using a digital BF indicator (Renco Lean Meter, S.E.C. Repro Inc., Ange-Gardien-de-Rouville, Québec, Canada) at d 85, d 109 and d 111 of gestation, and at d 1 of lactation. The BF was always measured at the same, marked spot on both sides of the sow. Values from the 2 measurements were averaged to obtain a single BF measurement. Devillers et al. (2006) described that the secretory activity of the mammary gland starts at d 85 of gestation. In this study, d 109 of gestation was the first whole day that sows were housed in the farrowing unit. Therefore, we calculated the change in BF between d 85 and d 109 of gestation (**ΔBF d 85-109**, mm) as BF d 109 minus BF d 85, and the change in BF between d 109 of gestation and d 1 of lactation (**ΔBF d 109-1**, mm) as BF d 1 minus BF d 109. The change in BF should be interpreted as follows: a negative value represents BF loss or BF mobilisation; a positive value represents BF gain or BF deposition.

The rectal body temperature (digital thermometer, accuracy 0.1°C) was recorded between 04.30 and 05.00 a.m. the day before, of and the day after farrowing to monitor health status. Parity, gestation length, number of liveborn and stillborn piglets, and parturition length were recorded for every sow. The daily feed intake (**DFI**) per sow was recorded from d 111 of gestation until d 3 of lactation. The sow's CY was calculated as the sum of the piglets' CI within a litter.

The piglets' CI (g) was estimated by a regression equation as described by Devillers et al. (2004b), based on BW_B, weight at 17-24 h of age (further referred to as weight at 24 h of age, $\mathbf{BW_{24}}$), duration of CI (t with $17h \leq t \leq 25h$), and time between birth and first suckling ($\mathbf{t_{FS}}$). The equation is the following:

$$CI = -217.4 + 0.217 \times t + 1861019 \times BW_{24}/t + BW_B \times (54.80 - 1861019/t) \times (0.9985 - 3.7 \times 10^{-4} \times t_{FS} + 6.1 \times 10^{-7} \times t^2_{FS})$$

The detailed handling of piglets at birth was as follows: when a piglet was born, the back of the piglet was dried with a paper towel, a number was written on the back with a marker and the piglet was ear-tagged allowing identification. The umbilical cord was shortened when it was longer than approximately 15cm. After weighing, they were placed against the sow's vulva again with their nose. The accuracy of the scale was 0.02 kg and the birth interval was recorded for every piglet.

Samples

Feed samples were taken from the silos at the end of the study.

Serum (8 mL, serum cloth activator tubes) of the sows was collected by punction of the *vena jugularis* while they were restrained by a snare. The sampling was done before the morning meal after a fasting period of 20h. As colostrum is mainly produced the week prior to farrowing (Devillers et al., 2006), we collected serum each other day during that week. In this way, we obtained serum from every sow 3-4 days before farrowing and only these were further analysed. We also collected and analysed serum samples of the sows at d 1 of lactation. The blood samples were stored in iced water, subsequently centrifuged at 671 x g for 10 min and serum was stored frozen at -20°C until further analysis. The serum was analysed for urea, creatinine, NEFA, C4, IgG and IgA.

The colostrum (35 mL) was collected at 3, 6 and 24 h after birth of the first piglet, equally divided from all teats on 1 side of the udder. Except for the sample at 3 h, 2 mL of oxytocin (10IU/mL) was administered intramuscularly 5 min before sampling. At the time of the sample collection at 6 h, 6 sows did not complete the farrowing and they were also given an injection of 2 mL of oxytocin. The samples were subdivided and frozen immediately at -20°C and stored until further analysis. Each colostrum sample was analysed for its chemical composition, IgG and IgA.

Analyses of samples

Feed. The nutritional composition of the diets were analysed according to the Association of Official Analytical Chemists methods (Thiex, 2002) (ISO 5983-1, 2005; ISO 1443, 1973; ISO 5498, 1981). The gestation diet contained 90.6% dry matter (**DM**), 3.9% of crude fat (**CF**), 13.5% of crude protein (**CP**), 4.7% of crude ash (**CA**) and 9.6% of crude fibre (**CFib**). The transition diet contained 88.7% DM, 3.5% CF, 13.6% CP, 6.2% CA and 8.5% CFib. The lactation diet contained 89.7% DM, 5.2% CF, 18.2% CP, 5.3% CA and 4.3% CFib.

Serum. Creatinine, urea and NEFA were measured spectrophotometrically (Ultrospec IIE, LKB, Biochrom, Cambridge, England) using a commercial colorimetric diagnostic kit (Randox Laboratories, Crumlin, United Kingdom). A quantitative electrospray tandem mass spectrometry was used to determine C4 as described by Vreken et al. (1999). (Iso)butyrylcarnitine is a catabolite of AA that can be metabolized to oxaloacetate, which is needed to react with acetyl CoA when entering the citric acid cycle (Michal, 1999a, b). Still, we need to be critical when interpreting this variable as not only amino acids but also fatty acids can be a source of C4. In the latter case, we should expect a same trend in NEFA and C4. As serum samples were obtained after an overnight fasting of 20 h, we can assume that C4 mainly reflects a catabolism of body fat or body protein. Immunoglobulins G and A were analysed by a porcine quantitative sandwich enzyme immunoassay technique (Bethyl Laboratories Inc., Montgomery, USA). All samples were analysed in duplicate.

Colostrum. The dry matter, fat, protein and lactose content were analysed by Lactoscope FTIR Advanced type FTA-3.0 (Delta Instruments, Drachten, Netherlands). The samples were diluted 1:2 with distilled water and calibrated curves were verified with Gerber and Kjeldahl analysis. These analyses were not done in duplicate because of the high amount of sample needed for 1 analysis.

Immunoglobulins G and A were analysed by a porcine quantitative sandwich enzyme immunoassay technique (Bethyl Laboratories Inc., Montgomery, USA) in duplicate and in the same array, in order to avoid inter-array variation.

Statistical analysis

The data is reported as LSMean ± standard deviation (**SD**) or median ± interquartile range (**IR**) when variables were normally or not normally distributed, unless mentioned otherwise. The Kolmogorov-Smirnov test was used to analyse whether variables were normally distributed. The correlation analysis was performed using Pearson or Spearman Rank correlation analysis when variables were distributed normal or not normal. Sows were divided into 2 groups based on parity: parity 1 to 3 (n = 18) and parity 4 to 7 (n = 19). This division differed from other studies (Devillers et al., 2007) but was based on graphical interpretation of the data. In order to analyse whether the variables differed between groups, we used an independent samples t-test or a Kruskall-Wallis analysis when variables were hence normally or not normally distributed.

In order to analyse which variables were associated with CY, multivariable regression analysis was performed using forward modelling. The statistical model is:

$$Y = \beta 0 + (\sum_{i=1}^{n} \beta i Xi) + \varepsilon i$$

with Y as the dependent variable, β0 as a constant value, βi as slope coefficients, Xi as the independent variable and εi as the random error term. The dependent variable was CY for each model. The independent variables and their slope coefficients are shown in the regression equations. For each regression model, the normality and homogeneity of variance, outliers and their influence and multicollinearity were tested through residual analysis, leverage, studentized deleted residuals, Cook's distance, DFFITS, DFBETAS, variance inflation factor and tolerance. When needed, variables were transformed and reported as such.

The overtime change of the colostrum composition was analysed by repeated measures ANOVA for normally distributed data and by Friedmann's 2-way ANOVA for not normally distributed data.

All statistical analyses were performed using SPSS 19.0 (IBM Company Headquarters, Chicago, Illinois), considering statistical significance when $P < 0.05$.

RESULTS

Production parameters

The range is marked between brackets. The parity was 3.8 ± 2.1 (1-7), the gestation length was 114.6 ± 1.7 days (112-117), the farrowing duration was 234 ± 117 min (53-591) and the litter size was 14.6 ± 2.4 (10-20). The number of liveborn piglets was 13.5 ± 2.2 (10-18), the number of stillborn piglets was 1.0 ± 2.0 (0-5), with a total litter BW_B of 19.0 ± 2.8 kg (13.3-24.3). The day before farrowing the sow's rectal body temperature was 38.1 ± 0.4 °C (37.3-39.0), on the day of farrowing it was 38.2 ± 0.5 °C (37.1-39.0) and the day after farrowing it was 38.9 ± 0.4 °C (38.0-39.7). For the individual piglets, the birth interval was 8.0 ± 14.0 min (0-108) and t_{FS} was 20.0 ± 31.0 min (4-207), the BW_B was 1305 ± 338 g (400-2380), their BW_{24} was 1393 ± 348 g (480-2420), and their weight gain during the first 24 h of life was 60 ± 100 g (-230-300). The BW_B of the liveborn piglets ($P = 0.204$) and t_{FS} ($P = 0.441$) did not differ between piglets born before d 114 of gestation or the ones born after.

Feed intake and BF of the sows

Data considering feed intake, BF and ΔBF are shown in **Table 1**. Colostrum yield was not correlated to the feed intake between d 111 of gestation and farrowing ($r = -0.07$, $P = 0.666$), and during the first 3 days of lactation ($r = -0.03$, $P = 0.874$). We observed a BF loss in 30 sows between d 85-109 and in 27 sows between d 109 - 1. Changes in BF during both periods did not correlate with the BF level at the beginning of the respective period ($-0.02 < r < 0.3$, $P > 0.05$).

Colostrum yield

The total CY was 3243 ± 132 g (1568 – 5017) per sow. The CI per piglet was 245 ± 154 g with a maximum of 635 g and the average CI/kg BW_B of the piglets was 196 ± 108 g with a maximum of 394 g (**Table 1**). Thirty-seven percent of the sows were not producing and 31% of the piglets did not consume 160 g colostrum/kg liveborn piglet, the threshold value as proposed by Le Dividich et al. (2005a).

Multivariable regression analysis, performed with all variables presented in **Table 2**, revealed 2 factors that were associated with CY: parity group and ΔBF d 85-109. The obtained regression equation ($R^2 = 0.41$, $P < 0.001$) was: CY = 4290 – 842 (parity group) – 113 (ΔBF d 85-109, mm). The details are shown in **Table 3**. Both variables were negatively associated with CY. The sows with a parity of 4 to 7 produced 840 g less colostrum compared to sows with a parity of 1 to 3 and within a parity group, an extra loss of 1 mm BF between d 85 and 109 of gestation was associated with an increase in CY of 113 g. Raw data of these variables are presented in **Table 2** and **Figure 1**.

Table 1 *Colostrum yield, feed intake, BF of sows (n = 37) and CI by piglets (n = 551). Mean ± SD or median ± IR are given for variables with a normal or non-normal distribution (indicated by *).*

Level	Variable	Mean/ Median	SD / IR	Min	Max
Sows	CY, g	3243	804	1568	5017
	Average CI / liveborn piglet, g	246	74	98	421
	Average CI /kg liveborn piglet, g	187	53	78	295
	DFI d 111-1, kg*	2.0	0.3	0.9	2.0
	Feed intake d 1-3, kg	10.4	2.5	4.5	14.6
	BF at d x of gestation, mm				
	d 85	18.5	5.7	9.0	34.0
	d 109	16.5	5.7	8.5	31.5
	d 111	16.5	5.7	8.5	31.5
	BF d 1 of lactation, mm	15.7	5.9	8.0	32.5
	ΔBF d 85-109, mm	-2.0	2.3	-6.0	4.5
	ΔBF d 109-1, mm	-0.8	1.2	-3.5	2.0
Piglets	CI, g*	245	154	0	635
	CI/kg BW_B, g*	196	108	0	394

ΔBF d 85-109: Change in BF between d 85 and d 109 of gestation; ΔBF d 109-1: Change in BF between d 109 of gestation and d 1 of lactation

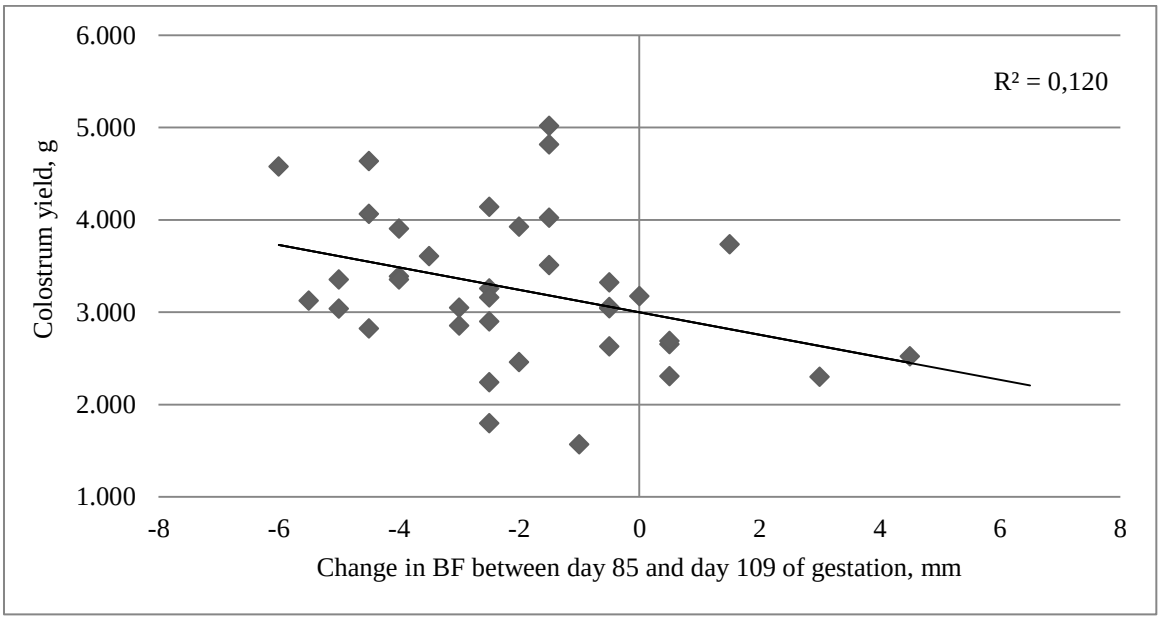

Figure 1 *The association between CY and the BF change between d 85 and d 109 of gestation is shown.*

Table 2 *Comparison of colostrum, feed intake, BF, farrowing and litter characteristics, between sows of different parity groups. Normally distributed variables were analysed with an independent samples T-test and mean ± SEM is given. Not normally distributed variables (indicated with *) were analysed with a Kruskal-Wallis analysis and median ± IR is given.*

Variable		Parity group		SEM / IR	*P*
		1-3	4-7		
Number of sows		18	19		
Colostrum characteristics	CY, g	3688	2821	132	< 0.001
	CY/kg liveborn piglet, g	210	165	9	0.008
Feed characteristics	DFI d 111-1, kg	2.0	2.0	0.04	0.599
	Feed intake d 1-3, kg	10.5	10.4	0.4	0.925
BF characteristics	BF d 85, mm	21.3	15.9	0.9	0.002
	BF d 109, mm	19.2	14.0	0.9	0.003
	BF d 111, mm	19.2	14.0	0.9	0.004
	BF d 1, mm	18.8	12.8	1.0	0.001
	ΔBF d 85-109, mm	-2.1	-1.9	0.4	0.782
	ΔBF d 109-1, mm	-0.4	-1.2	0.2	0.050
Farrowing characteristics	Gestation length, days	115.6	113.6	0.3	< 0.001
	Farrowing duration, min	208	256	19	0.205
	Litter size	14.1	15.1	0.4	0.247
	Liveborn piglets	13.4	13.7	0.4	0.685
	Stillborn piglets*	0.5	1.0	2	0.210
Litter characteristics	Litter $BW_{B,}$ kg	18.7	19.3	0.5	0.470
	Litter BW_B liveborn piglets, kg	17.8	17.7	0.4	0.916
	Average piglet $BW_{B,}$ kg	1.3	1.3	0.03	0.556
	Average BW_B liveborn piglets, kg	1.4	1.3	0.03	0.558
	Average t_{FS}*, min	27	27	16	0.443

d 111-1: d 111 of gestation until d 1 of lactation; d 1-3: d 1 of lactation until d 3 of lactation; ΔBF d 85-109: Change in BF between d 85 and d 109 of gestation; ΔBF d 85-109: Change in BF between d 109 of gestation until d 1 of lactation; t_{FS}: Time between birth and first suckle

Table 3 *Multivariable regression analysis when we used technical parameters (technical model) or metabolic parameters (metabolic model) as predictors. The dependent variable is the CY (g) per sow. For the technical model, the sows were divided in 2 parity groups: parity 1-3 and parity 4-7. In the regression equation, the x-value of the parity 1-3 sows is 0 and the x-value of the parity 4-7 sows is 1.*

Model	Predictor	Slope	SD	CI for slope	*P*
Technical model	Constant	4291	351	[3579 ; 5005]	< 0.001
	Parity group	-842	210	[-1269 ; -415]	< 0.001
	ΔBF d 85-109, mm	-113	46	[-206 ; -20]	0.018
Metabolic model	Constant	3582	460	[2645 ; 4520]	< 0.001
	C4 3-4 days before farrowing, µmol/L	-1604	631	[-2889 ; -318]	0.016
	10log C4 d 1 of lactation, µmol/L	1077	412	[238 ; 1915]	0.013
	10log NEFA d 1 of lactation, mmol/L	-922	367	[-1670 ; -174]	0.017

CI: confidence interval; ΔBF d 85-109: Change in BF between d 85 and d 109 of gestation

As parity *per se* did not provide further insights into how CY might be affected, we tried to identify factors underlying parity. Therefore, we first compared characteristics regarding feed intake, BF, the farrowing process and the litter performance between the 2 parity groups (**Table 2**). We could only identify a difference for the BF characteristics and gestation length. Older sows had a lower BF at all times ($P < 0.004$), tended to lose more BF between d 109 of gestation and d 1 of lactation ($P = 0.050$) and had a shorter gestation length ($P < 0.001$). Then, we investigated possible associations between these characteristics and CY. The ΔBF d 109-1 (r = 0.39, $P = 0.017$), BF d 85 (r = 0.39, $P = 0.017$) and gestation length (r = 0.39, $P = 0.017$) were correlated to CY, the latter 2 also mutually highly correlated (r = 0.680, $P < 0.001$).

Using forward linear modelling techniques, we were able to see the R^2 with each new variable added to the model. The first factor entered in the model was the ΔBF d 85-109 and this explained 13% (R^2) of the observed variability in CY. When the factor 'parity-group' was added to the model, an extra 28% of the variability in CY was explained, making a total of 41%. We rebuilt the model without the factor 'parity group' but with the 3 factors that were

identified as possibly underlying the parity group effect. Again, in a first step, the ΔBF d 85-109 explained 13% (R^2) of the observed variability in CY. When we added the 3 factors, an extra 21% of the variability in CY was explained with BF d 85 removed from the model due to confounding issues. This indicates that in this study, the ΔBF d 109-1 and gestation length are factors underlying to the factor parity group, without explaining all variation in CY explained by parity group. Raw data of ΔBF d 109-1 and gestation length are plotted against CY in **Figure 2** and **Figure 3**.

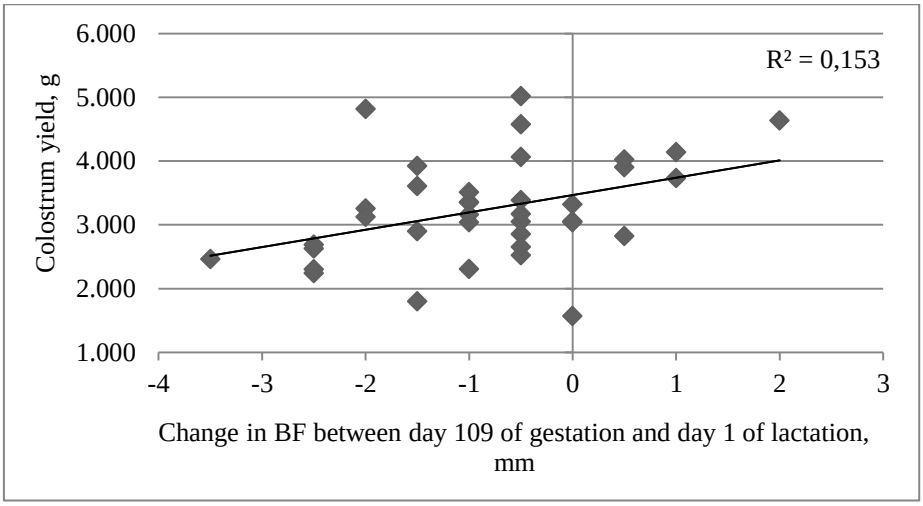

Figure 2 *The association between CY and the BF change between d 109 of gestation and d 1 is shown.*

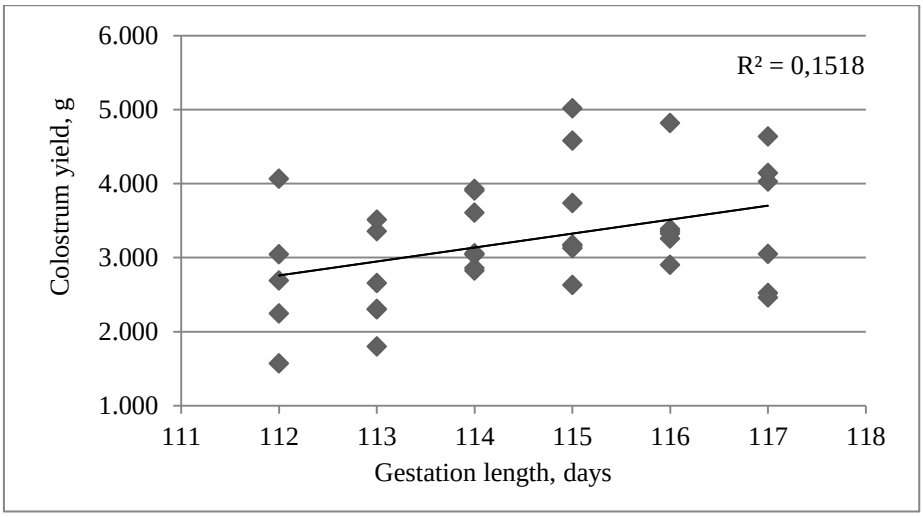

Figure 3 *The association between CY and gestation length is shown.*

Colostrum composition

The nutritional composition (%) and concentration of IgG and IgA (mg/mL) in the colostrum are shown in **Table 4**. The concentration of fat and lactose had increased, while all other parameters had decreased over time ($P < 0.001$). The colostrum composition was not correlated to CY (r between -0.3 to 0.3, $P > 0.05$). The total output of nutrients (fat, protein, lactose) through colostrum did correlate with CY ($0.64 < r < 0.94$, $P < 0.001$).

Table 4 *Mean composition based on fresh samples (%) and mean concentrations of IgG and IgA in colostrum 3, 6 and 24 h after birth of the first piglet. Statistical analysis of the time effect was performed.*

Variable	3h	6h	24h	*P*
Fat, %	8.9 (0.6)	9.9 (0.5)	14.2 (0.6)	< 0.001
Protein, %	25.2 (0.6)	21.9 (0.5)	11.6 (0.4)	< 0.001
Lactose, %	3.1 (0.1)	3.7 (0.1)	*5.5 (0.4)	< 0.001
Dry matter, %	37.2 (0.7)	35.5 (0.1)	31.2 (0.7)	< 0.001
IgG, mg/mL	*92 (40)	*85 (35)	18.3 (2.8)	< 0.001
IgA, mg/mL	*11 (8)	8.1 (0.8)	*2.8 (2.5)	< 0.001

*Not normally distributed variable

Serum analysis

The concentrations of the parameters measured in the serum are shown in **Table 5**. The concentration of C4 3-4 days before farrowing was higher in parity 4 to 7 sows compared to parity 1 to 3 sows, whereas at d 1 of lactation, the concentration of C4 tended to be lower in the parity 4 to 7 sows.

The serum concentration of C4 3-4 days before farrowing was negatively associated with CY and at d 1 of lactation, the logarithmic transformation of NEFA was negatively associated with CY and the logarithmic transformation of C4 was positively associated with CY ($R^2 = 0.39$, $P = 0.001$). The obtained regression equation was: CY = 3582 – 1603 C4 (µmol/L) + 1077 10log C4 (µmol/L) – 922 10log NEFA (mmol/L). Details of the regression equation are

shown in **Table 3** and raw data of these variables are plotted against CY in supplementary **Figure 4**, **Figure 5** and **Figure 6**.

Table 5 *Comparison of serum metabolites between sows of different parity groups. Variables were analysed with an independent samples T-test and mean ± SEM is given. All variables were normally distributed.*

Variable	Parity group		SEM	*P*
	1-3	4-7		
Number of sows	18	19		
Urea 3-4 days before farrowing, mg/dL	32.7	30.7	0.83	0.241
Creatinine 3-4 days before farrowing, mg/dL	2.7	2.9	0.06	0.153
NEFA 3-4 days before farrowing, mmol/L	0.67	0.79	0.07	0.431
C4 3-4 days before farrowing, µmol/L	0.43	0.55	0.03	0.047
Urea at d 1 of lactation, mg/dL	32.0	34.5	1.4	0.383
Creatinine at d 1 of lactation, mg/dL	2.9	3.0	0.06	0.160
NEFA at d 1 of lactation, mmol/L	0.24	0.25	0.03	0.641
C4 at d 1 of lactation, µmol/L	0.97	0.68	0.11	0.053
IgG at d 111 of gestation, mg/mL	14.1	16.4	0.77	0.138
IgA at d 111 of gestation, mg/mL	1.8	2.3	0.17	0.149
IgG at d 1 of lactation, mg/mL	13.0	14.5	0.69	0.305
IgA at d 1 of lactation, mg/mL	1.6	2.1	0.18	0.164

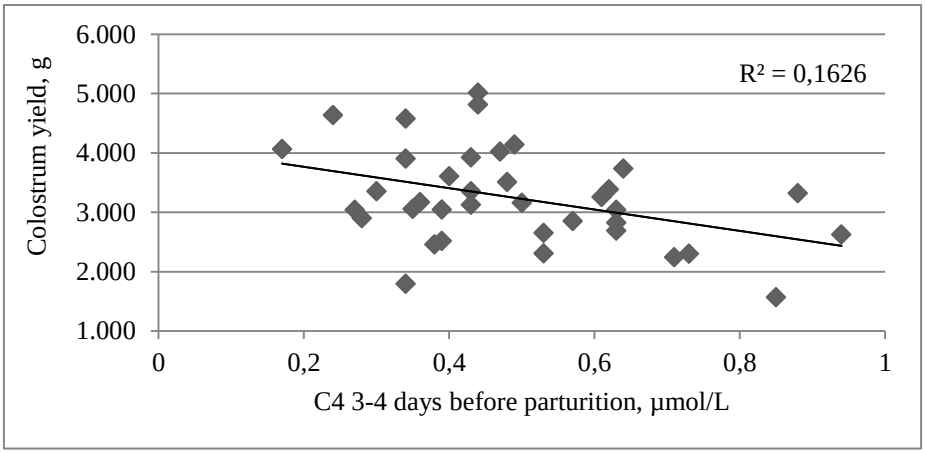

Figure 4 *The association between CY and C4 3 to 4 days before farrowing.*

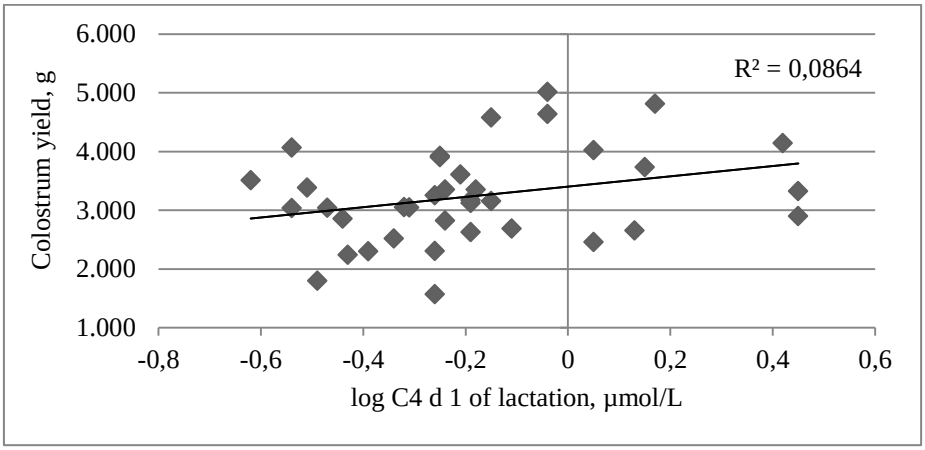

Figure 5 *The association between CY and the logarithmic serum concentration of C4 at d 1 of lactation.*

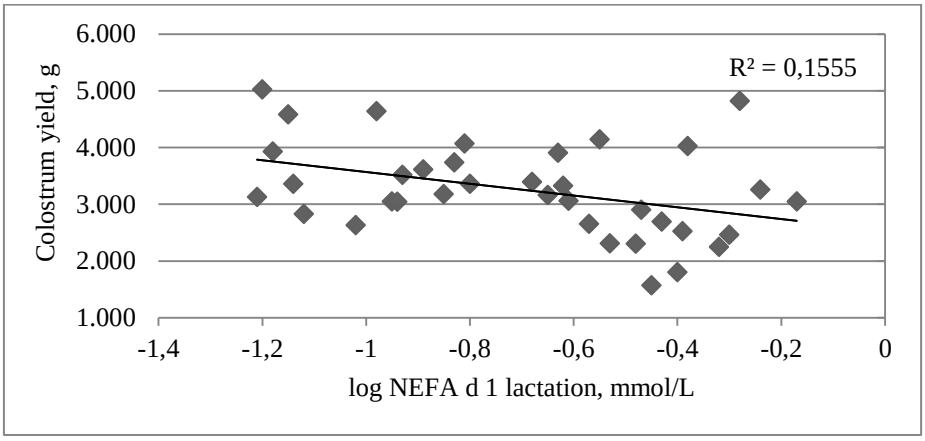

Figure 6 *The association between CY and the logarithmic serum concentration of NEFA at d 1 of lactation.*

DISCUSSION

The negative association between CY and ΔBF d 85-109 we observed has never been described before. As we did not collect more data between d 85 and d 109 of gestation, we can only propose some hypotheses that might explain this association. The period between d 85 and d 109 of gestation is considered to be important for mammogenesis (Kensinger et al., 1982; Ji et al., 2006) which was suppressed by keeping sows in an anabolic state during this period (Weldon et al., 1991). Our study population was mainly catabolic between d 85 and 109 of gestation and there is no information available to date whether this benefits gestational mammogenesis. The negative association between CY and ΔBF 85-109 could also be the result of a higher energy demand of sows with a higher mammary development. Aside from the possible association with mammogenesis, BF and changes in BF could also alter the sow's level of insulin sensitivity and thus its lactogenesis. Decreased insulin sensitivity is needed to a certain extent in order to direct glucose to the mammary gland (Père end Etienne, 2007) where it is used for lactose synthesis (Shennan and Peaker, 2000). Père et al. (2000) state that all sows develop an insulin resistance starting from d 85 of gestation and that this is more apparent in fat sows. A positive energy balance increases the concentration of leptin (Barb et al., 2001) which leads to a lower insulin sensitivity (Franks et al., 2007; Papadopoulos et al., 2009). It might be worthwhile looking further into the relations between the change of BC during late gestation, gestational mammogenesis, colostrogenesis and CY.

The higher CY in sows with parities 1 to 3 corresponds to the findings of Devillers et al., (2007) who reported that second and third parity sows tended to produce more colostrum than primiparous and older sows. As we were unable to detect differences between primiparous and second to third parity sows, perhaps due to lack of power, and because of graphical interpretation of the data, we combined first to third parity in one group. The observed association between parity group and CY cannot be explained by parity as such, but because

other factors differ between parity groups. As thoroughly described in the results section, we identified ΔBF d 109-1 and gestation length as the 2 factors differing between parity groups and being correlated to CY, thus proving to be candidates to partially explain the association between parity group and CY in this study. The variability in CY explained by parity group was higher than the variability explained by ΔBF d 109-1 and gestation length. This indicates that there are other factors associated to parity that contribute to the variability in CY; however, these have not been identified in this study. Furthermore, not all variability in CY explained by these 2 factors will be covered by the parity group. Nonetheless, this indicates that the gestation length and ΔBF d 109-1 might partially explain the difference in CY between parity groups observed in this study and, therefore, they will be further discussed. Back fat thickness at d 85 of gestation also differed between parity groups and was correlated to CY but was not kept in the model. We cannot explain the different BF between parity groups although the relatively low feeding practices during gestation at this farm might be the cause of a gradual decrease in BF over successive parities.

The negative association between gestation length and CY was also found by Devillers et al., (2007). Milon et al. (1983) suggested that CY and gestation length were negatively associated due to a decreased BW_B and vitality of the piglets. These litter characteristics have shown to be important in determining CY (Devillers et al., 2007), though we did not observe any differences in BW_B and t_{FS} between piglets born before d 114 of gestation and piglets born after.

We propose a relatively easy nutrient balance model of sows at the end of gestation where on the one hand, the input of nutrients available for metabolic processes are derived from either feed or body reserves, whereas on the other hand, the loss of nutrients at the end of gestation are determined by the total litter BW_B and the loss of nutrients through colostrum. The feed intake and the litter BW_B were not associated with CY and sows with a higher CY also had a

higher nutrient output through colostrum. Thus, as colostrum is mainly produced the week prior to farrowing (Devillers et al., 2006), we would expect the use of body fat and protein reserves to increase with an increasing CY in order to obtain the proposed nutrient balance. Our results showed the opposite. The elevated use of body fat (ΔBF d 109-1) and body fat or protein (C4 3-4 days before farrowing) was associated with a decreased CY. The parity 4 to 7 sows used more body fat and protein reserves during the last days before farrowing and this might be to cover their higher maintenance requirements compared to young sows (Noblet et al., 1998) made even more prominent due to the low feed supply. The higher catabolic state of older sows did likely prohibit sows from producing colostrum at their full potential. It is an interesting observation that sows that are catabolic during the last days of gestation eventually produce a lower CY as this indicates that the use of body reserves cannot fully compensate a nutrient intake below nutrient requirements.

Colostrum yield was negatively associated to C4 before farrowing, whereas it was positively associated to C4 at d 1 of lactation, where it is likely an indicator of body protein catabolism as the association between NEFA and CY was opposite. During the 24 h following parturition, the secretion of the mammary cells becomes abundant (Devillers et al., 2006) and hence the body's protein can be used to deliver AA or glucogenic substrates to the mammary gland (Boyd et al., 1995). Colostrum yield was negatively associated with NEFA at d 1 of lactation which again indicates the use of body fat reserves around farrowing should be prohibited.

The chemical composition of colostrum revealed high concentrations compared to other studies (Le Dividich et al., 2004; Devillers et al., 2007; Foisnet et al., 2010a) without showing a lower CY. Our study was performed in PIC sows of which colostrum composition was not described before. Farmer et al. (2007) showed that chemical colostrum composition differs between genotypes yet never as much as we observed. Sows in our study were mostly

catabolic during the month prior to farrowing and we should consider this as a factor affecting colostrum composition.

We should be careful when extrapolating the associations between CY and changes in BC observed in this study as most sows in our study were catabolic during observation probably due to the relatively low feed supply.

In conclusion, BF changes between d 85 and d 109 of gestation were negatively associated to CY and parity 4 to 7 sows had a lower CY than parity 1 to 3 sows. We identified gestation length and the extent in which the body's energy and protein reserves were used the last days before farrowing as possible underlying factors possibly explaining part of the parity effect. Sows that were catabolic the week prior to farrowing seemed unable to produce colostrum to their full potential. Colostrum composition did not alter when CY increased. These findings indicate that a proper management of the sow's BC during late gestation could be a tool to optimize the intrinsic capacity of the sow's CY.

3.2.

Effect of peripartal feeding strategy on colostrum yield and composition in sows

Adapted from

Decaluwé, R., D. Maes, A. Cools, B. Wuyts, S. De Smet, B. Marescau, P.P. De Deyn, and G. P. J. Janssens

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ABSTRACT

Research showed a positive association between BF change the week before farrowing and CY. This study tested the causality of this association, hence to optimize CY by altering the sow's peripartal feeding strategy. Sows were randomly divided into 2 treatment groups at d 108 of gestation. The first group (**L**, n = 28) received 1.5 kg feed/d, the second group (**H**, n = 22) received 3 times 1.5 kg feed/d until farrowing. The DFI and CY were measured. Colostrum was analyzed for nutrient composition, AA and fatty acids, IgG and IgA. Sow serum was obtained at d 108 of gestation and d 1 of lactation after overnight fasting, and analyzed for NEFA, C4, creatinine, urea, 3-hydroxy-butyrylcarnitine (**3-OH-C4**), IgG, and IgA. Based on BF at d 108, sows were divided into BC groups: skinny (< 17 mm, n = 15), moderate (17 to 23 mm, n = 21), fat (> 23 mm, n = 14). We performed ANOVA with treatment and BC as fixed factors and Scheffé *post hoc* test. The week before farrowing, the L-group had the lowest DFI (1.5 kg) and within the H-group, fat sows (3.8 kg) had a lower DFI than skinny sows (4.3 kg) ($P = 0.006$). The H-group tended to have a greater total CY ($P = 0.074$) and had a greater CY/kg liveborn piglet ($P = 0.018$) than the L-group. Compared to sows in moderate BC, fat sows had a lower total CY ($P = 0.044$), and a lower CY/kg liveborn piglet ($P = 0.005$). The H-group had a greater concentration of lactose ($P = 0.009$) and n-3 PUFA ($P < 0.001$) but a lower concentration of protein ($P = 0.040$) in colostrum than the L-group. The concentration of IgG and IgA did not differ between treatment and BC groups. Serum parameters at d 108 were similar between the treatment groups and BC groups. At d 1, the H-group mobilized less body fat (NEFA: $P = 0.002$) and protein (creatinine: $P < 0.001$) reserves but had a greater ratio urea:NEFA ($P < 0.001$) and less ketone bodies as indicated by 3-OH-C4 carnitine (3-OH-C4: $P < 0.001$) compared to the L-group. This indicates a more balanced entry of metabolites in the citric acid cycle and thus a better support of the maternal peripartal metabolism in the H-group. Serum parameters did not differ between BC groups.

Both CY and composition can be influenced by the peripartal feeding strategy and BC. The highest CY and most beneficial colostrum composition were obtained when sows entered the farrowing unit in a moderate BC and were provided a high peripartal feeding strategy.

Key words: colostrum, energy, feeding strategy, peripartal, protein

INTRODUCTION

Approximately 30% of sows produce insufficient colostrum for her litter (Foisnet et al., 2010a; Decaluwé et al., 2013). Assessing this problem could be rather complicated as the sows' CY is associated with sow, piglet and environmental traits (Farmer and Quesnel, 2009) and strategies that increase CY should not have negative effects on colostrum composition. Previous results show that for similarly managed sows there is no association between CY and colostrum composition (Decaluwé et al., 2013) but it might still be that increasing CY through changes in the management alters colostrum composition as adding fat to the sow's diet increases the colostral fat content (Jackson et al., 1995) and milk production (Coffey et al., 1982).

Martineau et al. (2013) report that a good transition from gestation to lactation metabolism is essential for a good lactation performance. During late gestation, the sow's metabolism adapts by sparing glucose for fetuses and lactation while the sow herself starts using more ketogenic energy substrates (Boyd and Kensinger, 1998). When the supply of nutrients through the sow's diet is low, sows become catabolic which increases the use of ketogenic energy substrates. This can result in ketosis (Theil et al., 2013) and although this generally does not result in clinical symptoms, it might lead to suboptimal production. Colostrum is produced during the last month of gestation but mainly during the last week before farrowing (Devillers et al., 2006) and the BF change during this last week of gestation is positively associated to CY (Decaluwé et al., 2013).

The hypothesis of the present study is, therefore, that the feeding strategy a week before farrowing could affect the maternal metabolism and the level of nutrients available for the mammary gland resulting in a different CY.

MATERIAL AND METHODS

Study population and experimental design

The experiment was approved by the ethical committee of the Faculty of Veterinary Medicine, Ghent University (EC2012/099).

The study was conducted from July until September 2012 in a commercial farm comprising 1700 PIC sows and practicing a 2-week-batch system. Ninety-five sows (parity 2 to 7), equally divided over 2 batches were observed from d 85 of gestation until weaning. Only sows with a gestation length of 114-116 days were included in the study and because estimating CY was labor-intensive, the number of sows that could be monitored correctly at the same time was limited. Therefore, we collected data of 50 sows. The day of first insemination was defined as d 0 of gestation, the day of parturition as the last day of gestation and d 0 of lactation.

From d 29 until d 106 of gestation, sows were similarly managed and group-housed with 15 sows per pen. Two feeders that dropped a small amount of the gestation diet (meal) at regular intervals throughout the day were present per pen. The total amount of feed provided was on average 2.5 kg•sow^{-1}•day^{-1}. Sows were moved to the farrowing unit on d 107 of gestation, where they were housed individually in conventional farrowing crates until weaning at 3 weeks of lactation. Floor heating and an infrared lamp were used to create a microclimate for the piglets.

Upon arrival in the farrowing unit, sows were stratified for parity, change in BF between d 85 and d 108 of gestation, and BF at d 108 of gestation and randomly divided into 2 treatment groups. The first group received a high peripartal feeding strategy (**H**, n = 22): 1.5 kg of a

transition diet (meal) 3 times a day (07.30 h, 11.30 h, 16.30 h) between d 108 of gestation and d 3 of lactation. The second group received a low peripartal feeding strategy (**L**, n = 28): 1.5 kg of the same transition diet once a day at 07.30 am until day of farrowing. At d 1 of lactation, the L-group was fed twice and at d 2 of lactation they were fed 3 times 1.5 kg of the transition diet. Approximately 4 h after each meal, feed left-overs were recorded. Starting from d 3 of lactation until weaning, all sows received the same lactation diet (meal) 4 times a day of which the amount gradually increased. When a sow had not finished the meal of the previous day, the trough was emptied and a 10 to 20 % smaller amount of fresh feed was given. The feeding pattern of both treatment groups between d 108 of gestation and weaning is shown in **Figure 1**. During the entire experiment, sows had free access to fresh drinking water (drinking nipple – flow 1.5 to 2 L/min).

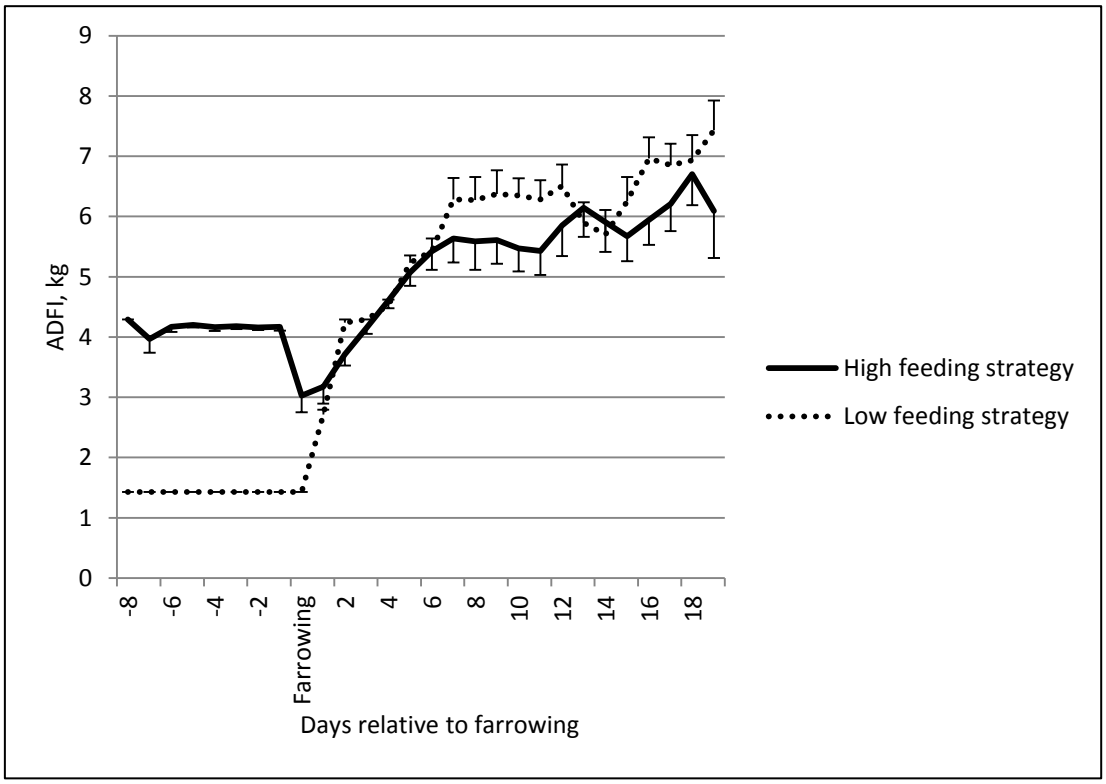

Figure 1. *ADFI pattern of both treatment groups from d 108 of gestation until the end of lactation are shown. Error bars represent the SEM.*

Farrowing induction was not applied, and farrowing intervention was minimized to manual extraction when the birth interval between 2 piglets exceeded 1 h. No oxytocin was administered during parturition as this might interfere with mammary secretion (Ellendorf et al., 1982). No additional help or care was given to the piglets unless there was a risk for them of getting crushed. On d 2 of lactation, litters were standardized to 11 ± 1 piglet by cross-fostering. From d 2 of lactation, piglets were offered creep feed. The feed intake of the piglets was not measured.

Parameters and measurements

All measurements of BF were performed by the same person on standing sows at the P2-position (Maes et al., 2004) at both sides of the spinal cord after hair removal using a digital BF indicator (Renco Lean Meter, S.E.C. Repro Inc., Ange-Gardien-de-Rouville, Québec, Canada). Values from the 2 measurements were averaged to obtain a single BF measurement. The BF was measured at d 85 and d 108 of gestation, at d 1 of lactation and at weaning.

The CY was calculated as the sum of the individual piglet's CI within a litter as described by Devillers et al. (2004b) using following variables: BW_B (kg), weight at 17 to 24 h of age (**BW_{24}**, kg), duration of CI (**t** in min and with 17 h ≤ t ≤ 25 h), and time between birth and first suckling (**t_{FS}**, min). The t_{FS} was estimated to be 35 min which was based on observations from a previous study performed at the same farm (Decaluwé et al., 2013). As explained by Devillers et al. (2004b), an error of 15 min of t_{FS} induces a miscalculation of intake by the piglet of 6 g/kg BW_B or less than 2 % error. The used regression equation was: $CI = -217.4 + 0.217 \times t + 1861019 \times BW_{24}/t + BW_B \times (54.80 - 1861019/t) \times (0.9985 - 3.7 \times 10^{-4} \times t_{FS} + 6.1 \times 10^{-7} \times t^2_{FS})$. When a piglet was born, the back of the piglets was dried with a paper towel and marked. Piglets were ear-tagged allowing identification. The umbilical cord was shortened when it was longer than approximately 15 cm. After weighing (scale accuracy 0.02 kg), they were placed in the farrowing pen again with their nose against the sow's vulva.

Observed sow parameters were parity, gestation length, farrowing duration, number of total, liveborn and stillborn piglets, and number of weaned piglets. Observed piglet parameters were birth interval, pre-weaning mortality, BW_B, BW_{24}, and body weight at d 3, d 7 and d 14 of age and at weaning. Piglets were cross-fostered after measuring the BW_{24} and from then on, litter weight gain was calculated per sow.

Samples

Feeds were sampled at the end of the study.

Sow's serum (serum cloth activator tubes, 18 mL) and plasma (sodium fluoride:potassium oxalate tubes, 2 mL) was collected by punction of the *vena jugularis* while restraining sows with a snare at d 108 of gestation and at d 1 of lactation before the morning meal after an overnight fasting period (minimum 10 h). Samples were stored in iced water, subsequently centrifuged at 1000 × g for 15 min at room temperature and stored frozen at -20 °C until further analysis.

Colostrum (40 mL) was collected from all teats of 1 side of the udder at 6 h after birth of the first piglet, after an i.m. injection of 2 mL of oxytocin (10IU/mL) 5 min before sampling. At the time of sample collection, 10 sows did not complete farrowing but they were also injected 2 mL of oxytocin. The colostrum samples were subdivided into 6 subsamples, frozen at -20 °C and stored until further analysis.

Analyses of samples

Feed. Nutritional composition of the diets was analyzed according to the Association of Official Analytical Chemists methods (Thiex, 2002) (ISO 5983-1, 2005; ISO 1443, 1973; ISO 5498, 1981). All percentages represent an as-fed basis. The gestation diet contained 89.9% dry matter (DM), 2.4% of crude fat (CF), 13.5% of crude protein (CP), 10.2% of crude ash (CA) and 8.0% of crude fiber (CFib). The transition diet contained 91.1% DM, 4.4% CF, 13.0% CP, 8.9% CA and 7.9% CFib. The lactation diet contained 89.6% DM, 3.3% CF,

17.3% CP, 10.4% CA and 3.7% CFib. The creep feed of the piglets' diet contained 93.7% DM, 10.1% CF, 19.7% CP, 6.3% CA and 4.3% CFib.

The fatty acid profile of the transition diet was determined as described by Stefanov et al. (2010) and is shown in **Table 1**.

Table 1. *Fatty acid profile of the sow's transition diet and intake in both treatment groups.*

Variable	Value/100 g fatty acids	Value/100 g feed	Daily intake H-group	Daily intake L-group
SFA, g	38.3	1.93	86.7	28.9
MUFA, g	26.6	1.34	60.4	20.1
n-6 PUFA, g	29.1	1.46	65.9	22.0
n-3 PUFA, g	4.8	0.24	10.8	3.6
Linoleic acid n-6 C18:2, g	29.1	1.46	65.8	21.9
Arachidonic acid n-6 C20:4, mg	10.0	0.50	22.5	7.5
Linolenic acid n-3 C18:3, g	4.6	0.23	10.4	3.5
EPA n-3 C20:5, mg	20.0	0.80	36.0	12.0
DHA n-3 C22:6, mg	50.0	2.70	121.5	40.5
(n-6):(n-3) PUFA	6.08	6.08	6.08	6.08

EPA: eicosapentaenoic acid; DHA: docosahexaenoic acid; H: high feeding level during the peripartal period; L: low feeding level during the peripartal period

Serum and plasma. Serum was analyzed for urea, creatinine, NEFA, C4, 3-OH-C4, IgG and IgA. Plasma was analyzed for glucose. (Iso)butyrylcarnitine is a catabolite of AA that can be metabolized to oxaloacetate, which is needed to react with acetyl-CoA when entering the citric acid cycle (Michal, 1999a,b). Still, we need to be critical when interpreting this variable as not only amino acids but also fatty acids can be a source of C4. In the latter case, we should expect a same trend in NEFA and C4. Urea, creatinine, NEFA, and glucose were measured spectrophotometrically (Ultrospec IIE, LKB, Biochrom, Cambridge, England) using a commercial colorimetric diagnostic kit (references UR107 for urea, CR510 for creatinine, FA115 for NEFA, and GL2623 for glucose, Randox Laboratories, Crumlin, United

Kingdom). Quantitative electrospray tandem MS was used to determine C4 and 3-OH-C4 as described by Zabielski et al. (2007). A porcine quantitative sandwich enzyme immunoassay technique was used to analyze IgG (dilution 1:100000) and IgA (dilution 1:40000) (references A100-104 for IgG and A100-102 for IgA, Bethyl Laboratories Inc., Texas, USA). All samples were analyzed in duplicate. The intra and interassay coefficient of variation were, respectively, 2.9 and 5.2% for urea, 2.8 and 2.9% for creatinine, 4.8 and 4.3% for NEFA, 9.6 and 9.5% for C4 and 3-OH-C4, 3.1 and 6.3% for IgG, and 3.2 and 9.8% for IgA.

Colostrum. Colostrum was analyzed for its macronutrient, fatty acid and AA acid composition, IgG and IgA. Nutritional composition (fat, protein and lactose content) was estimated by Lactoscope FTIR Advanced type FTA-3.0 (Delta Instruments, Drachten, Netherlands). Samples were diluted 1:2 with distilled water and calibrated curves were verified with Gerber and Kjeldahl analysis (R^2 between FTIR and Gerber = 0.9975; R^2 between FTIR and Kjeldahl = 0.9997). To determine the fatty acid profile, milk fat was extracted as described by Chouinard et al. (1997) and subsequently methylated and analyzed by gas liquid chromatography as described by Stefanov et al. (2010). The intra and interassay coefficient of variation were, respectively, 0.24 and 0.23%. For analysis of total AA, proteins and peptides in the colostrum samples were first hydrolyzed to break all peptide bounds. Therefore, colostrum samples were first dried with a Savant speed-vac system and then further dried into an exsiccator with potassium hydroxide platelets and phosphorus pentoxide. Next, 6 N HCl containing 1 % fenol and 5 % thioglycol acid was added to the dried colostrum samples. Hydrolysis of the colostrum samples was then performed under inert conditions using nitrogen gas to prevent oxidative degradation of AA during acid hydrolysis and under vacuum. The samples were heated at 110 °C for 24 h and subsequently dried under vacuum. To remove all acid traces the samples were washed several times with a solution of water, ethanol and tri-ethylamine (2:2:1 v/v). To the dry hydrolysis product sampling buffer (lithium

citrate buffer) was added and dilutions were made for the analysis of AA with a Biotronik LC 6001 Amino Acid Analyzer (Biotronik, Maintal, Germany). For colorimetric detection the ninhydrin method was used. In the analysis, we grouped the essential and non-essential AA according to Lewis (2001). A porcine quantitative sandwich enzyme immunoassay technique was used to analyze colostral IgG (dilution 1:500000) and IgA (dilution 1:50000) in duplicate (references A100-104 for IgG and A100-102 for IgA, Bethyl Laboratories Inc., Montgomery, Texas, USA). The intra and interassay coefficient of variation were, respectively, 2.3 and 9.7% for IgG, and 3.4 and 2.6% for IgA.

Statistical Analysis

All statistical analyses were performed using SPSS 19.0 (IBM Company Headquarters, Chicago, Illinois), considering statistical significance when $P < 0.05$ (2-sided tests).

Normally distributed variables are reported as LSmean ± SEM and not normally distributed variables as median ± IR. Normality of the data was analyzed with the Kolmogorov-Smirnov test, the Levene's test was used to verify homogeneity of variance.

Data were subjected to GLM with treatment group and BC group as fixed factors. Interaction terms were tested, removed from the model if not significant and only presented if significant ($P < 0.05$). Sows were assigned to 1 of 3 BC groups according to their BF at d 108 of gestation: skinny (< 17 mm), moderate (17 to 23 mm) and fat (> 23 mm) BC. These 3 groups based on BC contained 15, 21 and 14 sows, respectively. The number of sows within the skinny, moderate and fat BC group was 8, 12, and 8 within the L-group, and 7, 9 and 6 within the H-group, respectively. The number of sows in both treatment groups was not identical (L-group: n = 28, H-group: n = 22) because the number of sows that could be correctly observed while estimating CY was limited by the practical conditions. Normality and homogeneity of variance of the residuals were examined graphically and verified using the Kolmogorov-Smirnov test, Q-Q plot and the Levene's test. To determine significant differences, a *post hoc*

Scheffé test was performed when appropriate. When data were not-normally distributed, a Kruskall-Wallis analysis was performed and pairwise comparisons were executed when appropriate. The odds ratio for producing/consuming less than 160 g of colostrum per kg liveborn piglet, which is proposed as the minimum required amount of CI (Le Dividich et al., 2005a), was calculated for the L-group compared to the H-group.

RESULTS

Feed intake and BF

An interaction effect was observed between treatment and BC group in average daily feed intake (**ADFI**) between d 108 of gestation and d 1 of lactation (**Figure 2**). It was lower for the L-group (1.5 ± 0 kg) than for the H-group but within the H-group, skinny sows (4.3 ± 0.01 kg) had a greater ADFI than fat sows (3.8 ± 0.2 kg; $P = 0.006$) and tended to have a greater ADFI than sows in moderate BC (4.0 ± 0.07 kg; $P = 0.092$). The ADFI during lactation did not differ across treatment and BC groups. Total feed intake between d 108 of gestation and weaning tended ($P = 0.054$) to be greater in the H-group than in the L-group (**Table 2**).

The L-group lost more BF than the H-group ($P = 0.001$) between d 108 of gestation and d 1 of lactation and this was independent of BC group. The L-group lost less BF during lactation ($P = 0.072$) as did skinny sows compared to sows in moderate ($P = 0.046$) and fat BC ($P = 0.003$). The loss of BF during the entire period of observation (d 108 of gestation until weaning) did not differ between treatment groups ($P = 0.188$), while skinny sows lost less BF than sows in moderate ($P = 0.003$) or fat BC ($P < 0.001$). The BC of sows at d 108 of gestation was similar to the BC at d 85 of gestation. Furthermore, skinny sows lost BF between d 85 and d 108 of gestation while fat sows gained BF during this period ($P = 0.005$). Feed intake, BF and BF changes are presented in **Table 2**.

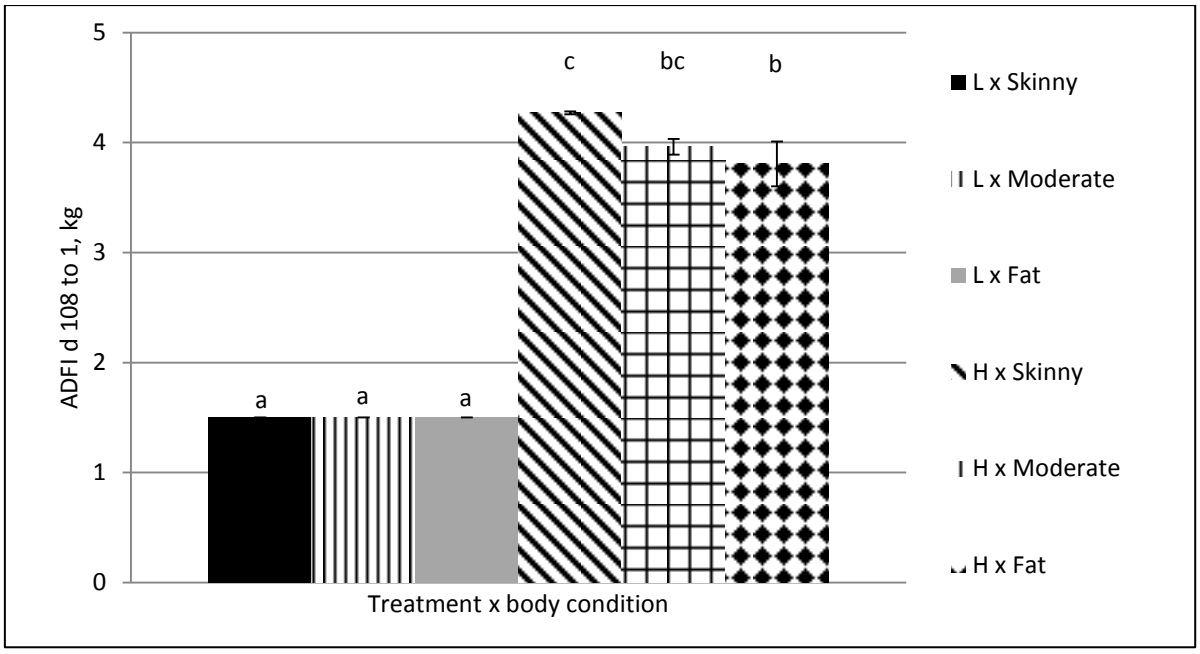

Figure 2. *ADFI between d 108 of gestation and d 1 of lactation for both treatment groups interacted with BC group. Means without a common letter superscript differ (P < 0.05). H: high feeding level during the peripartal period; L: low feeding level during the peripartal period*

Table 2. *Feed intake, BF and BF change for treatment (TR) and BC groups at d 108 of gestation. Interaction terms were tested but were not significant (P > 0.05).*

Variable	TR		BC			SEM	*P*	
	H	L	Skinny	Moderate	Fat		TR	BC
ADFI lactation, kg	5.3	5.8	5.7	5.6	5.4	0.1	0.166	0.648
FI d 108-weaning, kg	129 [£]	117 [$]	126	123	118	2.9	0.054	0.650
BF d 85, mm	18.5	19.2	13.4 [a]	18.9 [b]	24.6 [c]	0.7	0.553	< 0.001
BF d 108, mm	19.4	19.6	12.8 [a]	19.7 [b]	26.5 [c]	0.8	0.876	< 0.001
ΔBF d 85-108, mm	0.9	0.4	-0.7 [a]	0.8 [ab]	1.9 [b]	0.3	0.353	0.004
ΔBF d 108-1, mm	-0.05 [b]	-1.7 [a]	-0.8	-1.0	-1.1	0.2	0.001	0.004
ΔBF lactation, mm	-2.6 [a]	-1.6 [b]	-0.7 [c]	-2.2 [b]	-3.1 [a]	0.3	0.034	0.002
ΔBF d 108-weaning, mm	-2.6	-3.3	-1.5 [b]	-3.2 [a]	-4.2 [a]	0.2	0.188	< 0.001

a - c Within a row and within main effect, means without a common letter superscript differ ($P < 0.05$); $ - £ Within a row and within main effect, means without a common symbol superscript tend to differ ($0.05 < P < 0.10$); FI: feed intake; ΔBF: BF change; H: high feeding level during the peripartal period; L: low feeding level during the peripartal period

Colostrum yield

The CY was affected by both treatment and BC at d 108 of gestation with no interaction observed. Sows of the H-group tended to have a greater total CY (P = 0.074) and secreted more colostrum per kg liveborn piglet (P = 0.018) than sows of the L-group. Compared to sows in moderate BC, fat sows had a lower total CY (P = 0.044), a lower CY per liveborn piglet (P = 0.016) and a lower CY per kg liveborn piglet (P = 0.005). Colostrum yield parameters are shown in **Table 3**.

Table 3. *Colostrum yield, macronutrient and Ig composition of colostrum in treatment (TR) and BC groups at d 108 of gestation. Interaction terms were tested but not significant (P > 0.05).*

Variable	TR		BC			SEM	*P*	
	H	L	Skinny	Moderate	Fat		TR	BC
CY								
Total CY, g	3999 $^{£}$	3508 $^{\$}$	3874 ^{ab}	3991 ^{b}	3163 ^{a}	141	0.074	0.036
CY/liveborn piglet, g	312	287	297 ^{ab}	345 ^{b}	230 ^{a}	17	0.435	0.016
CY/kg liveborn piglet, g	239 ^{b}	200 ^{a}	215 ^{ab}	245 ^{b}	178 ^{a}	9	0.018	0.005
Colostrum Composition								
Macronutrients								
% fat	5.0	5.2	4.7	4.9	5.8	0.2	0.562	0.108
% protein	14.7 ^{a}	15.3 ^{b}	14.5 ^{a}	15.2 ^{ab}	15.4 ^{b}	0.1	0.040	0.040
% lactose	2.5 ^{b}	2.2 ^{a}	2.5 $^{£}$	2.3 $^{\$£}$	2.2 $^{\$}$	0.1	0.009	0.057
% DM	22.2	22.7	21.7 ^{a}	22.4 ^{ab}	23.4 ^{b}	0.2	0.225	0.018
Total fat, g	195	183	184	196	183	9	0.540	0.819
Total protein, g	589	531	558 $^{\$£}$	605 $^{£}$	487 $^{\$}$	22	0.185	0.081
Total lactose, g	99 ^{b}	75 ^{a}	98 ^{b}	89 ^{ab}	69 ^{a}	4	0.001	0.005
Total DM, g	883	788	841	889	738	32	0.140	0.144
Ig								
IgG, mg/mL	50.1	59.0	65.0	39.1	47.5	4.2	0.620	0.123
IgA, mg/mL	9.8	10.0	8.3 $^{\$}$	10.4 $^{\$£}$	11.0 $^{£}$	0.52	0.828	0.097
Total IgG, g	202	208	249	209	153	18	0.786	0.127
Total IgA, g	37.7	35.2	31.0	41.8	33.8	2.3	0.665	0.124

a - c Within a row and within main effect, means without a common letter superscript differ (P < 0.05)

$ - £ Within a row and within main effect, means without a common symbol superscript tend to differ (0.05 < P < 0.10).

H: high feeding level during the peripartal period; L: low feeding level during the peripartal period

Fourteen percent of the H-group and 32% of the L-group produced less than 160 g colostrum per kg liveborn piglet. Odds of a sow producing less than 160 g colostrum per kg liveborn piglet were 3.0 times higher in L-group than in the H-group. Twenty-seven % of piglets born in the H-group, and 34% of the piglets born in L-group, consumed less than 160 g colostrum per kg BW_B. Odds of a piglet consuming less than 160g colostrum per kg BW_B were 1.38 times higher in the L-group than piglets in the H-group.

Colostrum composition

Macronutrient and immunoglobulin composition. The percentage of colostral protein was lower for the H-group compared to the L-group (P = 0.040), and lower for skinny sows compared to fat sows (P = 0.048). Total g of colostral protein output did not differ between treatment groups and tended to be greater for sows in moderate BC compared to fat sows (P = 0.077). Percentage of lactose was greater for the H-group compared to the L-group (P = 0.009) and tended to be greater for skinny sows compared to fat sows (P = 0.060). Total g of lactose output was greater for the H-group compared to the L-group (P = 0.001). Fat sows had a lower total lactose output than skinny sows (P = 0.005) and tended to have a lower lactose output than sows in a moderate BC (P = 0.053). Percentage of colostral DM was greater for fat sows compared to skinny sows (P = 0.017) but this difference was not observed when total output of colostral DM was considered. Fat sows tended to have a greater concentration of IgA compared to skinny sows (P = 0.062). The concentration of IgG and total output of IgG and IgA did not differ across treatment or BC groups. Macronutrient and Ig composition of colostrum are shown in **Table 3**.

Amino acids and fatty acids composition. Concentration of essential (P = 0.015) and non-essential AA (P = 0.009) was greater for sows in the L-group compared to the H-group and lower for skinny sows compared to the other BC groups (essential AA: P = 0.010, non-

essential AA: P = 0.009). Total colostral output of essential and non-essential AA did not differ between treatment and BC groups. Details are shown in **Table 4**.

Sows in the H-group had greater colostral concentrations of MUFA, n-6 PUFA, n-3 PUFA, linoleic acid and linolenic acid and a lower concentration of arachidonic acid compared to the L-group (for all $P < 0.001$). The (n-6):(n-3) ratio was lower for sows in the H-group compared to the L-group (P = 0.008). Fat sows had lower concentrations of SFA compared to the other BC groups (P = 0.001). Concentration of n-6 PUFA (P = 0.050) and linoleic acid (P = 0.033) was greater for fat sows than skinny sows. The fatty acid composition is shown in **Table 4**.

Table 4. *Amino acid and fatty acid composition of colostrum in treatment (TR) and BC groups at d 108 of gestation. Interaction terms were tested but were not significant (P > 0.05).*

Variable	TR		BC			SEM/	*P*	
	H	L	Skinny	Moderate	Fat	IR	TR	BC
AA								
EAA, mmol/L	569 [a]	620 [b]	551 [a]	612 [b]	627 [b]	11	0.015	0.010
NEAA, mmol/L	447 [a]	491 [b]	434 [a]	481 [b]	497 [b]	9	0.009	0.009
Total EAA, mmol	2151	2282	2124	2438	1977	93	0.490	0.109
Total NEAA, mmol	1795	1700	1678	1917	1564	74	0.536	0.128
Fatty acids, g/100 g FA								
SFA	32.6	32.6	33.5 [b]	32.8 [b]	31.4 [a]	0.23	0.857	0.001
MUFA	33.0 [a]	37.1 [b]	35.0	35.1	35.9	0.37	< 0.001	0.406
*n-3 PUFA	4.2 [b]	2.5 [a]	2.6	2.7	2.8	1.8	< 0.001	0.444
n-6 PUFA	23.6 [b]	21.0 [a]	21.6 [a]	22.1 [ab]	22.8 [b]	0.26	< 0.001	0.030
*(n-6):(n-3) PUFA	5.5 [a]	8.6 [b]	8.9	7.9	8.1	3.5	0.008	0.782
Linoleic acid n-6 C18:2	21.8 [b]	18.8 [a]	19.6 [a]	20.1 [ab]	20.8 [b]	0.28	< 0.001	0.017
Arachidonic acid n-6 C20:4	0.81 [a]	0.92 [b]	0.90	0.90	0.82	0.01	< 0.001	0.062
Linolenic acid n-3 C18:3	2.8 [b]	1.6 [a]	1.9	2.2	2.2	0.12	< 0.001	0.307
EPA n-3 C20:5	0.13	0.12	0.13	0.13	0.12	0.004	0.272	0.738
DHA n-3 C22:6	0.23	0.22	0.23	0.23	0.22	0.005	0.338	0.369

a - c Within a row and within main effect, means without a common letter superscript differ ($P < 0.05$)

*: not normally distributed variables; EAA: essential AA; NEAA: non-essential AA; FA: fatty acids; EPA: eicosapentaenoic acid; DHA: docosahexaenoic acid; H: high feeding level during the peripartal period; L: low feeding level during the peripartal period

(Re)productive performance

Parity (5 ± 1), gestation length (115 ± 1 d), farrowing duration (257 ± 18 min), average birth interval (20 ± 2 min), total born (15 ± 0.5), liveborn (14 ± 4) and stillborn piglets (0 ± 1), number of piglets that died before (1 ± 2) and after (0 ± 1) cross-fostering, and percentage of stillborn piglets (0 ± 6.8%) and percentage of piglets that died after cross-fostering (0 ± 9.1%) did not differ between treatment and BC groups. Percentage of piglets that died before cross-fostering tended (P = 0.075) to be greater in the H-group (10.1 ± 10.8%) than in the L-group (6.7 ± 18.3%) and no differences across BC groups were observed (7.4 ± 16.5%).

Piglets' BW_B, BW_{24} and weight gain during different periods of lactation is shown in **Table 5**. Litter weight gain between birth and 24 h of age tended to be greater for the H-group compared to the L-group (P = 0.058) and was lower for fat sows compared to sows in moderate BC (P = 0.031). Average piglet weight gain between birth and 24 h of age was lower for fat sows than for sows in moderate BC (P = 0.017). Litter (P = 0.013) and average (P = 0.006) piglet weight gain between d 3 and d 7 of lactation was greater for fat sows than for skinny sows. Average piglet weight gain during lactation tended to be greater for sows in moderate BC compared to skinny sows (P = 0.064).

Blood parameters sow

Concentrations of the blood parameters are shown in **Table 6**. At d 108 of gestation, fat sows tended to have a lower creatinine concentration than sows in moderate BC (P = 0.097). At d 1 of lactation, sows in the H-group had a greater concentration of urea (P = 0.001), a lower concentration of creatinine (P < 0.001), NEFA (P = 0.002), C4 (P = 0.016), 3-OH-C4 (P < 0.001) and IgA (P = 0.044). Sows in moderate BC tended to have a greater concentration of creatinine than fat sows (P = 0.084) and a greater concentration of C4 compared to other BC groups (P = 0.083). The ratio urea/NEFA (P < 0.001) and creatinine/NEFA (P = 0.015) was greater for sow in the H-group compared to sows in the L-group.

Table 5. *Piglets'* BW_B *and weight gain during lactation in treatment (TR) and BC groups at d 108 of gestation. Interaction terms were tested but were not significant (P > 0.05).*

Variable		TR		BC			SEM	*P*	
		H	L	Skinny	Moderate	Fat		TR	BC
Litter weight (gain), kg	BW_B TBP	18.28	18.70	18.73	17.96	19.12	0.57	0.699	0.953
	BW_B LBP	17.27	18.14	18.48	16.95	18.21	0.52	0.952	0.995
	BW_B SBP	2.20	1.56	1.24	2.11	1.82	0.25	0.304	0.645
	0 - 24h	1.36 £	1.01 $	1.23 ab	1.39 b	0.78 a	0.10	0.058	0.029
	24h - 3d	3.19	3.39	3.11	3.50	3.21	0.16	0.852	0.017
	3d - 7d	8.55	8.55	7.38 a	8.71 ab	9.55 b	0.29	0.246	0.014
	7d - 14d	17.06	17.00	15.48	18.44	17.50	0.57	0.961	0.169
	14d - weaning	9.60	10.56	9.32	10.97	9.75	0.52	0.161	0.080
	0 - weaning	39.48	40.04	35.98	42.05	40.48	1.3	0.880	0.136
Average piglet weight (gain), kg	BW_B TBP	1.29	1.39	1.34	1.39	1.28	0.038	0.321	0.592
	BW_B LBP	1.31	1.40	1.37	1.40	1.30	0.037	0.301	0.616
	BW_B SBP	1.33	0.92	0.71	1.30	1.05	0.13	0.203	0.445
	0 - 24h	0.11	0.090	0.10 ab	0.13 b	0.060 a	0.010	0.254	0.019
	24h - 3d	0.26	0.28	0.26	0.29	0.26	0.014	0.491	0.035
	3d - 7d	0.77	0.74	0.66 a	0.77 ab	0.85 b	0.022	0.629	0.003
	7d - 14d	1.55	1.46	1.36	1.57	1.54	0.046	0.780	0.006
	14d - weaning	0.90	0.94	0.84	1.01	0.88	0.042	0.474	0.128
	0 - weaning	3.60	3.51	3.22 $	3.77 £	3.58 $£	0.10	0.572	0.060

a - c Within a row and within main effect, means without a common letter superscript differ ($P < 0.05$)

$ - £ Within a row and within main effect, means without a common symbol superscript tend to differ ($0.05 < P < 0.10$)

TBP: total born piglets; LBP: liveborn piglets; SBP: stillborn piglets; H: high feeding level during the peripartal period; L: low feeding level during the peripartal period

Table 6. *Serum and plasma biochemical variables at d 108 of gestation and d 1 of lactation in treatment (TR) and BC groups at d 108 of gestation. Interaction terms were tested but were not significant (P > 0.05).*

Time	Variable	TR		BC			SEM/ IR	*P*	
		H	L	Skinny	Moderate	Fat		TR	BC
d 108 of gestation	Urea, mmol/L	4.4	4.3	4.7	4.0	4.5	0.19	0.758	0.217
	Creatinine, µmol/L	233	238	242 $^{\$£}$	241 $^{£}$	221 $^{\$}$	3.8	0.530	0.059
	Glucose, mmol/L	3.2	3.2	3.1	3.2	3.2	0.080	0.549	0.728
	NEFA, mmol/L	0.68	0.58	0.64	0.57	0.70	0.058	0.434	0.650
	C4, µmol/L	0.21	0.25	0.22	0.25	0.21	0.012	0.150	0.434
	*3-OH-C4, µmol/L	0.020	0.020	0.020	0.020	0.020	0.020	0.840	0.639
	IgG, mg/mL	17.8	19.5	19.9	18.8	17.3	0.54	0.576	0.159
	IgA, mg/mL	1.8	2.1	1.8	2.1	1.9	0.12	0.519	0.720
d 1 of lactation	Urea, mmol/L	4.4 ^{b}	3.6 ^{a}	4.3	3.9	3.8	0.12	0.001	0.138
	Creatinine, µmol/L	214 ^{a}	263 ^{b}	247 $^{\$£}$	246 $^{£}$	229 $^{\$}$	4.8	< 0.001	0.038
	Glucose, mmol/L	4.0	3.9	3.9	4.0	3.9	0.065	0.898	0.532
	*NEFA, mmol/L	0.25 ^{a}	0.45 ^{b}	0.23	0.32	0.48	0.44	0.002	0.331
	*C4, µmol/L	0.36 ^{a}	0.47 ^{b}	0.32 $^{\$}$	0.42 $^{£}$	0.30 $^{\$}$	0.25	0.016	0.083
	3-OH-C4, µmol/L	0.031 ^{a}	0.052 ^{b}	0.030	0.040	0.040	0.020	< 0.001	0.717
	IgG, mg/mL	13.6	15.6	14.7	14.9	14.4	0.43	0.136	0.842
	IgA, mg/mL	1.9 ^{b}	1.3 ^{a}	1.4	1.6	1.5	0.13	0.034	0.776
	*Urea:NEFA	28 ^{b}	7.5 ^{a}	19	10	9.1	23	< 0.001	0.260
	*Creatinine:NEFA	1.2 ^{b}	0.58 ^{a}	1.2	0.87	0.53	1.3	0.047	0.371

a - c Within a row and within main effect, means without a common letter superscript differ ($P < 0.05$)

$ - £ Within a row and within main effect, means without a common symbol superscript tend to differ ($0.05 < P < 0.10$)

*: not normally distributed variables; H: high feeding level during the peripartal period; L: low feeding level during the peripartal period

DISCUSSION

Both CY and (nutritional) composition were influenced by the sow's BC and the peripartal feeding strategy with the effect of these 2 being mainly independent. The highest CY and the highest colostral output of nutrients was achieved when sows entered the farrowing unit in a moderate BC (17 to 23 mm BF) and were provided with a high peripartal feeding strategy.

Feeding sows *ad libitum* for prolonged periods during gestation reduced voluntary feed intake during lactation (Weldon et al., 1994; Prunier et al., 2001; Sinclair et al., 2001; van der Peet-Schwering et al., 2004). However, when sows were fed *ad libitum* only during the week before farrowing, this decrease in feed intake was not observed (Cools et al., 2013), which corroborated with observations in this study. It is well described that the sow's BC affects voluntary feed intake (Prunier et al., 2001; Young et al., 2004) and this was also observed in the H-group as skinny sows had a greater ADFI compared to other sows the week before farrowing. A similar BF change was observed for both treatment groups between d 108 of gestation and weaning, but the period in which this change was achieved differed. The H-group lost less BF during the week before farrowing which was expected due to the greater ADFI but lost more BF during lactation. It was assumed that this is not due to a greater milk production as piglet weight gain did not differ across treatment groups. The ADFI during lactation was 0.5 kg lower in the H-group compared to the L-group which was not statistically significant but might have been biologically relevant and could explain the difference in BF change. The sow's BC at d 108 of gestation did not affect the BF change the week before farrowing but skinny sows lost less BF during lactation compared to other sows. This was similar to results reported by Cools et al. (2014).

Total CY (1.7 to 5.7 kg) was within normal ranges according to literature (Devillers et al., 2004b; Foisnet et al., 2010a; Decaluwé et al., 2013). Dourmad et al. (1999) stated that the effect of feed restriction at the end of gestation on CY would be rather small as sows

compensate by mobilizing their body reserves. Sows in the L-group indeed mobilized more body fat and protein reserves as was indicated by the change in BF the week before farrowing and serum concentrations of NEFA, creatinine and C4 at d 1 of lactation although it was not clear whether C4 originated from fat or protein. Nonetheless, this mobilization of body reserves seemed insufficient to fully compensate for reduced intake of nutrients as CY was lower. These findings supported the statement of Noblet et al. (1997) that adapting feeding strategies to the sow's need at different periods during the reproductive cycle was critical for minimizing the difference between actual and potential performance of the sows.

Housing and management up to d 108 of gestation, BF at d 108 of gestation, BF change between d 85 and 108 of gestation, and serum parameters at d 108 of gestation did not differ between treatment groups and were within ranges reported earlier by Verheyen et al. (2007). It was, therefore, assumed that the physiological background of sows at the start of the treatment was similar for both treatment groups. The difference in CY between treatment groups had to result from the difference in feed intake in the week before farrowing and we hypothesized that the greater CY in the H-group resulted from the increased availability of nutrients. Around farrowing, the sow's metabolism adapts to spare glucose for fetuses and mammary secretion by guiding the maternal metabolism towards a greater use of energy substrates derived from fat (Boyd and Kensinger, 1998). These ketogenic energy substrates enter the citric acid cycle as acetyl-CoA and should react with oxaloacetate which can originate from glucose and AA. The availability of oxaloacetate can be easily depleted when fat mobilization is high, putting pressure on the sow's metabolism. This pressure can be lowered by decreasing precursors of acetyl-CoA and increasing precursors of oxaloacetate. This situation was achieved in sows receiving the high feeding strategy as they mobilized less body fat reserves but had more protein catabolites available as was shown by the BF change the week before farrowing, and serum concentrations of NEFA, urea and the ratio

urea/NEFA. The greater availability of protein catabolites in the H-group did not originate from the body protein reserves as there were lower concentrations of creatinine at d 1 of lactation and thus had to originate directly from the feed. When the acetyl-CoA that is delivered to the citric acid cycle exceeds the availability of oxaloacetate, it is converted to ketone bodies (Theil et al., 2013). These ketone bodies as indicated by 3-OH-C4carnitine were greater in the L-group.

A high feeding strategy in the week before farrowing thus reduced pressure on the maternal energy metabolism but it also increased the amount of nutrients secreted through colostrum as shown by the increased content of lactose and several fatty acids. Glucose is the precursor of lactose (Shennan and Peaker, 2000) but plasma glucose concentration at d 1 of lactation did not differ between treatment groups although intake of glucose precursors through feed differed 3-fold. This could be explained by the fasted state of the sows at the time of sampling indicating that plasma glucose already returned to basal levels. Nonetheless, the greater concentration and total output of lactose in colostrum in the H-group showed that more glucose delivered to the mammary gland was available for lactose production. Based on this experiment, it could not be concluded whether this was a result of a greater glucose delivery to the mammary gland, a decreased use of glucose for other processes than lactose production (Boyd and Kensinger, 1998), or a combination of both. The fatty acid profile of sow colostrum is mainly a reflection of the fat composition of the diet (Farmer and Quesnel, 2009) but colostral fat originates from the diet as well as from body fat reserves and *de novo* synthesis in the mammary gland (Boyd and Kensinger, 1998). In this study, all sows were offered the same diet but the fatty acid profile of the diet was better reflected in colostrum of the H-group although concentration and total fat output in colostrum did not differ between treatment groups. In the L-group, the relative share of fatty acids in colostrum originating from the diet was smaller. Thus, the fatty acid profile in sow's colostrum could be altered by

adapting the feed composition (Farmer and Quesnel, 2009) but this might only be successful when a certain level of feed intake was achieved. The protein content of colostrum in the H-group was lower compared to the L-group but the total output of colostral protein did not differ. When sows were provided the same feeding level the week before farrowing, there was no association between colostrum protein content and CY (Decaluwé et al., 2013). In this study, nutrient intake the week before farrowing differed across experimental groups and perhaps a dilution effect of the colostral protein with nutritional value was induced as the difference in colostral protein content was not due to differences in Ig-content. As most colostral protein with nutritional value is synthesized within the alveolar cells of the mammary gland (Devillers et al., 2006), a dilution effect should mean that the synthesis of colostral protein was not increased by greater ADFI or was already at its maximal capacity with lower ADFI. However, the origin of AA for this alveolar protein synthesis might have differed as sows in the L-group had to mobilize a greater amount of body protein compared to sows in the H-group.

The serum concentration of IgA at d 1 of lactation was greater in the H-group compared to the L-group but this did not result in differences in IgA concentration or total output in colostrum which might be due to the fact that approximately 60% of colostral IgA is synthesized by plasmocytes in the mammary gland (Salmon et al., 2009).

In contrast to the treatment groups, differences in CY and composition across BC groups did not seem to be due to physiological differences in the week before farrowing as most blood variables at d 108 of gestation and d 1 of lactation, and the BF change in the week before farrowing did not differ across BC groups. Still, BF change between d 85 and d 108 of gestation differed across BC groups, levels of creatinine tended to be lower in fat sows compared to sows in moderate BC and voluntary ADFI was lower for fat than for skinny sows the week before farrowing within the H-group. It was, therefore, assumed that the

physiological background at d 108 of gestation differed across BC groups and that this might have been the underlying cause of the observed differences across BC groups. Leptin and insulin are 2 major metabolic parameters regulating energy metabolism (Barb et al., 2001). Père and Etienne (2007) showed that insulin sensitivity of all sows decreased from d 85 of gestation onwards but that this was more prominent for fat sows and concentration of leptin varies with the amount of body fat (Barb et al., 2001).

Reproductive performance of sows did not differ between treatment groups and BC groups. The observed change in piglets' weight gain during the first 24 h of life was greater in the groups with the highest CY. During the whole lactation period, piglets from skinny sows had the lowest weight gain whereas feeding strategy did not affect piglet weight gain. Cross-fostering might have affected these results but this will have been minimal as only 5% of piglets were removed from the trial at d 2 of lactation. The effect of the increased CY and intake in the H-group was probably too low to affect piglet performance in this trial.

In conclusion, both CY and composition were influenced by the sow's BC and the peripartal feeding strategy with the effects being mainly independent of each other. The highest CY and the highest colostral output of nutrients were achieved when sows entered the farrowing unit in moderate condition and were provided with the high peripartal feeding strategy.

3.3.

Evidence that gestational mammogenesis is important for sows' colostrum yield

Adapted from

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ABSTRACT

We previously showed a negative correlation between CY and BF change between d 85 and 108 of gestation (**ΔBF d 85-108**) and proposed 2 hypotheses 1) gestational mammogenesis, and 2) insulin sensitivity. Both hypotheses require intensive and invasive study designs involving culling for mammogenesis and catheterization for insulin sensitivity. This study explored which is the most likely hypothesis by alternatively measuring and correlating performance and metabolic parameters in a group of sows fed at different feeding levels during late gestation.

At d 85 of gestation, 47 sows were stratified for BF and parity, and *randomly* divided into 6 groups differing in daily feed allowance between d 85 and 108 of gestation (**DFA d 85-108**). Group 1 was allowed 1.8 kg feed•sow^{-1}•day^{-1}. Feed allowance for each next group increased with 300 g feed•sow^{-1}•day^{-1} and reached 3.3 kg feed•sow^{-1}•day^{-1} in group 6. From d 108 of gestation until weaning at 3 weeks of lactation, all sows were managed and fed similarly. The DFI from d 108 onwards, CY, sow's reproductive parameters, and piglet performance were recorded. Colostrum was analyzed for nutrient composition, IgG and IgA. Sows' blood, collected after a fasting period at d 85 and d 108 of gestation and at d 1 of lactation, was analyzed for several metabolites including glucose and insulin. The ΔBF d 85-108, DFA d 85-108 and CY were correlated to all observed variables.

The CY was correlated with ΔBF d 85-108 (r = -0.446, P = 0.002) but not with DFA d 85-108 (r = -0.156, P = 0.312). We found 3 indications to support the hypothesis of mammogenesis: 1) Gestational mammogenesis occurs between d 85 and 108 of gestation. A negative ΔBF d 85-108 might partially evolve from an increased mammogenesis. 2) Colostrum composition was not correlated to CY or ΔBF d 85-108 (P > 0.10) which is indicative for more functional mammary tissue. 3) Piglets' daily weight gain was correlated to ΔBF d 85-108 up to d 3 of lactation (r = -0.359, P = 0.019) which is right before the start of lactational mammogenesis.

Although ΔBF d 85-108 and DFA d 85-108 affected the glucose and insulin metabolism, CY was not correlated to the changes in insulin (r = 0.025, *P* = 0.876) and glucose (r = -0.149, *P* = 0.359) between d 85 and 108 of gestation which makes this hypothesis less promising.

We conclude that the ΔBF d 85-108 is negatively correlated with CY and there are several indications that this is due to the level of gestational mammogenesis.

Key words: colostrum, insulin, mammogenesis, sow

INTRODUCTION

Approximately 30% of the sows have a CY which is insufficient for their litter (Foisnet et al., 2010a; Decaluwé et al., 2013) but sow factors that are correlated with CY are not well known (Farmer and Quesnel, 2009). We previously demonstrated a negative correlation (r = -0.35, *P* = 0.032) between CY and BF change between d 85 and 108 of gestation (**ΔBF d 85-108**) (Decaluwé et al., 2013). We propose 2 hypotheses that might explain this correlation. First, mammogenesis might be an underlying factor as the amount of functional mammary tissue was positively correlated with milk yield (Nielsen et al., 2001). Mammogenesis accelerates during the last month of gestation (Ji et al., 2006) and the use of more body energy reserves during this period might partially evolve from an increased mammogenesis finally resulting in a higher CY. Secondly, the ΔBF d 85-108 might be concomitant to a metabolic change. Insulin sensitivity decreases after d 85 of gestation (Père et al., 2000). This might be beneficial as it drives glucose to the insulin independent mammary gland (Shennan and Peaker, 2000). Glucose is the main precursor for lactose and acts as a major osmotic component that might affect CY (Foisnet et al., 2010a). Decreased insulin sensitivity forces sows to use more ketogenic substrates which might lead to ketosis (Theil et al., 2013). We previously demonstrated that sows with an increased use of ketogenic substrates at d 1 of lactation had a lower CY (Decaluwé et al., 2014a).

This experiment was set up to further explore the correlation between CY and ΔBF d 85-108 and to investigate whether this correlation was due to differences in mammogenesis or due to changes in nutrient metabolism. This is important as both hypotheses lead to different solutions for impaired CY from gilt management, genetic selection and feeding strategies in case of an effect of mammogenesis or fine-tuning of nutrition towards energy metabolism in case of an effect of insulin-sensitivity.

MATERIAL AND METHODS

Study population and experimental design

The experiment was approved by the ethical committee of the Faculty of Veterinary Medicine, Ghent University (EC2013/92).

The study was conducted from June until September 2013 in a commercial farm comprising 1700 PIC sows. The farm practiced a 2-week-batch system. Forty-seven healthy sows (parity 1 to 7), were observed from d 85 of gestation until weaning. The day of first insemination was defined as d 0 of gestation, the day of parturition as the last day of gestation and d 0 of lactation. From weaning until d 28 of gestation, sows were housed and fed individually in crates. At d 29 of gestation, sows were moved from the insemination unit to the gestation unit where they were group-housed. Upon entering the gestation unit, 90 sows were stratified for parity and BF and *randomly* divided into 6 groups. Each group was housed in a separate pen (15 sows per pen) containing 2 feeders (no animal-recognition system) that dropped small amounts of the gestation diet (meal) every 2 min throughout the day. From d 29 until d 85 of gestation, 37.5 kg feed•day^{-1} was offered per pen through these 2 feeders or on average 2.5 kg of feed•sow^{-1}•day^{-1}. From d 85 of gestation onwards, each group was offered a different amount of feed per day. Daily feed allowance as-fed between d 85 and 108 of gestation (**DFA d 85-108**) per sow was 1.8 kg for group 1, 2.1 kg for group 2, 2.4 kg for group 3, 2.7 kg for group 4, 3.0 kg for group 5 and 3.3 kg for group 6.

At d 107 of gestation, sows were moved to the farrowing unit where they were housed individually in conventional farrowing crates until weaning. We were able to observe sows from 2 farrowing units (2 x 26 sows), meaning that we had to select 9 sows per treatment group. For each treatment group, we excluded the 2 sows with the highest BF gain and the 2 sows with the highest BF loss between d 85 and 108 of gestation, and then randomly selected 9 out of the remaining 11 sows for each treatment group. From d 108 of gestation until d 2 of lactation, sows were fed 3 times a day for a total of 3.3 kg of feed•sow^{-1}•day^{-1}. Starting from d 3 of lactation until weaning, sows received a lactation diet (meal) 4 times a day of which the amount gradually increased. Every day, approximately 4 h after the last feeding, the amount of feed left-overs of each sow was estimated by the same person who emptied the trough of each sow with the same scoop and left-overs were discarded. In case of left-overs, the trough was emptied and a reduced portion of fresh feed was offered. All sows received the same gestation, transition, and lactation feed throughout the entire experiment. During the entire experiment, sows had free access to fresh drinking water (2 drinking nipples per pen in the gestation unit and 1 drinking nipple in each farrowing pen – flow 1.5 to 2 l/min).

Farrowing induction was not applied, and farrowing intervention was minimized to manual extraction when the birth interval between 2 piglets exceeded 1 h. No oxytocin was administered during parturition as this might interfere with mammary secretion (Ellendorf et al., 1982) except in 3 sows that were still farrowing at time of colostrum collection. No additional help or care was given to the piglets unless there was a risk for them of getting crushed. Floor heating and an infrared lamp were used to create a microclimate for the piglets. On d 2 of lactation, litters were standardized to 11 ± 1 piglet by cross-fostering. From d 2 of lactation, piglets were offered creep feed. The feed intake of the piglets was not measured.

Parameters and measurements

All measurements of BF were performed by the same person on standing sows at the P2-position (Maes et al., 2004) at both the left and right side of the sow after hair removal using a digital BF indicator (Renco Lean Meter, S.E.C. Repro Inc., Ange-Gardien-de-Rouville, Québec, Canada). Values from the 2 measurements were averaged to obtain a single BF measurement. We measured BF at d 85 and d 108 of gestation, at d 1 of lactation and at weaning.

The CY was calculated as the sum of the individual piglet's CI within a litter as described by Devillers et al. (2004b) using following variables: BW_B (kg), weight at 17-24 h of age (**BW_{24}**, kg), duration of CI (t in min and with 17 h $\leq$ t $\leq$ 25 h), and time between birth and first suckling (**t_{FS}**, min). Based on observations from a previous study performed at the same farm (Decaluwé et al., 2013), we standardized t_{FS} to 35 min. As explained by Devillers et al. (2004b), an error of 15 min of t_{FS} leads to a miscalculation of CI by the piglet of 6g/kg BW_B or less than 2% error. The used regression equation was: $CI = -217.4 + 0.217 \times t + 1861019 \times BW_{24}/t + BW_B \times (54.80 - 1861019/t) \times (0.9985 - 3.7 \times 10^{-4} \times t_{FS} + 6.1 \times 10^{-7} \times t^2_{FS})$. When a piglet was born, the back of the piglets was dried with a paper towel and marked. Piglets were ear-tagged allowing identification. The umbilical cord was shortened when it was longer than approximately 15cm. After determining BW_B, piglets were immediately put back in the farrowing pen with their nose against the sow's vulva. The accuracy of the scale was 0.02 kg.

Observed sow parameters were parity, gestation length, farrowing duration, number of total, liveborn and stillborn piglets, and number of weaned piglets. Observed piglet parameters were birth interval, pre-weaning mortality, BW_B, BW_{24}, and weight at d 3, d 7, d 14 of age and at weaning. Piglets were cross-fostered after determining BW_{24} and from then on, litter daily weight gain (**DWG**) was calculated per sow.

Samples

Sow's serum (serum clot activator tubes) and plasma (sodium fluoride/potassium oxalate tubes) was collected by punction of the *vena jugularis* while restraining sows with a snare at d 85 and d 108 of gestation and at d 1 of lactation after overnight fasting period (minimum 10 h). Samples were stored in iced water (4°C, maximum 2 h), subsequently centrifuged at 1000 × g for 10 min and stored frozen at -20°C until further analysis.

Colostrum (40 mL) was collected from all teats of 1 side of the udder at 6 h after birth of the first piglet, following an i.m. injection of 2 mL of oxytocin (10 IU/mL, Oxytocin, VMD) 5 min before sampling. At the time of sample collection, 3 sows did not complete farrowing but they were also injected 2 mL of oxytocin. The samples were subdivided, frozen at -20°C and stored until further analysis.

Analyses of samples

Feed. Nutritional composition of the diets was analyzed according to the Association of Official Analytical Chemists (AOAC) methods (Thiex, 2002) (ISO 5983-1, 2005; ISO 1443, 1973; ISO 5498, 1981). All percentages represent an as-fed basis. The gestation diet contained 90.1% dry matter (DM), 4.3% of crude fat (CF), 15.7% of crude protein (CP), 5.8% of crude ash (CA) and 4.1% of crude fiber (CFib). The transition diet contained 90.4% DM, 4.6% CF, 13.1% CP, 5.4% CA and 4.0% CFib. The lactation diet contained 90.5% DM, 5.7% CF, 14.1% CP, 5.6% CA and 3.4% CFib. The creep feed of the piglets' diet contained 90.7% DM, 8.4% CF, 18.7% CP, 7.2% CA and 2.6% CFib.

Serum and plasma. Serum was analyzed for urea, creatinine, NEFA, and TG spectrophotometrically (Ultrospec IIE, LKB, Biochrom, Cambridge, England) using a commercial colorimetric diagnostic kit (references UR107 for urea, CR510 for creatinine, FA115 for NEFA, and TR210 for TG; Randox Laboratories, Crumlin, United Kingdom). Insulin was analyzed using an immunoradiometric kit (BioSource INS-IRMA Kit, BioSource

Europe S.A., Nivelles, Belgium). Fasting plasma glucose concentration was measured by enzymatic colorimetric assay method (REF 3L82-21 and 3L82-41) using an Abbott Architect C16000 auto-analyzer (Abbott Diagnostic Laboratories, Chicago, IL, USA) with the hexokinase-G6PDH method. Quantitative electrospray tandem MS was used to determine C4 and 3-OH-C4 as described by Zabielski et al. (2007). A porcine quantitative sandwich enzyme immunoassay technique (Bethyl Laboratories Inc., Montgomery, USA) was used to analyze IgG (dilution 1:100000) and IgA (dilution: 1:40000) (references A100-104 for IgG and A100-102 for IgA, Bethyl Laboratories Inc., Montgomery, Texas, USA). The intra and interassay coefficient of variation were, respectively, 2.9 and 5.2% for urea, 2.8 and 2.9% for creatinine, 4.8 and 4.3% for NEFA, 3.5 and 3.8% for TG, 9.6 and 9.5% for C4 and 3-OH-C4, 3.1 and 6.3% for IgG, and 3.2 and 9.8% for IgA.

Colostrum. Nutritional composition (fat, protein and lactose content) was analyzed by Lactoscope FTIR Advanced type FTA-3.0 (Delta Instruments, Drachten, Netherlands). Samples were diluted 1:2 with distilled water and calibrated curves were verified with Gerber and Kjeldahl analysis on 4 reference colostrum samples (R^2 between FTIR and Gerber = 0.9975; R^2 between FTIR and Kjeldahl = 0.9997). To determine the fatty acid profile, milk fat was extracted as described by Chouinard et al. (1997) and subsequently methylated and analyzed by gas liquid chromatography as described by Stefanov et al. (2010). The intra and interassay coefficient of variation were, respectively, 0.24 and 0.23%.

A porcine quantitative sandwich enzyme immunoassay technique was used to analyze IgG (dilution1:500000) and IgA (dilution 1:50000) in duplicate (references A100-104 for IgG and A100-102 for IgA, Bethyl Laboratories Inc., Montgomery, Texas, USA). The intra and interassay coefficient of variation were, respectively, 2.3 and 9.7% for IgG, and 3.4 and 2.6% for IgA.

Statistical analysis

All statistical analyses were performed using SPSS 19.0 (IBM, Chicago, Illinois), considering statistical significance when $P < 0.05$ (2-sided tests).

Normally distributed variables are reported as LSmean ± SEM and not normally distributed variables as median ± IR (Field, 2009). Normality of the data was analyzed with the Kolmogorov-Smirnov test, the Levene's test was used to analyze homogeneity of variance.

The effect of DFA d 85-108 on ΔBF d 85-108 was analyzed by ANOVA using a Scheffé *post hoc* test. Normality and homogeneity of the residuals were analyzed.

The CY, DFA d 85-108 and ΔBF d 85-108 were correlated with the outcome variables considering feed intake, BF (change), CY, colostrum composition, sow reproductive parameters, average piglet and litter DWG**,** and blood parameters using Pearson or Spearman correlation analysis when data were normally or not normally distributed, respectively. Linearity of the correlation and the possible influence of outliers were checked graphically on beforehand.

RESULTS

Exclusion of 3 sows

Three sows were excluded from analysis since the voluntary dDFI the week prior to farrowing was lower (-25 %, $P < 0.001$, 2-sided t-test) compared to the other sows and their CY was below 1 kg. As DFI the week prior to farrowing affects CY (Decaluwé et al, 2014a) and we wanted to rule out interference of this low DFI, these 3 sows were deleted from analysis. Two of these sows were first parity sows, 1 from the groups that received 1.8 kg feed•sow^{-1}•day^{-1} and 1 from the group that received 2.1 kg feed•sow^{-1}•day^{-1} between d 85 and 108 of gestation. The third sow (parity 7) belonged to the group receiving 2.4kg of feed•sow^{-1}•day^{-1}.

Correlation between DFA d 85-108 and ΔBF d 85-108

The DFA d 85-108 was correlated with the ΔBF d 85-108 (r = 0.57, $P < 0.001$). The ΔBF d 85-108 differed significantly between the groups with the lowest and highest DFA d 85-108 (**Figure 1**). The variance of ΔBF d 85-108 did not differ between groups differing in DFA d 85-108 (Levene's test: $P = 0.436$; **Figure 1**). It can also be observed that the 4 groups with an intermediate DFA d 85-108 have both sows with a positive or negative ΔBF d 85-108. Only the groups with the lowest and highest DFA d 85-108 had no sows with a positive or negative BF change respectively, but both groups had sows with no BF change between d 85 and 108 of gestation.

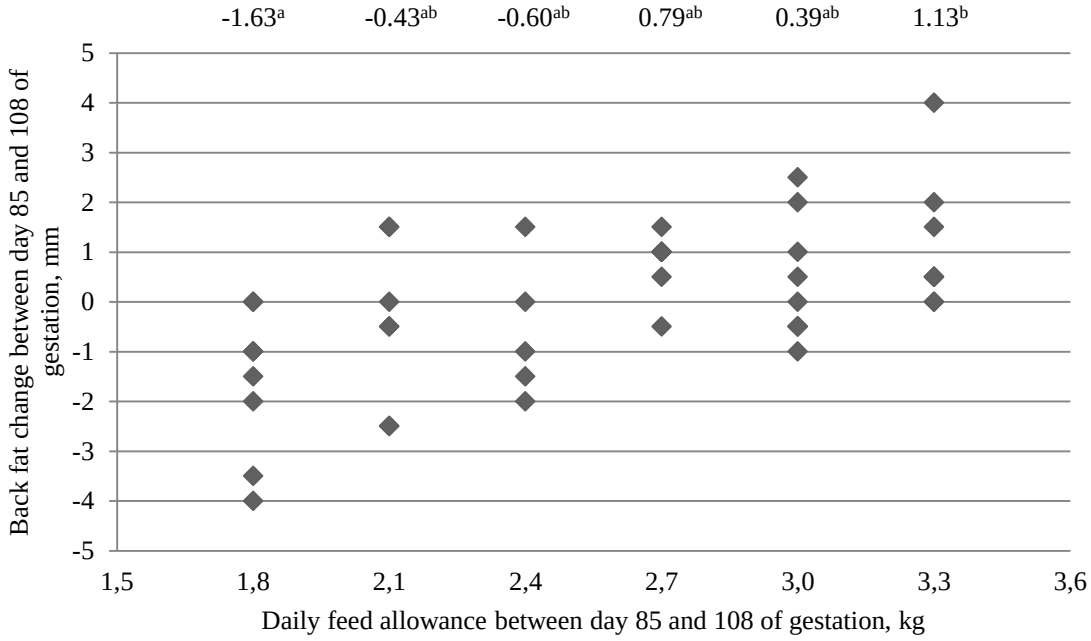


Figure 1. *DFA d 85-108 and ΔBF d 85-108 is shown for each sow. Mean per group of DFA d 85-108 is shown on top of the graph. Means without a common letter superscript differ ($P < 0.05$) between daily feed allowance groups (ANOVA with Scheffé post hoc test, $P = 0.002$).*

Feed intake and BF (change): correlations with DFA d 85-108, ΔBF d 85-108, and CY

The correlation coefficients are presented in **Table 1**.

The DFA d 85-108 tended to be correlated with the BF at d 108 of gestation (r = 0.265, *P* = 0.082).

The ΔBF d 85-108 tended to be correlated with the BF at d 108 of gestation (r = 0.260, *P* = 0.089) and was correlated with the BF change between d 108 of gestation and d 1 of lactation (r = -0.537, *P* < 0.001).

The CY was correlated with the ΔBF d 85-108 (r = -0.446, *P* = 0.002).

Table 1 *Mean/median ± SEM/IR and correlation coefficients with CY, ΔBF 85-108, and DFA 85-108 of variables considering feed intake, BF, and BF change.*

Variable	Mean Median	SEM IR	r CY	r ΔBF 85-108	r DFA 85-108	*P* CY	*P* ΔBF 85-108	*P* DFA 85-108
Total feed intake, kg								
d 108 of gestation until d 1 of lactation	19.8	0.6	-0.172	0.154	0.113	0.264	0.317	0.465
During lactation	101.9	4.0	0.225	-0.072	0.078	0.147	0.646	0.618
DFI, kg								
* d 108 of gestation until d 1 of lactation	3.29	0.13	0.058	0.066	0.161	0.710	0.670	0.296
During lactation	5.1	0.2	0.194	-0.044	0.083	0.213	0.780	0.598
BF, mm								
d 85 of gestation	18.3	0.6	0.082	-0.104	0.062	0.597	0.504	0.689
d 108 of gestation	18.3	0.7	-0.081	0.260	0.265	0.600	0.089	0.082
d 1 of lactation	18.2	0.7	-0.025	0.097	0.220	0.873	0.533	0.151
At weaning	15.7	0.6	-0.024	0.090	0.183	0.877	0.565	0.241
BF change, mm								
d 108 of gestation until d 1 of lactation	-0.11	0.2	0.186	-0.537	-0.134	0.226	<0.001	0.387
During lactation	-2.5	0.3	0.008	-0.047	-0.172	0.958	0.763	0.271

ΔBF 85-108: BF change between d 85 and 108 of gestation; DFA 85-108: daily feed allowance between d 85 and 108 of gestation; *: not normally distributed variable

Colostrum yield and composition: correlations with DFA d 85-108, ΔBF d 85-108, and CY

The correlation coefficients are presented in **Figure 2**. The correlation coefficients considering the fatty acid profile are presented in **Table 2**.

Table 2 *Mean ± SEM and correlation coefficients with CY, ΔBF 85-108, and DFA 85-108 of variables considering the colostral FA profile (g/100g FA).*

Variable	Mean	SEM	r CY	r ΔBF 85-108	r DFA 85-108	*P* CY	*P* ΔBF 85-108	*P* DFA 85-108
Saturated FA	33	0.3	0.117	-0.042	0.042	0.457	0.787	0.788
Mono-unsaturated FA	34	0.4	-0.077	-0.314	-0.178	0.623	0.041	0.253
N-6 PUFA	24	0.5	0.005	0.292	0.155	0.974	0.057	0.322
N-3 PUFA	2.8	0.1	-0.114	0.232	0.107	0.467	0.135	0.494
Linoleic acid	22	0.5	-0.001	0.285	0.137	0.996	0.064	0.382
Arachidonic acid	1.0	0.02	-0.026	0.016	0.181	0.867	0.917	0.244
Linolenic acid	1.7	0.06	-0.102	0.263	0.096	0.517	0.088	0.540
Eicosapentaenoic acid	0.16	0.004	-0.165	0.261	0.337	0.292	0.091	0.027
Docosahexaenoic acid	0.34	0.01	-0.006	0.018	-0.025	0.970	0.908	0.876

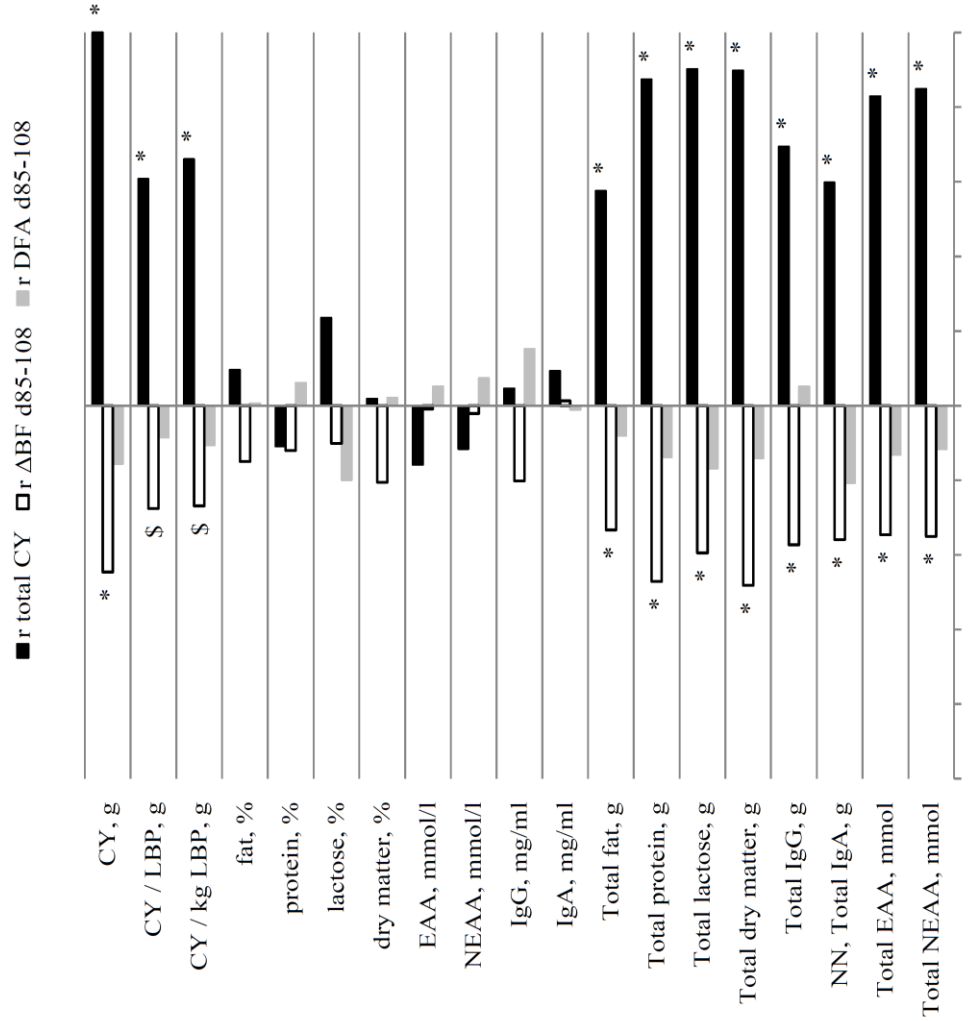
ΔBF 85-108: BF change between d 85 and 108 of gestation; DFA 85-108: daily feed allowance between d 85 and 108 of gestation; FA: fatty acid

The DFA d 85-108 was not correlated with CY and composition except for EPA (g/100g fatty acids) (r = 0.337, *P* = 0.027).

The ΔBF d 85-108 was correlated with the total CY (r = -0.446, *P* = 0.002) and tended to be correlated with the CY per liveborn piglet (r = -0.276, *P* = 0.070) and the CY per kg liveborn piglet (r = -0.269, *P* = 0.078). There was no correlation with the colostrum composition (fat, protein, lactose, dry matter, essential AA, non-essential AA, IgG and IgA) but there were correlations with the total output of fat (r = -0.333, *P* = 0.029), protein (r = -0.471, *P* = 0.001), lactose (r = -0.395, *P* = 0.009), dry matter (r = -0.482, *P* = 0.001), essential AA (r = -0.346, *P* = 0.021), non-essential AA (r = -0.350, *P* = 0.020), and IgG (r = -0.373, *P* = 0.016). The ΔBF d 85-108 was correlated with the colostral mono-unsaturated fatty acids (r = -0.314, *P* =

0.041) and tended to be correlated with the colostral n-6 PUFA (r = 0.292, *P* = 0.057), linoleic acid (r = 0.285, *P* = 0.064), linolenic acid (r = 0.263, *P* = 0.088), and EPA (r = 0.261, *P* = 0.091).

The CY was correlated with the CY per liveborn piglet (r = 0.607, *P* < 0.001) and the CY per kg liveborn piglet (r = 0.660, *P* < 0.001). The CY was not correlated with colostrum composition (fat, protein, lactose, dry matter, and IgG and IgA) and the colostral fatty acid profile but was correlated with the total output of fat (r = 0.575, *P* < 0.001), protein (r = 0.874, *P* < 0.001), lactose (r = 0.902, *P* < 0.001), dry matter (r = 0.898, *P* < 0.001), essential AA (r = 0.829, *P* < 0.001), non-essential AA (r = 0.849, *P* < 0.001), and IgG (r = 0.694, *P* < 0.001) and IgA (r = 0.542, *P* < 0.001).



	Mean	SEM	r CY	r ΔBF d	r DFA d
	Median	IR		85-108	85-108
CY, g	3267	126	1.000	-0.446	-0.156
CY / LBP, g	255	12	0.607	-0.276	-0.085
CY / kg LBP, g	199	9	0.660	-0.269	-0.106
fat, %	4.8	0.3	0.095	-0.150	0.006
protein, %	15.5	0.3	-0.109	-0.120	0.061
lactose, %	2.6	0.1	0.235	-0.101	-0.199
dry matter, %	22.9	0.4	0.018	-0.205	0.021
EAA, mmol/l	470.8	10.2	-0.158	-0.009	0.051
NEAA, mmol/l	571.5	11.2	-0.116	-0.021	0.074
IgG, mg/ml	73.6	2.7	0.046	-0.202	0.152
IgA, mg/ml	10.3	0.7	0.093	-0.013	0.011
Total fat, g	158	14	0.575	-0.333	-0.080
Total protein, g	502	22	0.874	-0.471	-0.138
Total lactose, g	86	4	0.902	-0.395	-0.168
Total dry matter, g	746	34	0.898	-0.482	-0.141
Total IgG, g	243	13	0.694	-0.373	0.051
NN, Total IgA, g	30	22	0.598	-0.359	-0.207
Total EAA, mmol	1502.5	62.4	0.829	-0.346	-0.131
Total NEAA, mmol	1828.0	76.1	0.849	-0.350	-0.117

Figure 2. *Descriptives of the CY and composition and their correlation coefficients with the DFA d 85-108, the ΔBF d 85-108 and the CY. Significant ($P < 0.05$) correlations are flagged with *, tendencies are flagged with $. Not normally distributed variables are indicated with NN.*

ΔBF d 85-108: back fat change between d 85 and 108 of gestation, DFA d 85-108: daily feed allowance between d 85 and 108 of gestation, LBP: liveborn piglet

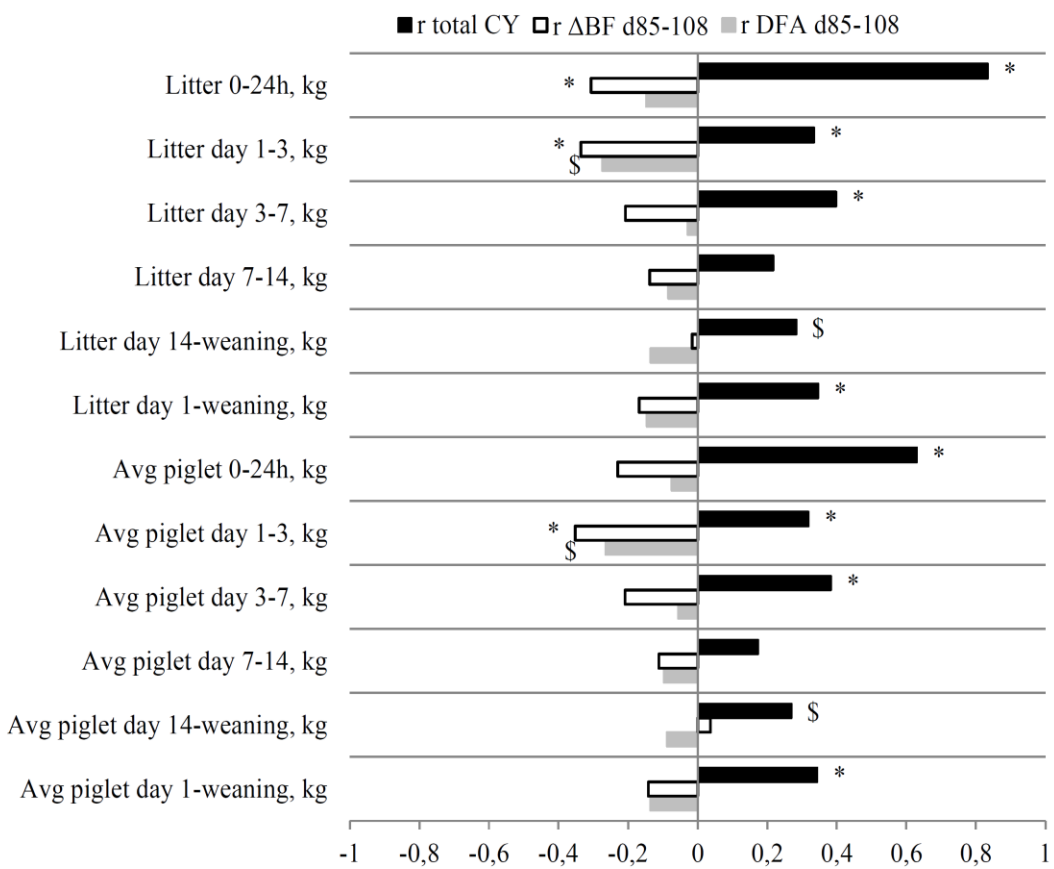
Piglets' daily weight gain: correlations with DFA d 85-108, ΔBF d 85-108, and CY

The correlation coefficients are presented in **Figure 3**.

The DFA d 85-108 tended to be correlated with the litter DWG between d 1 and 3 of lactation (r = -0.275, *P* = 0.070) and average piglet DWG between d 1 and 3 of lactation (r = -0.265, *P* = 0.082).

The ΔBF d 85-108 was correlated with the litter DWG between birth and 24 h of age (r = -0.307, *P* = 0.042), the litter DWG between d 1 and 3 of lactation (r = -0.336, *P* = 0.026) and the average piglet DWG between d 1 and 3 of lactation (r = -0.352, *P* = 0.019).

The CY was correlated with the litter DWG between birth and 24h of age (r = 0.834, *P* < 0.001), between d 1 and 3 of lactation (r = 0.335, *P* = 0.026), between d 3 and 7 of lactation (r = 0.398, *P* = 0.007), and between d 1 of lactation and weaning (r = 0.346, *P* = 0.023). The CY was correlated with average piglet DWG between birth and 24h of age (r = 0.630, *P* < 0.001), between d 1 and 3 of lactation (r = 0.319, *P* = 0.035), between d 3 and 7 of lactation (r = 0.383, *P* = 0.010), and between d 1 of lactation and weaning (r = 0.344, *P* = 0.024). The CY tended to be correlated with the litter DWG (r = 0.284, *P* = 0.065) and the average piglet DWG (r = 0.270, *P* = 0.080) between d 14 of lactation and weaning.



	Mean	SEM	r CY	r ΔBF d 85-108	r DFA d 85-108
Litter 0-24h, kg	0.86	0.09	0.834	-0.307	-0.148
Litter day 1-3, kg	1.34	0.08	0.335	-0.336	-0.275
Litter day 3-7, kg	1.89	0.09	0.398	-0.208	-0.029
Litter day 7-14, kg	2.41	0.10	0.218	-0.138	-0.085
Litter day 14-weaning, kg	2.53	0.09	0.284	-0.016	-0.135
Litter day 1-weaning, kg	2.22	0.08	0.346	-0.168	-0.146
Avg piglet 0-24h, kg	0.070	0.01	0.630	-0.230	-0.075
Avg piglet day 1-3, kg	0.11	0.01	0.319	-0.352	-0.265
Avg piglet day 3-7, kg	0.17	0.01	0.383	-0.209	-0.056
Avg piglet day 7-14, kg	0.22	0.01	0.173	-0.111	-0.097
Avg piglet day 14-weaning, kg	0.24	0.01	0.270	0.037	-0.088
Avg piglet day 1-weaning, kg	0.21	0.01	0.344	-0.142	-0.136

Figure 3. *Descriptives of the litter daily weight gain and average piglet daily weight gain and their correlation coefficients with the DFA d 85-108, the ΔBF d 85-108 and the CY. Significant (P < 0.05) correlations are flagged with *, tendencies are flagged with $.*

ΔBF d 85-108: BF change between d 85 and 108 of gestation, DFA d 85-108: daily feed allowance between d 85 and 108 of gestation

(Re)productive performance: correlations with DFA d 85-108, ΔBF d 85-108, and CY

Figure 4 shows the correlation coefficients considering the BW_B and BW_{24}. **Table 3** shows the correlation coefficients considering the reproduction parameters.

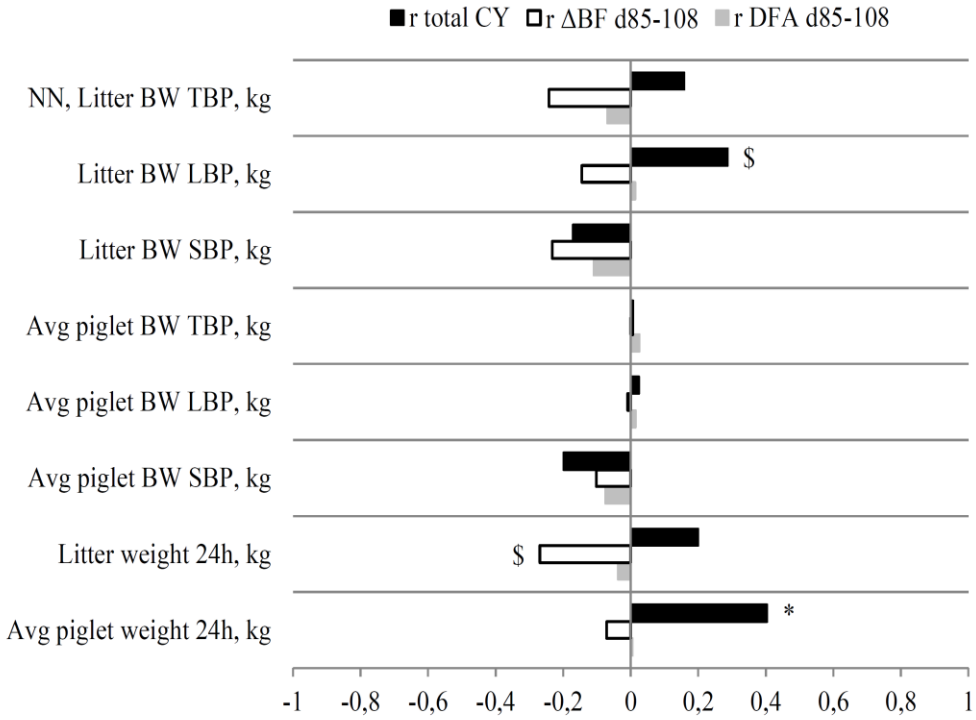
The ΔBF d 85-108 tended to be correlated with the litter BW_{24} (r = -0.269, *P* = 0.077).

The CY tended to be correlated with the litter BW_B of the liveborn piglets (r = 0.287, *P* = 0.059) and was correlated with the litter BW_{24} (r = 0.404, *P* = 0.007).

Table 3 *Mean/median ± SEM/IR and correlation coefficients with CY, ΔBF 85-108, and DFA 85-108 of variables considering the (re)productive parameters of the sow.*

Variable	Mean Median	SEM IR	r CY	r ΔBF 85-108	r DFA 85-108	*P* CY	*P* ΔBF 85-108	*P* DFA 85-108
Parity	4.3	0.3	-0.168	0.144	-0.026	0.275	0.350	0.867
Gestation length, d	115.1	0.2	-0.231	0.176	0.043	0.132	0.254	0.781
* Farrowing duration, min	173	100	-0.188	0.134	0.129	0.220	0.386	0.405
* Birth interval, min	13.5	8.3	-0.198	0.267	0.127	0.198	0.080	0.413
Total born piglets	14.6	0.5	0.072	-0.161	-0.013	0.645	0.296	0.935
Liveborn piglets	13.4	0.5	0.196	-0.072	0.054	0.201	0.642	0.730
* Stillborn piglets	1.0	2.0	-0.229	-0.135	-0.097	0.135	0.383	0.533
* Weaned piglets	10.0	3.0	0.036	-0.070	-0.005	0.820	0.655	0.973
* Stillborn piglets, %	5.6	13.3	-0.229	-0.132	-0.131	0.135	0.392	0.397
* mortality before d 2, %	8.7	22.7	0.008	0.152	0.055	0.960	0.326	0.724
* mortality after d 2, %	8.7	11.1	-0.013	0.038	0.119	0.936	0.808	0.440

ΔBF 85-108: BF change between d 85 and 108 of gestation; DFA 85-108: daily feed allowance between d 85 and 108 of gestation; *: not normally distributed variable



Mean	SEM	r CY	r ΔBF d 85-108	r DFA d 85-108
18.3	0.6	0.158	-0.242	-0.069
16.9	0.6	0.287	-0.145	0.013
1.6	1.7	-0.171	-0.232	-0.110
1.3	0.04	0.007	0.006	0.026
1.3	0.04	0.024	-0.009	0.014
1.1	0.06	-0.199	-0.102	-0.075
16.8	0.6	0.200	-0.269	-0.038
1.4	0.04	0.404	-0.071	0.005

Figure 4. *Descriptives of the litter* BW_B *and weight at 24h, average piglet* BW_B *and weight at 24h and their correlation coefficients with the DFA d 85-108, the* Δ *BF d 85-108 and the CY. Significant (P < 0.05) correlations are flagged with *, tendencies are flagged with $. Not normally distributed variables are indicated with NN.*

ΔBF d 85-108: BF change between d 85 and 108 of gestation, DFA d 85-108: daily feed allowance between d 85 and 108 of gestation, BW_B: BW_B, TBP: total born piglets, LBP: liveborn piglets, SBP: stillborn piglets

Sow blood variables: correlations with DFA d 85-108, ΔBF d 85-108, and CY

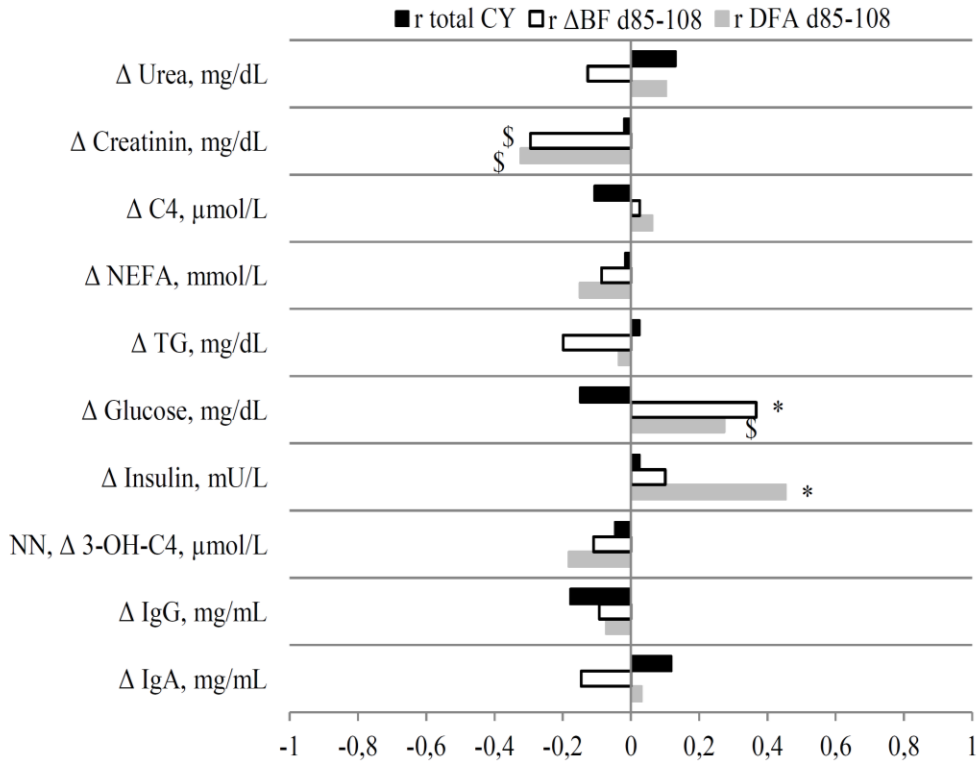
The correlation coefficients of the changes in serum concentration of the blood variables are presented in **Figure 5** and **Figure 6**. The correlation coefficients for the blood variables at d 85 and 108 of gestation and d 1 of lactation are shown in **Table 4**.

We were mainly interested in how the metabolites' concentrations changed between d 85 and 108 of gestation and between d 108 of gestation and d 1 of lactation. At d 85 of gestation, the blood variables were neither correlated with the DFA d 85-108, ΔBF d 85-108, nor with the CY.

The DFA d 85-108 was correlated with the change in insulin (r = 0.453, P = 0.003), and tended to be correlated with the change in creatinine (r = -0.323, P = 0.063) and the change in glucose (r = 0.274, P = 0.087) between d 85 and 108 of gestation. The DFA d 85-108 was correlated with the change in IgA (r = -0.366, P = 0.020) and tended to be correlated with the change in creatinine (r = 0.273, P = 0.093) between d 108 of gestation and d 1 of lactation.

The ΔBF d 85-108 was correlated with the change in glucose (r = 0.367, P = 0.020), and tended to be correlated with the change in creatinine (r = -0.295, P = 0.090) between d 85 and 108 of gestation. The ΔBF d 85-108 was correlated with the change in glucose (r = -0.374, P = 0.016) and creatinine (r = 0.363, P = 0.023) between d 108 of gestation and d 1 of lactation.

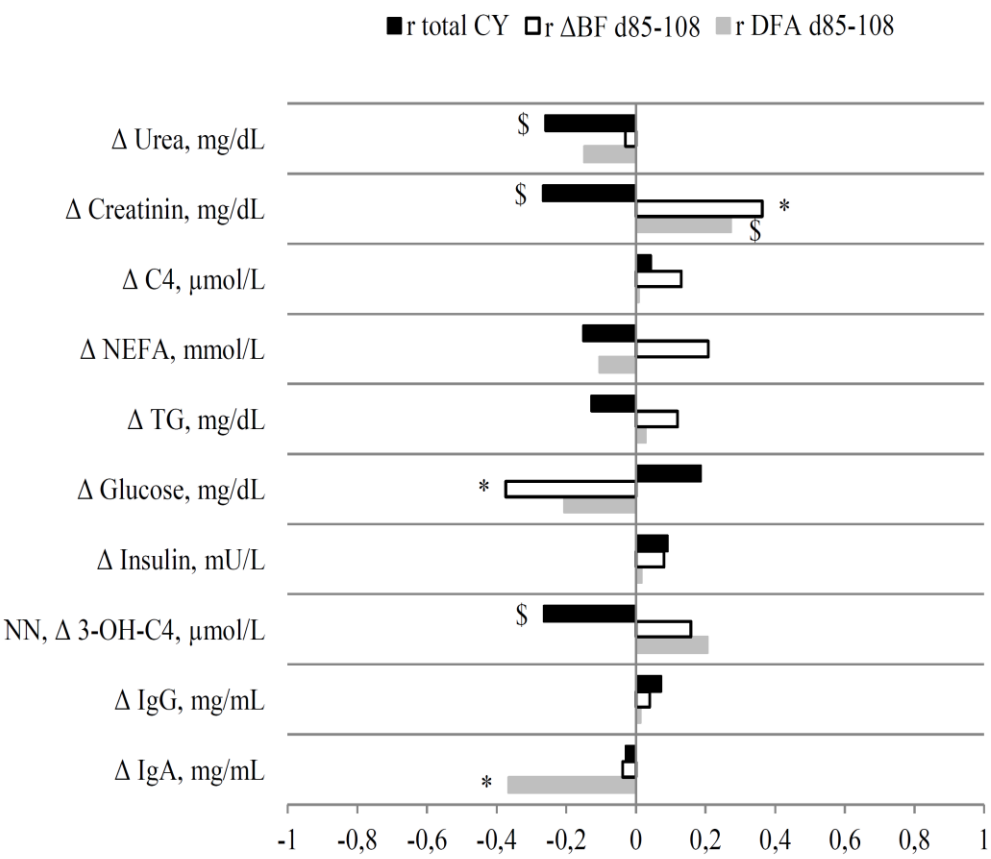
The CY was correlated with the change in 3-OH-C4 (r = -0.464, P < 0.001) and tended to be correlated with the change in urea (r = -0.260, P = 0.097) and creatinine (r = -0.267, P = 0.101) between d 108 of gestation and d 1 of lactation.



Mean Median	SEM IR	r CY	r ΔBF d 85-108	r DFA d 85-108
-1.38	1.36	0.131	-0.127	0.103
0.34	0.06	-0.020	-0.295	-0.323
-0.026	0.02	-0.107	0.026	0.063
0.55	0.06	-0.017	-0.086	-0.150
31.01	4.05	0.025	-0.199	-0.036
-9.80	2.59	-0.149	0.367	0.274
-1.03	0.43	0.025	0.100	0.453
0.010	0.03	-0.047	-0.110	-0.182
-0.19	0.78	-0.178	-0.093	-0.073
0.32	0.06	0.118	-0.146	0.031

Figure 5. *Descriptives of the change in sow's blood variables between d 85 and 108 of gestation, and their correlation coefficients with the DFA d 85-108, the ΔBF d 85-108 and the CY. Significant (P < 0.05) correlations are flagged with *, tendencies are flagged with $. Not normally distributed variables are indicated with NN.*

ΔBF d 85-108: BF change between d 85 and 108 of gestation, DFA d 85-108: daily feed allowance between d 85 and 108 of gestation



Mean Median	SEM IR	r CY	r ΔBF d 85-108	r DFA d 85-108
2.97	1.06	-0.260	-0.030	-0.149
-0.21	0.07	-0.267	0.363	0.273
0.010	0.02	0.043	0.130	0.008
-0.56	0.08	-0.151	0.208	-0.105
-53.35	4.74	-0.128	0.120	0.028
26.49	2.75	0.186	-0.374	-0.206
11.94	1.40	0.091	0.080	0.016
0.00	0.02	-0.264	0.158	0.206
-4.89	0.62	0.072	0.039	0.014
0.0045	0.05	-0.029	-0.038	-0.366

Figure 6. *Descriptives of the change in sow's blood variables between d 108 of gestation and d 1 of lactation, and their correlation coefficients with the DFA d 85-108, the ΔBF d 85-108 and the CY. Significant (P < 0.05) correlations are flagged with *, tendencies are flagged with $. Not normally distributed variables are indicated with NN.*

ΔBF d 85-108: BF change between d 85 and 108 of gestation, DFA d 85-108: daily feed allowance between d 85 and 108 of gestation

Table 4 *Mean/median ± SEM/IR and correlation coefficients with CY, ΔBF 85-108, and DFA 85-108 of variables considering the sow's blood variables at d 85 and d 108 of gestation and d 1 of lactation.*

Variable	Mean Median	SEM IR	r CY	r ΔBF 85-108	r DFA 85-108	*P* CY	*P* ΔBF 85-108	*P* DFA 85-108
Metabolites d 85 of gestation								
Urea, mg/dL	27.8	0.86	-0.177	0.006	-0.065	0.257	0.968	0.677
Creatinin, mg/dL	2.6	0.05	0.183	-0.072	0.030	0.278	0.671	0.860
C4, µmol/L	0.23	0.01	0.053	-0.141	-0.258	0.731	0.360	0.091
NEFA, mmol/L	0.34	0.03	0.280	-0.165	0.069	0.066	0.285	0.658
TG, mg/dL	43.6	2.3	-0.108	0.014	0.134	0.495	0.930	0.396
Glucose, mg/dL	62.9	0.72	-0.022	0.009	-0.94	0.888	0.957	0.555
Insulin, mU/L	6.9	0.32	-0.071	0.104	-0.207	0.647	0.504	0.178
*3-OH-C4, µmol/L	0.010	0.01	0.017	0.084	0.092	0.912	0.588	0.553
IgG, mg/mL	20.5	0.51	-0.096	0.079	0.019	0.535	0.610	0.902
IgA, mg/mL	0.90	0.06	0.260	0.237	0.123	0.101	0.135	0.442
Metabolites d 108 of gestation								
*Urea, mg/dL	26.1	10.7	0.054	-0.140	0.107	0.735	0.376	0.501
Creatinin, mg/dL	2.92	0.05	0.202	-0.359	-0.345	0.212	0.023	0.029
C4, µmol/L	0.21	0.01	-0.121	-0.081	-0.122	0.435	0.602	0.431
NEFA, mmol/L	0.88	0.06	0.102	-0.158	-0.124	0.511	0.304	0.424
*TG, mg/dL	71.9	43.6	0.048	-0.129	0.075	0.763	0.416	0.636
*Glucose, mg/dL	58.0	26.0	0.027	0.228	0.178	0.865	0.068	0.265
Insulin, mU/L	6.01	0.35	-0.022	0.227	0.363	0.889	0.148	0.018
*3-OH-C4, µmol/L	0.025	0.03	-0.042	-0.126	-0.210	0.789	0.417	0.172
IgG, mg/mL	20.44	0.81	-0.205	-0.024	-0.053	0.187	0.876	0.737
IgA, mg/mL	1.21	0.08	0.182	0.062	0.111	0.260	0.706	0.497
Metabolites d 1 of lactation								
Urea, mg/dL	30.3	1.21	-0.195	-0.199	-0.080	0.205	0.196	0.604
Creatinin, mg/dL	2.79	0.09	-0.119	-0.004	-0.112	0.447	0.978	0.476
C4, µmol/L	0.21	0.01	-0.114	0.065	-0.170	0.483	0.691	0.295
*NEFA, mmol/L	0.26	0.26	0.068	-0.065	-0.269	0.674	0.686	0.089
*TG, mg/dL	22.65	13.23	-0.125	0.046	-0.141	0.456	0.784	0.397
Glucose, mg/dL	79.8	1.05	0.022	-0.062	-0.068	0.887	0.691	0.663
*Insulin, mU/L	15.9	11.6	0.051	0.131	0.090	0.744	0.404	0.564
*3-OH-C4, µmol/L	0.020	0.02	-0.464	0.066	-0.003	0.001	0.673	0.983
IgG, mg/mL	15.52	0.43	-0.400	-0.023	-0.196	0.009	0.887	0.214
IgA, mg/mL	1.20	0.07	0.220	0.051	-0.146	0.156	0.746	0.351

ΔBF 85-108: BF change between d 85 and 108 of gestation; DFA 85-108: daily feed allowance between d 85 and 108 of gestation; *: not normally distributed variable

DISCUSSION

The ΔBF d 85-108 was negatively correlated with the CY without affecting colostrum composition. Although the DFA d 85-108 and the ΔBF d 85-108 were clearly correlated, we did not observe a correlation between CY and the DFA d 85-108.

Sows were group housed during the treatment period and as such, we could not measure the DFI per sow. We are aware of the fact that sow's feed intake within a treatment group might have varied and that this could bias the results. Nonetheless, 2 feeders were present per pen and they dropped a certain amount of feed every 2 min throughout the day, which minimized the possibility of 1 sow eating the meal of another sow. After the treatment period, the 2 sows with the highest BF gain and the 2 sows with the highest BF loss of each treatment group were excluded from further observation as the actual DFI of these sows had the highest risk to deviate from the daily feed allowance. Even with these sows excluded, actual DFI during the treatment period might have differed between sows within a treatment group. The treatments showed a similar variance in BF change during the treatment period, which suggests that the variance in actual feed intake within a treatment group was also similar between treatment groups.

We previously demonstrated a negative correlation between CY and ΔBF d 85-108 (Decaluwé et al., 2013) and this was confirmed in the present study. A first hypothesis to explain this correlation is mammogenesis. As studies estimating mammogenesis imply culling of the sow, we selected some non-invasive parameters that are indicative for mammogenesis. Functional mammary tissue is critical for milk production and piglets' weight gain (Nielsen et al., 2001) and the higher the number of functional mammary secretory cells, the higher the milk production (Head et al., 1991). Unfortunately, a correlation between CY and the amount of functional mammary tissue was not yet investigated but we can assume that the available functional mammary tissue is determinant for its potential production, both for colostrum and

milk. Three observations support the hypothesis that mammogenesis might be the missing link between CY and the ΔBF d 85-108. First, gestational mammogenesis occurs between d 85 and 108 of gestation (Ji et al., 2006). The development of functional mammary tissue is under hormonal control (Devillers et al., 2006), but to build mammary tissue, energy and protein are needed (Noblet et al., 1985; Ji et al., 2006). Nielsen et al. (2001) estimated that 1g of mammary tissue produces 1.3g of milk per day. When we extrapolate the latter to colostrum, then 240g of colostrum (the change in CY for each mm of ΔBF d 85-108 according to our results) is produced by 185g of mammary tissue. Noblet et al. (1985) showed that during the last month of gestation approximately 40MJ ME and 456 g of protein are retained per kg gain of mammary tissue or approximately 7.5MJ ME and 85g of protein for 185 g of mammary tissue gain. When we assume a k value of 0.7 for energy and a maternal efficiency of 0.5 for protein (Whittemore, 1998), then 185g of mammary tissue gain demands 11MJ ME and 170g CP. This amount of energy and protein can be provided by approximately 0.9kg and 1.2kg of feed respectively (with 12.5MJ ME and 140g CP / kg feed). The increased need of nutrients for maintenance of the gained tissue is not considered in this estimation. Although the energy and protein needed for mammogenesis is relatively small, we can assume that sows using more body reserves between d 85 and 108 of gestation might partially do this to develop functional mammary tissue and thus increase their potential to produce more colostrum. A second indication is the similar colostrum composition for each mm of ΔBF d 85-108. Compounds of the colostrum are mainly produced within the mammary alveolar cell or originate directly from the serum (Devillers et al., 2006). The concentration of colostral nutrients and immunoglobulins was not correlated with CY and thus, CY was strongly correlated with total colostral output. This can be due to a higher number of alveolar cells or an increased efficiency of the available alveolar cells. The latter is less plausible as it was shown that milk production is relatively constant per alveolar cell (Nielsen et al., 2001)

which leaves the hypothesis of a better gestational mammogenesis. The concentration of IgG also was not correlated with CY, meaning that when CY increased, the total delivery of IgG from serum to colostrum also increased. As IgG is transferred from the serum to colostrum mainly in a receptor-mediated way by the FcRn-receptor (Schnulle and Hurley, 2003; Salmon et al., 2009), this increase of IgG transfer from serum to colostrum had to result from an increase in FcRn-receptors per unit of mammary tissue or an increase in functional mammary tissue. A third indication is that the negative correlation between the ΔBF d 85-108 and piglets' DWG is present until d 3 of lactation. At that point, mammary secretions were the major source of nutrition for the piglets. Next to the prepuberal and gestational mammogenesis, sows also have a significant lactational mammogenesis (Farmer et al. 2013) which is abundant from d 5 of lactation (Kim et al., 1999a). Therefore, gestational mammogenesis might determine piglet weight gain during early lactation whereas lactational mammogenesis might diminish this effect when the lactation period extends. Nonetheless, CY was correlated with piglets' DWG until weaning which supports earlier findings in literature (Devillers et al., 2011; Decaluwé et al., 2014b). Thus, the ΔBF d 85-108 is negatively correlated with the CY and the hypothesis that mammogenesis is the missing link in this correlation is supported by 1: the observed period during gestation which is important for gestational mammogenesis, 2: the lack of an effect on colostrum composition, and 3: the piglets' DWG until d 3 of lactation.

Next to mammogenesis, we also explored a second hypothesis that insulin sensitivity could explain the negative correlation between CY and the ΔBF d 85-108. Indeed, Foisnet et al. (2010a) showed that sows with a low CY had higher serum concentrations of glucose 1 week before farrowing and Kemp et al. (1996) showed that sows with a decreased glucose tolerance at d 104 of gestation had a greater piglet mortality during the first week of lactation, the latter being highly affected by CI (Decaluwé et al., 2014b). The ΔBF d 85-108 was positively

correlated with the change in plasma glucose and not correlated with the change in serum insulin concentrations during the same period. As concentrations of glucose and insulin at d 85 of gestation were similar for all sows, this is an indication that insulin sensitivity is negatively correlated with the ΔBF d 85-108 which is in accordance with Père et al. (2000) who showed that insulin sensitivity decreases in all sows at the end of gestation but even more so in fat sows. The DFA d 85-108 also affected the glucose metabolism as both basal insulin and glucose increased with increasing feed allowance. Although we were able to alter the glucose metabolism by the treatment and it was also affected by the ΔBF d 85-108, the changes in glucose and insulin between d 85 and 108 of gestation were not correlated with CY. This indicates that CY was not determined by the insulin sensitivity, at least not within ranges observed in this study. Even more, CY was not correlated with changes in any measured blood variable between d 85 and 108 of gestation but was negatively correlated with changes in 3-OH-C4 and negatively correlated with changes in variables indicating protein catabolism between d 108 of gestation and d 1 of lactation. This means that sows that start producing more ketone bodies as indicated by 3-OH-C4carnitine or start using more body protein reserves the week prior to farrowing, have a reduced CY which is concomitant with our previous results (Decaluwé et al., 2013; Decaluwé et al., 2014a). Still, Loisel et al. (2014) reported a positive association between body protein mobilization and CY.

We can conclude that the BF change between d 85 and 108 of gestation is negatively correlated with CY but this correlation cannot be induced by changing the sows' feed allowance between d 85 and 108 of gestation as changing the BF through feed allowance had no effect on CY. The period during gestation, the lack of an effect on colostrum composition and the piglets' daily weight gain during the first days of lactation, support the hypothesis that gestational mammogenesis might be the underlying, explanatory variable and this should be studied thoroughly. On the other hand, insulin sensitivity seems not involved.

3.4.

Piglets' colostrum intake associates with daily weight gain and survival until weaning

Adapted from

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ABSTRACT

The aim of this study was to identify sow and piglet parameters that were associated to piglets' daily weight gain (**DWG**) and survival. We were especially interested in associations with CI and how CI affects AA use in neonatal piglets.

Survival and DWG was recorded of piglets born to 37 PIC sows (parity 1-7) until weaning at 3 weeks of age. Parameters regarding reproduction, sow BC, CY, and colostrum nutritional and immunological composition were noted. Four piglets per litter were randomly selected for serum collection 24-30 h after birth and this was analysed for urea, creatinine, NEFA, IgG, IgA, and 7 free AA.

The DWG was positively associated with BW_B and CI/kg BW_B, and negatively with time between birth and first suckle ($\mathbf{t_{FS}}$) until d 3 of lactation ($R^2 = 0.39$, $P < 0.001$), d 7 of lactation ($R^2 = 0.26$, $P < 0.001$) and weaning ($R^2 = 0.18$, $P < 0.001$). The mortality rate was higher for piglets with a BW_B < 1kg ($P < 0.001$), a CI/kg BW_B < 160g ($P < 0.001$) and a t_{FS} > 60 min ($P < 0.01$).

The CI/kg BW_B was negatively associated to urea ($P = 0.002$), positively to some free AA ($P < 0.05$) but not to creatinine, NEFA, IgG and IgA in piglets' serum. The DWG was negatively associated to urea and positively to leucine until d 3 of lactation ($R^2 = 0.19$, $P < 0.001$), until d 7 of lactation ($R^2 = 0.13$, $P < 0.001$) and until weaning ($R^2 = 0.08$, $P < 0.001$).

A lower CI/kg BW_B was accompanied by a higher catabolism of protein that did not seem to originate from the piglets' body reserves. It seems that piglets with a lower CI/kg BW_B use a larger proportion of colostral protein as a substrate for energy production instead of other purposes such as lean growth, as there was a negative association between parameters indicating protein catabolism and DWG at least until weaning.

In conclusion, the study demonstrated that piglet' daily weight gain and survival until weaning was positively associated with BW_B, CI/kg BW_B and negatively to time between

birth and first suckle. The effect of CI/kg BW_B seems to be related to a shift in nutrient use. With a decreasing CI/kg BW_B, piglets use a relatively higher amount of colostral protein in catabolic processes.

Key words: colostrum – daily weight gain – survival – piglet - protein

INTRODUCTION

Pre-weaning piglet mortality, ranging from 10 to 13% in the main pig producing countries, remains a major problem (Quesnel, 2008a) and mostly occurs during the first 3 days after birth (Tuscherer et al., 2000). Crushing is often identified as the major cause of neonatal mortality (Alonso-Spilsbury et al., 2007), but in most cases this is secondary to insufficient CI (Edwards, 2002; Le Dividich et al., 2005a).

At birth, piglets have very limited body reserves (Le Dividich et al., 2005a) and due to the epitheliochorial structure of the placenta, they hardly receive antibodies prenatally (Salmon et al., 2009). Colostrum is the sole external resource providing the neonatal piglet with nutrients (Le Dividich et al., 2005a), maternal immunity (Rooke and Bland, 2002) and factors promoting development of the gastro-intestinal tract (Xu et al., 2000). Le Dividich et al. (2005a) state that piglets need a minimal CI of 160-170 g/kg BW_B. Our earlier work showed that approximately one third of the sows do not produce 160 g colostrum per kg live born litter (Decaluwé et al., 2013).

The CI was positively associated with survival and weight gain (further referred to as performance) during the first 6 weeks of life (Devillers et al., 2011) stressing the importance of CI to optimize piglet long-term performance. The CI was also positively associated with rectal temperature and plasma glucose concentration (Devillers et al., 2011), which emphasises that colostrum prevents hypothermia and hypoglycaemia. Flynn et al. (2000) showed a very active protein metabolism in sow-reared piglets during lactation. The main function of AA is to be used as building blocks for protein synthesis, but they can also be used

as a substrate for energy production although this is not preferable as it is less efficient (Wu, 2009). To our knowledge, the rather small number of publications investigating the importance of colostrum for piglet performance has mainly focused on piglets' energy metabolism. The relation between CI and protein metabolism has, apart from Ig, not been described.

This study was set up to identify sow and piglet parameters affecting piglets' pre-weaning daily weight gain (**DWG**) and survival. A particular focus was piglets' CI as this was expected to be a major risk factor. Amino acid concentrations were monitored in 24-30 h old piglets to evaluate its relationship with CI and DWG during lactation.

MATERIAL AND METHODS

Description of the study population

This study was approved by the Ethical committee of the Faculty of Veterinary Medicine, Ghent University (EC2011/005). The experiment was performed during April and May 2011 at a commercial farm with 1700 PIC sows in a 2-week batch system. Five-hundred fifty-one piglets from 37 sows (parity 1-7) were observed from birth to weaning at 3 weeks of age. Day of birth was defined as d 0 of age. During suckling, piglets were housed in conventional farrowing crates with floor heating and infrared lamps. From d 5 of lactation, piglets were offered creep feed but intake could not be measured. Cross-fostering was performed at d 2 of age to standardise litters to 11 ± 1 piglet and, therefore, 37 piglets were cross-fostered out of the study population and not further observed.

The farrowing process was not induced and manual birth assistance was only performed when the birth interval exceeded 1 h. Oxytocin was not administered during parturition as this interferes with mammary secretion (Ellendorf et al., 1982), except when sows had not finished farrowing before the colostrum sampling 6 h after birth of the first piglet, which was the case for 6 sows. The detailed handling of piglets at birth was as follows: when a piglet was

born, the back of the piglet was dried with a paper towel, a number was written on the back with a marker and the piglet was ear-tagged allowing identification. The umbilical cord was shortened when it was longer than approximately 15cm. After weighing, they were placed against the sow's vulva again with their nose. No additional help or care was given to the piglets unless there was a risk for them getting crushed.

Bodyweight of the individual piglets was measured at birth, between 17-24 h after birth (**BW_{24}**), at d 3, 5 and 7 of lactation and at weaning. Day of mortality was recorded when applicable. The piglets' CI was estimated by the regression equation described by Devillers et al., (2004b) based on BW_B, BW_{24}, time between birth and first suckle (**t_{FS}**), and duration of CI (**t** with $17h \leq t \leq 25h$). The equation is the following:

$$CI = -217.4 + 0.217 \times t + 1861019 \times BW_{24}/t + BW_B \times (54.80 - 1861019/t) \times (0.9985 - 3.7 \times 10^{-4} \times t_{FS} + 6.1 \times 10^{-7} \times t^2_{FS})$$

Along this paper, CI is expressed per kg BW_B.

Collection and analyses of samples

The creep feed was analysed for its nutritional composition according to the methods outlined by the Association of Official Analytical Chemists (Thiex, 2002) (ISO 5983-1, 2005; ISO 1443, 1973; ISO 5498, 1981). It was composed of 96.5% dry matter with 16.2% crude fat, 18.0% crude protein, 7.2% crude ash and 1.3% crude fibre.

Blood (5 mL, serum cloth activator tubes) was collected from 2 randomly selected male and 2 female piglets per litter between 24 to 30 h after birth by puncture of the *vena jugularis*, stored in iced water and subsequently centrifuged at 671 x *g* for 10 min. Serum was collected and stored at -20°C until further analysis. Serum was analysed for urea, creatinine, NEFA, IgG, IgA, acylcarnitine profile and 7 free AA, i.e. valine (**Val**), leucine (**Leu**), methionine, phenylalanine (**Phe**), tyrosine (**Tyr**), glycine (**Gly**) and alanine (**Ala**). Urea, creatinine and NEFA were measured spectrophotometrically (Ultrospec IIE, LKB, Biochrom, Cambridge,

England) using a commercial colorimetric diagnostic kit (Randox Laboratories, Crumlin, United Kingdom). IgG and IgA were analysed by a porcine quantitative sandwich enzyme immunoassay technique (Bethyl Laboratories Inc., Montgomery, USA). Quantitative electrospray tandem mass-spectrophotometry as described by Vreken et al. (1999) was used to determine the acylcarnitine profile and the earlier described 7 free AA in serum. This technique does not analyse the other free AA and thus, no information is available on them. All samples were analysed in duplicate.

Colostrum (35 mL) was collected at 3, 6 and 24 h after birth of the first piglet, equally divided from all teats of 1 side of the udder. Except for the sample at 3 h, 2 mL of oxytocin (10IU/mL) was administered intramuscularly 5 min before sampling. At the time of the sample collection at 6 h, 6 sows did not complete the farrowing and they were also given an injection of 2 mL of oxytocin. The samples were subdivided and stored at -20°C until further analysis. Each colostrum sample was analysed for its chemical composition, IgG and IgA. Dry matter, fat, protein and lactose content were predicted by Lactoscope FTIR Advanced type FTA-3.0 (Delta Instruments, Drachten, Netherlands) as used by van den Brand et al. (2000) and Laws et al. (2009). The FTIR-analyses were not done in duplicate because of the high amount of sample needed but samples of 8 sows were also analysed by the Gerber method to determine the fat content (R^2 between FTIR and Gerber = 0.9975) and by the Kjeldahl method to determine the protein content (R^2 between FTIR and Kjeldahl = 0.9997). This was used to linearly correct all results. Immunoglobulins G and A were analysed by a porcine quantitative sandwich enzyme immunoassay technique (Bethyl Laboratories Inc., Montgomery, USA) in duplicate.

Statistics

Multilevel multivariable regression analysis was performed using MLwiN (University of Bristol, UK) to identify predictors for the piglets' individual DWG until d 3 and d 7 of

lactation and until weaning. Sow was included as a random effect to account for the clustering of piglets within a sow. First, predictors with a *P*-value < 0.15 in a multilevel univariable regression model were identified. Linearity of the relationship between predictor and outcome variable was examined graphically. When a correlation coefficient > 0.6 was detected between 2 predictors, 1 of these possible predictors was not entered in the model based on biological importance in the first place and on statistical importance in the second place. Then, the remaining predictors were included in a multilevel multivariable regression model and a backward modelling procedure was performed. Goodness-of-fit of each model was tested in SAS (PROC MIXED) (SAS Institute Inc., USA) including the goodness-of-fit measures, 2 x log-likelihood, the Akaika information criterion, and the Bayesian information criterion. Conditional studentized residuals were evaluated graphically and graphed against the predicted values. Regression analysis was performed separately for the technical variables presented in **Table 1** (technical model) and for the piglets' serum variables that were associated with CI/kg BW_B (metabolic model). The individual sow's/piglets' nutrient and Ig output/intake via colostrum was estimated by measuring the area under the curve of the regression line of the colostral chemical composition and Ig content. For the metabolic model only piglets' serum parameters associated with CI/kg BW_B were included in the model as the aim was to focus on the metabolic processes that could explain the relation between CI/ kg BW_B and piglets' daily weight gain.

Table 1 *List of all technical variables explored as possible predictors for daily weight gain in piglets. Total output/intake of different colostral components by the sow/piglets was estimated by measuring the area under the curve of the respective regression equation.*

Sow level	
Technical parameters	Parity
	Gestation length, days
	Total born piglets
	Liveborn piglets
Condition parameters	BF d 109 of gestation, mm
	BF d 1 of lactation, mm
	ΔBF between d 85 and 109 of gestation, mm
	ΔBF/d between d 109 of gestation and d 1 of lactation, mm
CY	Total CY, g
Colostrum nutritional composition (fat, protein, lactose, dry matter)	Concentration 3, 6, 24h after onset of farrowing, %
	Total output via colostrum, g
Colostrum immunological composition (IgG, IgA)	Concentration 3, 6, 24h after onset of farrowing, mg/mL
	Total output via colostrum, mg
Piglet level	
Technical parameters	Time between birth and first suckle, min
	Birth interval, min
	Birth rank
	BWB, kg
CY	CI, g
	CI/kg BW_B, g
Colostrum nutritional composition (fat, protein, lactose, dry matter)	Total intake via colostrum, g
	Total intake/kg BW_B via colostrum, g
Colostrum immunological composition (IgG, IgA)	Total intake via colostrum, mg
	Total intake/kg BW_B via colostrum, mg

ΔBF: change in BF; ΔBF/d: daily change in BF

A Cox proportional hazard model with sow included as a stratum was fit to determine the association between fixed effects BW_B, CI/kg BW_B and t_{FS}, and the estimated time to death using STATA10 (StataCorp LP, USA). Variables associated with DWG were converted to categorical variables: BW_B (< 1 kg, 1-1.6 kg, > 1.6 kg), CI/kg BW_B (< 160 g/kg BW_B, 160-

250 g/kg BW_B, > 250 g/kg BW_B) and t_{FS} (< 30 min, 30-60 min, > 60 min). The thresholds of the lower categories were based on literature. Piglets with a BW_B < 1kg are defined as intra-uterine growth retarded piglets (Michiels et al., 2011), Le Dividich et al. (2005a) state that piglets need at least 160g CI/kg BW_B and the time between birth of a piglet and its first suckle averages 30 min (De Passillé and Rushen, 1989b). Upper thresholds were chosen arbitrarily but it was taken into account that each category needed to contain a sufficient number of piglets and that on a representative farm, it would be realistic to find piglets belonging to each category. Survival analysis based on piglet's serum variables was not performed as only 6 out of 145 piglets of which serum was collected, died during lactation.

The over-time changes of the colostrum composition were analysed by repeated measures ANOVA.

Data are reported as LSMean ± SEM unless otherwise mentioned and results were considered to be statistically significant with a *P*-value < 0.05. Normality of the data was verified performing a Kolmogorov-Smirnov test. Correlation analysis was performed using Pearson or Spearman Rank correlation analysis when data were normally or not normally distributed.

RESULTS

Colostrum

The total CY was 3243 ± 132 g per sow. The CI per piglet was 245 ± 12 g with a maximum of 635 g and the average CI/kg BW_B of the piglets was 196 ± 8 g with a maximum of 394 g. Thirty-seven per cent of the sows did not produce and 31% of the piglets did not consume 160 g colostrum per kg live born piglet. Average t_{FS} was 36 ± 2 min.

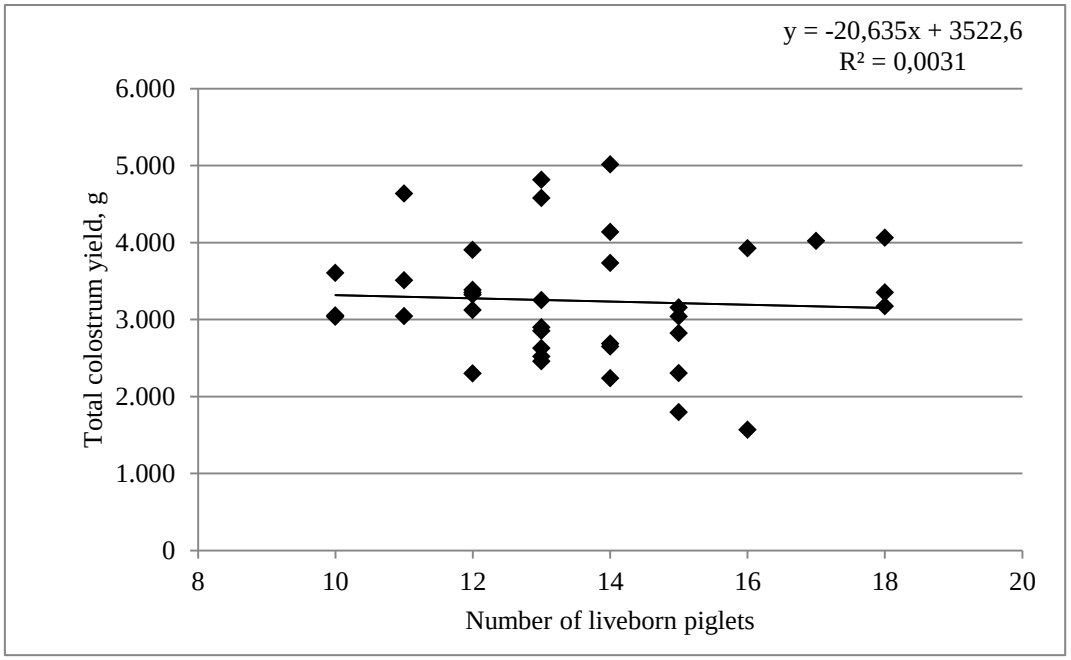
The CY was not associated with number of liveborn piglets (R^2 = 0.003, *P* = 0.74) while the average CY per liveborn piglet decreased 20g for each extra liveborn piglet (R^2 = 0.34, *P* < 0.001) (**Figure 1**). The nutritional composition and concentration of IgG and IgA in colostrum 3, 6 and 24h after birth of the first piglet are shown in **Table 2**. Nutritional composition of

colostrum was independent of CY except for protein content 24 h after birth of the first piglet which was correlated with CY but the correlation coefficient remained small (r = -0.372; *P* = 0.023).

The CI/kg BW_B was associated with piglets' serum concentration of urea (negative), Val, Leu, Phe, Tyr and Ala (positive), and tended to be associated with the serum concentration of IgG (*P* = 0.09). Details are presented in **Table 3**. No clear associations were observed between the CI/kg BW_B and the variables of the acylcarnitine profile (results not shown).

Table 2 *Mean nutritional composition and mean concentrations of IgG and IgA in colostrum 3, 6 and 24 h after birth of the first piglet. The SEM is shown between brackets. Statistical analysis of the time effect was performed.*

Variable	3h	6h	24h	*P*
Fat, %	8.9 (0.6)	9.9 (0.5)	14.2 (0.6)	< 0.001
Protein, %	25.2 (0.6)	21.9 (0.5)	11.6 (0.4)	< 0.001
Lactose, %	3.1 (0.1)	3.6 (0.1)	5.4 (0.1)	< 0.001
Dry matter, %	37.2 (0.7)	35.5 (0.6)	31.2 (0.7)	< 0.001
IgG, mg/mL	92 (12)	85 (13)	18.3 (3)	< 0.001
IgA, mg/mL	11 (1.3)	8.1 (0.8)	2.8 (0.3)	< 0.001



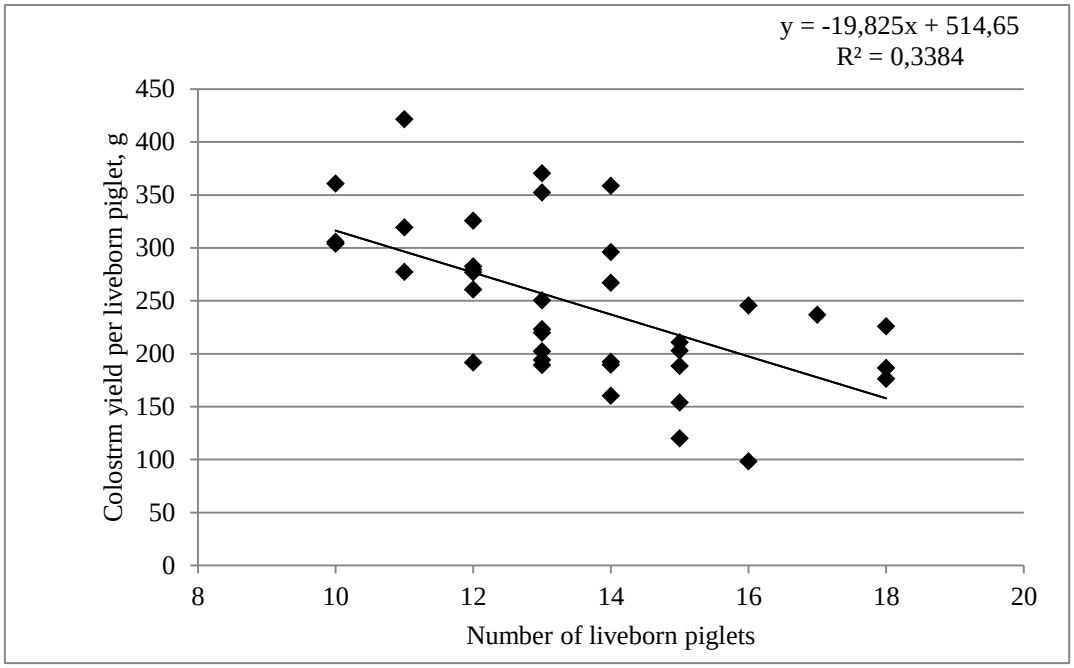


Figure 1 *In the first graph, the association between the number of liveborn piglets and total CY is shown. In the second graph, the association between the number of liveborn piglets and the available CY per liveborn piglet is shown. Total CY was not associated to the number of liveborn piglets and as a consequence, the available amount of colostrum for each liveborn piglet, decreases as the number of liveborn piglets increases.*

Table 3 *Serum concentrations of metabolites, Ig and free AA in piglets (24-30h old), and their association with the CI/kg BW_B obtained by multilevel regression analysis using CI/kg BW_B as predictor and each metabolite as dependent variable. No association between carnitine acids and CI/kg BW_B were observed and these data are not shown.*

	Serum concentration				Association with CI/kg BW_B		
Variable	Mean	SEM	Minimum	Maximum	Slope	SEM	*P*
NEFA, µmol/L	242	12.5	ND	664	0.19	0.14	0.16
Urea, µg/mL	430	13.1	180	1090	-480	158	0.002
Creatinine, µg/mL	10	1.4	5.0	14	-1.0	1.8	0.57
IgG, mg/mL	28	1.2	0.32	108	24	14	0.09
IgA, mg/mL	16	1.6	1.1	209	0.50	22	0.99
Valine, µmol/L	64	1.9	28	128	0.047	0.02	0.03
Leucine, µmol/L	338	6.4	206	543	0.19	0.08	0.02
Methionine, µmol/L	41	2.0	11	119	0.016	0.03	0.53
Phenylalanine, µmol/L	150	2.9	61	229	0.17	0.03	< 0.001
Tyrosine, µmol/L	201	5.4	55	397	0.27	0.07	< 0.001
Glycine, µmol/L	545	14.2	221	1363	-0.082	0.17	0.63
Alanine, µmol/L	809	16.6	415	1276	0.60	0.20	0.004

ND: not detectable (for NEFA < 72 µmol/L)

Daily weight gain

Total litter BW_B was 19.0 ± 0.5 kg, BW_B of the liveborn piglets was 1311 ± 72 g and BW_B of stillborn piglets was 1224 ± 15 g. Piglet body weight at 24h, 3 and 7 days of age and at weaning was 1393 ± 33 g, 1675 ± 39 g, 2449 ± 56 g and 5439 ± 105 g. Piglet's DWG until d 3 and 7 of lactation and until weaning was 104 ± 3 g, 154 ± 3 g and 205 ± 3 g.

During the 3 observed time periods, DWG was associated with the same 3 predictors, all of them located at pig level. Birth weight and CI/kg BW_B both showed a significant positive association with DWG during all observed time periods. The negative association between DWG and t_{FS} was significant until d 3 and tended to be significant ($P < 0.10$) when observed time periods prolonged (**Table 4**).

As we were mainly interested in the role of CI/kg BW_B, serum parameters that were significantly associated with CI/kg BW_B (**Table 3**) were used as predictors for piglets' DWG in a multivariable multilevel regression analysis (**Table 5**). Metabolic parameters that were maintained in the model are urea and Leu. Serum concentration of urea was negatively associated while Leu was positively associated with DWG during the observed time periods. Two other AA, Phe and Tyr, were also significantly associated with DWG but were highly correlated mutually as well as with Leu (r between 0.65 and 0.73). The choice to continue with Leu was made as this offered the strongest model.

Table 4 *Details of the multilevel multivariable regression analysis with daily weight gain (DWG) during different periods as dependent variable and technical parameters described in* ***Table 1*** *as possible predictors. For all time periods, BW_B and CI/kg BW_B were positively associated and time until first suckle (t_{FS}) was negatively associated with DWG.*

Model	DWG until d 3, g/d			DWG until d 7, g/d			DWG until weaning, g/d		
	Slope	SEM	*P*	Slope	SEM	*P*	Slope	SEM	*P*
Intercept	-82.3	13.9	< 0.001	-30.0	16.3	0.08	44.8	17.2	0.01
BW_B, g	0.082	0.01	<0.001	0.094	0.01	< 0.001	0.087	0.01	< 0.001
CI/kg BW_B, g	0.43	0.03	< 0.001	0.29	0.03	< 0.001	0.23	0.04	< 0.001
t_{FS}, min	-0.19	0.07	0.007	-0.14	0.08	0.07	-0.16	0.08	0.04
R^2 and *P* total model	$R^2 = 0.39$, $P < 0.001$			$R^2 = 0.26$, $P < 0.001$			$R^2 = 0.18$, $P < 0.001$		

Table 5 *Multilevel multivariable regression analysis using daily weight gain (DWG) until d 3 and 7 of lactation and until weaning as dependent variables and metabolites and free AA significantly affected by CI/kg* BW_B *as possible predictors.*

Model	DWG until d 3, g/d			DWG until d 7, g/d			DWG until weaning, g/d		
	Slope	SEM	*P*	Slope	SEM	*P*	Slope	SEM	*P*
Intercept	110	22	< 0.001	160	23	< 0.001	198	23	< 0.001
Urea, mg/dL	-1.84	0.32	< 0.001	-1.83	0.36	< 0.001	-1.69	0.36	< 0.001
Leucine, µmol/L	0.21	0.06	0.01	0.22	0.06	< 0.001	0.25	0.06	< 0.001
R^2 and *P* total model	$R^2 = 0.19$, $P < 0.001$			$R^2 = 0.13$, $P < 0.001$			$R^2 = 0.08$, $P < 0.001$		

Piglet survival

Total pre-weaning piglet mortality was 11.6% and 85% of these piglets died within the first 3 ds after birth. Pre-weaning mortality during the 3 periods was analysed using the technical variables associated with DWG after converting them to categories as described above. Details of survival analysis are shown in **Table 6**. Piglet mortality was higher with a BW_B lower than 1kg and a CI/kg BW_B lower than 160 g during all observed time periods. According to our classification, once BW_B exceeded 1kg or the CI/kg BW_B exceeded 160 g, chance of survival did not increase with a higher BW_B or CI/kg BW_B. When t_{FS} took longer than 60 min, survival rate was significantly lower compared to a t_{FS} below 30 min. In the time period until d 3, piglets with a t_{FS} between 30 and 60 min had a better chance of survival than piglets with an interval that took longer than 60 min.

Table 6 *Percentage mortality until d 3 of lactation, d 7 of lactation and weaning. Analysed risk factors (3 categories each) were BW_B, CI/kg BW_B and time between birth and first suckle (t_{FS}).*

Variable	Group	N	Until d 3	Until d 7	Until weaning
BW_B, kg	< 1.0	57	42.1 [a]	50.9 [a]	50.9 [a]
	1 – 1.6	301	6.0 [b]	6.0 [b]	6.3 [b]
	> 1.6	95	4.2 [b]	6.3 [b]	6.3 [b]
CI/kg BW_B, g	< 160	157	23.0 [a]	26.8 [a]	27.4 [a]
	160-250	198	3.0 [b]	3.0 [b]	3.0 [b]
	> 250g	98	4.1 [b]	5.1 [b]	5.1 [b]
t_{FS}, min	< 30	290	4.1 [a]	5.2 [a]	5.5 [a]
	30-60	86	12.8 [a]	16.3 [ab]	16.3 [ab]
	> 60	67	19.4 [b]	20.9 [b]	20.9 [b]

Superscripts indicate significant differences ($P < 0.05$) between groups within a time period (not between time periods).

Reproductive performance

Total number, number of liveborn and number of stillborn piglets was 14.6 ± 0.4, 13.5 ± 0.4 and 1.05 ± 0.2. The percentage of stillborn piglets was 6.3 ± 9.6. The farrowing process lasted 234 ± 19 min with an average birth interval of 14 ± 0.8 min for liveborn piglets and 40 ± 11 min for stillborn piglets.

DISCUSSION

Distinct positive long-term associations with piglets' performance were observed for BW_B and CI/kg BW_B which agrees with findings of Devillers et al. (2011) who showed this association up to 6 weeks of age. The relationship between BW_B and piglet performance has already been well described (Milligan et al., 2002, Quiniou et al., 2002). One explanation for the long-term association of CI/kg BW_B on DWG might be that piglets that consume enough colostrum provide in their nutritional needs and, therefore, are able to keep suckling high amounts of mammary secretion e.g. because piglets become stronger and more vital and/or because suckling is the best lactation stimulator in the sow (Hurley, 2001). Also, colostrum and milk are rich in various bioactive compounds, including growth promoting factors that promote gastro-intestinal development and benefit absorption of nutrients (Xu et al., 2000). As our data only show an association, we cannot exclude that other, not measured variables might affect this association. The positive relationship between CI/kg BW_B and survival of the piglets is probably due to prevention of starvation. Indeed, Devillers et al. (2011) showed that piglets consuming less than 200g of colostrum are more prone to develop hypothermia and hypoglycaemia which is a main underlying cause of neonatal mortality (Le Dividich et al., 2005a). Beyond 3 days of age, the association between t_{FS} and DWG changed from clearly significant towards a trend. A large part of piglets with a t_{FS} exceeding 30 min died during the first 3 days of lactation so that they could not be included in models for DWG during longer lasting periods. Also, piglets that did survive beyond 3 days might have partially recovered from a prolonged t_{FS} but the negative association with DWG remains until weaning.

Parameters representing nutritional and immunological composition of colostrum (**Table 1**) were also entered in the model but none of them were retained. Total grams of nutrient output through colostrum and nutrient intake/kg BW_B via colostrum contributed to the model but were highly correlated with total CY produced by the sow (r between 0.74 and 0.95) or CI/kg

BW_B by the piglets (r between 0.95 and 0.98). Correlation between mg intake/kg BW_B of Ig through colostrum and CI/kg BW_B was lower (r between 0.45 and 0.59), probably due to the wide variability of colostral Ig concentrations which is in agreement with other studies (Farmer and Quesnel, 2009). In the present study, CI/kg $BW_{B,}$ therefore, seemed a good estimator of total nutrient but not of IgG and IgA intake. The latter 2 were entered but not retained in the model predicting DWG. Absorption of intact Ig is only possible prior to gut closure and this gut closure is not directly induced by the amount of Ig but rather by the amount of nutrients absorbed. Also, Ig absorption might be saturated with increasing amounts of CI (Rooke and Bland, 2002; Le Dividich et al., 2005a; Devillers et al., 2011). After gut closure, Ig mainly exhibit an immunological function at the level of the gut or they are digested as a protein (Salmon et al., 2009). This suggests that during the pre-weaning period and within the observed ranges, nutrient intake rather than Ig intake is the underlying reason for the positive association between CI/kg BW_B and DWG as has already been stated for neonatal survival (Le Dividich et al., 2005a). Nonetheless, it is important for piglets to obtain a high level of passive immunity as this assures long-term health which is an important requirement for weight gain and post-weaning performance (Rooke and Bland, 2002).

The chemical composition of colostrum revealed high concentrations of protein and dry matter compared to other studies (Le Dividich et al., 2004; Devillers et al., 2007; Foisnet et al., 2010a) without showing a lower CY. Our study was performed in PIC sows of which colostrum composition was not described before. Farmer et al. (2007) showed that chemical composition of colostrum differs between genotypes although they did not observe concentrations similar to the ones in this study.

We wanted to unravel the metabolic processes that could explain the association between CI/kg BW_B and DWG before weaning. In a first step, metabolic parameters in piglets' serum that were associated with CI/kg BW_B were identified. Interpretation of these parameters

should be done carefully, as the time between sampling and last suckle was not standardised. Some parameters might have responded more dramatically to the time after suckling than others, but nevertheless, relative sampling times were completely random, hence should not render bias, but might only generate larger SD. The fact that increasing CI/kg BW_B was associated with lower urea and higher free AA concentrations in serum indicates that in the case of a low CI, a higher proportion of absorbed AA are used for (maintenance) energy requirements instead of lean growth. The lack of association of CI/kg BW_B with serum NEFA and creatinine suggests that mobilisation of piglets' body reserves was not into play, but rather their absorbed proteins were directed to either energy substrate for maintenance requirements or building block for lean growth. This is not surprising as piglets' body reserves at birth have shown to be very low (Le Dividich et al., 2005a). The rather high variability of colostral IgG and IgA concentrations and the fact that gut closure is induced by the uptake of nutrient per se rather than the amount of absorbed IgG (Rooke and Bland, 2002) might explain the absence of an association between Ig intake via colostrum and CI/kg BW_B.

In a second step, we analysed whether serum metabolites that were significantly associated with CI/kg BW_B, were also associated with DWG. Only urea and Leu were retained in the models for all observed time periods. The negative association between DWG and urea supports the hypothesis that the direct use of absorbed nutrients can shift between anabolism and catabolism. With a low CI, the colostral protein intake also decreases and then a part of the colostral protein is catabolised probably as energy substrate which decreases the amount of colostral protein available for lean weight gain. An association between a piglet's serum AA and CI/kg BW_B did not necessarily mean an association with the DWG. An association with CI/kg BW_B and DWG was only observed for Leu, Phe and Tyr. This indicates that the importance of intake might differ between AA as e.g. some AA might be more limiting or some could exert special functions. It has already been shown that Leu acts as a signal

molecule which promotes muscle protein synthesis in neonatal piglets (Escobar et al., 2006; Suryawan et al., 2008). At the moment it is unclear which factor in CI caused the shift between AA usage for lean growth or for energy requirements, but total amount of ingested nutrients is likely important because CI/kg BW_B was highly correlated with intake of colostral nutrients. It is notable that this effect lingered on until weaning.

In accordance to other studies (Devillers et al., 2007; Foisnet et al., 2010a), our results show that providing sufficient colostrum to each piglet is not evident and becomes more difficult as litter size increases. Also, colostrum is not divided equally among piglets so to assure 160 g CI/kg BW_B for every piglet, CY should, therefore, exceed 160 g per kg litter weight. As it is shown that colostrum has long-term effects on DWG and survival rate, research aiming to increase CY in sows, both via a breeding and management approach, should be of high priority. Optimizing colostrum composition might also be important as it has already been shown that sow's milk stimulates fat deposition rather than optimizing lean tissue gain (Pluske and Dong, 1998). Our results point to the association of specific AA with DWG. The fact that they can be altered through CI warrants further investigation in their eventual contribution to piglet development.

CONCLUSION

In conclusion, the study demonstrated that piglet' daily weight gain and survival until weaning is positively associated with BW_B, CI/kg BW_B and negatively to time between birth and first suckle. The effect of CI/kg BW_B seems to be related to a shift in nutrient use, rather than the effect of maternal Ig supply. With a decreasing CI/kg BW_B, piglets use a relatively higher amount of colostral protein in catabolic processes instead of using it for weight gain.

CHAPTER 4

GENERAL DISCUSSION

1. CRITICAL COMMENTS RELATED TO THE STUDY DESIGN

1.1. Estimation of colostrum yield

Because our trials were performed under commercial conditions and a large number of sows needed to be observed at the same time, we used the weight equation model developed by Devillers *et al.* (2004b) to estimate CY. There are some critical remarks that need to be considered on methods for estimating CY. There are 2 major drawbacks.

First, the technique is intensive and requires continuous supervision of the sows. There is only minor manipulation of the piglets, but still this manipulation might interfere both in a positive and negative way. The manipulations might stimulate piglets that are born weak and hypoxic but could also disturb normal born piglets. Also, continuous attendance might be a stress factor for the observed sows which could negatively affect the farrowing process. Indeed, high level of fear of humans was correlated with a longer farrowing duration and a longer birth interval between piglets as well as a decreased survival rate of the piglets (Thodberg *et al.*, 2002; Janczak *et al.*, 2003; Mosnier *et al.*, 2009).

Second, CY in sows is measured indirectly through the piglets. Therefore, we should wonder whether the sum of CI by the piglets is a good estimate of CY or rather a measure of maximal CI by the piglets. The ability of the piglets to suckle can be affected by many variables such as presentation of the teats, splayleg, early parturition and runt piglets (Damm *et al.*, 2002). Indeed, Devillers *et al.* (2007) showed that piglets with indications of lower vitality had a reduced CI. The impact of some piglets with lower vitality at birth on estimated CY was not shown yet but can be expected to be minor as the sow's CY is considered lower than the potential intake by the litter. When kept in similar environments, bottle-fed piglets had a voluntary CI which was over double the average intake by sow-reared piglets (Le Dividich *et al.*, 1997). Also, the large within-litter (15 – 110%) and between-litter (30%) variation in CI (Le Dividich *et al.*, 2005a) indicate that not all piglets can consume their full potential when

sow-reared. Therefore, it is generally accepted that the sow's capacity to produce colostrum is the limiting factor in CY and thus the total sum of individual CI by the piglets is a good estimate of total CY. Of course, when a sow does not allow the piglets to suckle, then the estimated CY might be an underestimation of the true yield.

1.2. Extrapolation of the results

Most studies considering CY in sows are performed on 1 farm and with 1 breed (Flummer and Theil, 2002; Hansen *et al.*, 2012; Devillers *et al.*, 2007; Foisnet *et al.*, 2010a, b). This was also the case in our studies. The labor-intensive methods related to estimating CY can explain this. Indeed, continuous (24/24) supervision of a group of sows is needed when estimating CY. In our studies, we focused on sow factors that affected CY. Using different herds in these studies might have biased the results due to possible effects at herd level (Declerck *et al.*, unpublished results).

All our studies were performed on 1 commercial sow farm, with 1700 PIC sows. A sow was never used in more than 1 experiment. The sows used in our studies had an average of 14.5 total born piglets, 13.4 liveborn piglets, 1.1 stillborn piglets, 10.9 weaned piglets and 18.9% pre-weaning mortality. Based on these figures, the sows can be considered as high-prolific. Pre-weaning mortality was quite high. Based on productivity, we can state the sows used in our experiments are representative for the current sow population in NW Europe. The range of the sows' CY observed in our experiments was comparable to those reported in other publications (Devillers *et al.*, 2007; Foisnet *et al.*, 2010a, b). Nonetheless, extrapolation of our results to other sow breeds and herds should be done with caution. Experiments that confirm our results with other breeds and on other farms are warranted.

2. STRATEGIES TO IMPROVE COLOSTRUM YIELD

Previous research reported that one third of sows has an insufficient CY for nursing the litter (Le Dividich *et al.*, 2005a; Foisnet *et al.*, 2010a, b) and that CY is highly variable between sows (Devillers *et al.*, 2007; Foisnet *et al.*, 2010a; Quesnel, 2011). These observations were confirmed by our research (**chapter 3.1., 3.2., and 3.3.**). This large variation offers a window for improvement. Apparently, some sows are able to produce more colostrum than others and thus by examining differences between these sows, we could unravel how CY is determined and which strategies could be implemented to improve CY. When aiming to improve CY, we should develop 2 strategies, always keeping in mind that an improvement in CY should not be at cost of the colostrum composition.

A first strategy can be considered a short-term strategy which should focus on optimizing the management of the sow, in all its aspects. The large variation in CY between sows indicates that some sows likely do not achieve their full potential. Indeed, nowadays, sows are expected to deliver top performances i.e. CY and thus, optimal conditions need to be created for these sows to allow them to achieve these top performances. The short-term strategy thus should focus on how we can decrease the difference between the actual and potential CY.

A second strategy can be considered a long-term strategy which should look beyond optimizing CY within 1 reproductive cycle but focus on a complete life-span of the sow and even look at improving CY potential at population level. Indeed, on a longer term, we should not only aim that sows achieve their potential CY but also aim for an increased CY potential. The potential of sows to produce piglets increased significantly during the last decades (Tribout *et al.*, 2003). It is not clear whether this change affected CY. Nonetheless, CY is independent of litter size (**chapter 3.4.**), and thus the increase in litter size probably resulted in a decreased amount of colostrum available per piglet.

2.1. Short term strategy

Most research focused on the importance of hormonal changes in the peripartal period and how this could influence CY. Indeed, the peripartal period is characterized by many hormonal alterations (Devillers *et al.*, 2006). Especially the increase in prolactin and the concomitant decrease in progesterone concentrations seem important in determining CY by regulating the closure of the mammary gland barrier (Foisnet *et al.*, 2010a). Unfortunately, these peripartal hormonal changes are not easy to manipulate. Supplementation of altrenogest (Foisnet *et al.*, 2010b) or prostaglandins (Foisnet *et al.*, 2011) to sows in the peripartal period had no effect on changes in reproductive hormones and no or very limited effect on CY. Silymarin is a plant extract from the plant *Silybum marianum* and when fed to gilts between d 90 and 100 of gestation, it tended to increase serum prolactin concentration (Farmer *et al.*, 2014). When fed during the last 4 days of gestation, it increased serum prolactin concentrations 24 h before farrowing (Loisel *et al.*, 2013b). A study that investigated the effects of silymarin supplementation during the last week of gestation showed no effects on CY, but prolactin concentrations were also not affected in this study (Loisel *et al.*, 2014). With comparable hormonal patterns around farrowing, still much variation in colostrum production between sows can be observed. This indicates that hormonal regulation is important in setting the scene for colostrum and milk production after which other factors like nutrient availability might determine the success rate.

The peripartal period is, next to important changes in reproductive hormones, also characterized by the shift from an anabolic gestation homeorhesis to a catabolic lactation homeorhesis (Martineau *et al.*, 2013). This metabolic change is accompanied by changes in feed-intake regulating hormones (Cools *et al.*, 2013). Colostrum is mostly produced during the last week of gestation and as a result, the mammary gland is highly demanding for nutrients during this period. We showed that the BF change in the last week before farrowing

was positively correlated with CY (**chapter 3.1.**) which indicates that a negative energy balance around farrowing should be avoided. Nonetheless, studies considering peripartal feeding strategies are scarce and mostly sows are fed restrictedly at the end of gestation. Cools *et al.* (2014) showed that *ad libitum* feed intake during the peripartal period is beneficial as it prohibits a negative energy balance before farrowing and leads to higher litter weaning weights while no drawback in feed intake was observed. Dourmad *et al.* (1999) stated that a restricted feed intake at the end of gestation can only have minor negative effects on CY as the sow can mobilize her body reserves. We showed that sows with a restricted feed intake at the end of gestation indeed compensated by mobilizing body fat and protein reserves but apparently this was insufficient to achieve their full potential CY (**chapter 3.2.**) and the more they had to compensate, the lower the resulting CY was (**chapter 3.1.**). One explanation could be the reduced availability of nutrients in the mammary gland in case of restricted feed intake. This is less plausible as the amount of nutrient output in colostrum was much lower than the amount of extra nutrient input via the feed in the high fed group. Another explanation is that the extra input of nutrients reduced the negative energy balance, resulting in a lower fat mobilization and less production of acetyl-CoA. In this way, there is less unbalance in the citric acid cycle. This was supported by the higher serum concentrations of 3-OH-C4 as a marker for ketone bodies when sows were fed restrictively (**chapter 3.2.**). Protein catabolites can serve as precursors of oxalo-acetate and thus might reduce the relative shortage of oxalo-acetate compared to acetyl-CoA. We observed a decreased CY with increasing body protein catabolism 3-4 days before farrowing (**chapter 3.1.**), whereas a positive relation between CY and body protein catabolism was shown at d 1 of lactation (**chapter 3.1.**). Loisel *et al.* (2014) observed an increased CY with higher mobilization of body protein reserves the day before farrowing. The discrepancy might be due to the different energy balance of sows in both studies, being negative in our study and positive in the study by Loisel *et al.* (2014). A high

feeding strategy the week prior to farrowing led to more feed derived protein catabolites which were accompanied by a higher CY (**chapter 3.2.**). Although the mechanisms underlying the correlation between CY and the availability of protein catabolites remains unclear, it is clear that suboptimal feeding strategies around farrowing put the balance of the sow's metabolism under pressure and can only be partially compensated by the sow which leads to suboptimal performances. This, together with the work of Cools (2013), provides a growing body of evidence that peripartal feeding strategies are important for production performances and that feeding higher amounts of feed to the sows during the peripartal period is beneficial for production although restricted peripartal feeding strategies are *legio* in practice.

By the end of gestation, insulin sensitivity decreases (Père and Etienne, 2007) and glucose is redirected towards the insulin independent placenta and mammary gland (Shennan and Peaker, 2000), with the sows metabolism becoming more dependent on ketogenic substrates. Decreased insulin sensitivity might have negative effects on CY. Foisnet *et al.* (2010a) showed that sows with a low CY had higher serum concentrations of glucose 1 week before farrowing compared to sows with a normal CY. Kemp *et al.* (1996) showed that sows with a decreased glucose tolerance at d 104 of gestation had a greater piglet mortality during the first week of lactation. Neonatal piglet mortality is an indicator of reduced CI (Devillers *et al.*, 2011). Hansen *et al.* (2012) showed that the weight gain of the liveborn piglets during the colostral phase was negatively correlated with sow plasma glucose concentration at d 112 of gestation. On the other hand, increasing the glucose availability in the mammary gland might not alter the glucose metabolism of the mammary gland as acute glucose infusion did not alter glucose uptake by the mammary gland (Holmes *et al.*, 1988) and it seems that glucose uptake by the mammary gland is not regulated by the arterial glucose concentration but by intra-mammary demand (Bell and Bauman, 1997). We observed a negative correlation between CY

and BF change between d 85 and 108 of gestation (**chapter 3.1.**). It is during this period that insulin sensitivity in gestating sows changes (Père *et al.*, 2000). A more positive energy balance leads to an increase of the concentration of leptin (Barb *et al.*, 2001) and a decrease of the insulin sensitivity (Franks *et al.*, 2007; Papadopoulos *et al.*, 2009). Also, we showed that a fat BC upon entering the farrowing unit is detrimental for the CY (**chapter 3.2.**). Although this indicates that decreased insulin sensitivity might result in a decreased CY, we were able to alter insulin sensitivity at the end of gestation but this did not affect CY (**chapter 3.3.**).

In conclusion, the short-term strategy should focus on how we can diminish and eliminate the difference between the actual and potential CY and thus should focus on optimizing the management of the sow, in all its aspects. Changes in reproductive hormones are important in the onset of lactogenesis but are difficult to alter and manage. Nonetheless, some feeding supplements such as silymarin show opportunities to interfere with the peripartal hormonal changes and this warrants further investigation. Feeding strategies in the peripartal period do affect CY without negatively affecting colostrum composition and there were indications that a support of the balance of the maternal metabolism might be determining. We used, however, a quite robust study design and further research should elucidate which nutrients were determinant for the higher CY. Nonetheless, a negative energy balance the week prior to farrowing is not beneficial. Altering the insulin sensitivity, and thus the partitioning of glucose between insulin dependent and insulin independent tissues, is possible with feeding strategies during gestation (**chapter 3.3.**) but this seems less promising in altering CY. These indications should be confirmed by studies particularly focusing on this hypothesis and in which glucose and insulin profiles after a meal test or (oral) glucose tolerance test at the end of gestation are linked to CY.

2.2.Long term strategy

Functional mammary tissue is critical for milk production and piglets' weight gain (Nielsen *et al.*, 2001) and the higher the number of functional mammary secretory cells, the higher the milk production (Head and Williams, 1991). We can assume that the available functional mammary tissue is determinant for its potential production, both for colostrum and milk. Indeed, we found indications that the amount of functional mammary tissue is related to CY (**chapter 3.1., and 3.3.**). As a result, we should aim for a maximal development of functional mammary tissue which starts at d 90 of gestation (Sorensen *et al.*, 2002). In fact, the long term strategy to increase the sows' potential CY already starts at the gilt farm. During the prepuberal period, mammary gland development is stimulated by feeding phyto-oestrogens (Farmer *et al.*, 2010a) and *ad libitum* feed intake (Sorensen *et al.*, 2006) and diminished by reduced feed intake (Sorensen *et al.*, 2006; Farmer *et al.*, 2012a). Mammogenesis continues during the last third of gestation and is negatively affected by a high energy intake (Weldon *et al.*, 1991). Mammogenesis during lactation is mostly determined by the suckling stimulus and a non-suckled teat has a reduced amount of functional mammary tissue in the next lactation (Farmer *et al.*, 2012c). This has implications for cross-fostering strategies as in fact all teats should be suckled to optimize functional mammary tissue in the next lactation. Indeed, a non-functional or suboptimal teat should be considered as a loss of potential. It is not yet clear for how long a teat should be suckled to prevent negative effects in the subsequent lactation. Total parenchymal tissue is lower in small litters (Kim *et al.*, 1999c), meaning that extra piglets should be added to these litters as soon as possible, and definitely before regression of the non-suckled teats after 36-72 h (Hurley *et al.*, 2001).

Mammogenesis could also be improved at population level. Indeed, feeding linseed to sows during gestation and lactation increased functional mammary tissue of the offspring at first insemination (Farmer and Palin, 2008). Genetic selection might also be effective to improve

mammary gland development as differences between breeds were observed (Farmer *et al.*, 2000a). Whether there are differences in CY between breeds has not been shown yet. When we compare our studies (PIC) to the studies of Foisnet *et al.* (2010a, 2010b, 2011) and Devillers *et al.* (2004a, 2011) (Landrace x Large White), CY is within the same range. Nonetheless, it is worthwhile to look into this. In cattle, heritability of milk yield is about 0.25-0.35 and selection strategies increased milk yield with 40% between 1970 and 1990 (Rauw *et al.*, 1998). Genetic selection can lead to an increase in functional teats (Hirooka *et al.*, 2001) but it is not clear yet whether this also leads to a higher CY. One difficulty is that colostrum and milk yield in sows are difficult to measure compared to dairy cattle. Piglet survival at 3-5 days of lactation might be considered as an alternative parameter. Indeed, 50% of pre-weaning mortality occurs during the first 3 days of lactation (Tuchscherer *et al.*, 2000) and insufficient CI has been identified as 1 of the major primary causes (de Passillé and Rushen, 1989a; Edwards *et al.*, 2002; Milligan *et al.*, 2002). Still, it should be kept in mind that neonatal mortality can only serve as an indicator of insufficient CI. A high neonatal mortality does not necessarily mean that CY is low as it is related to many other factors.

2.3. Colostrum composition

Colostrum of dairy cattle contains fewer nutrients per liter compared to colostrum of beef cows (Guy *et al.*, 1994) but also between different breeds of dairy cattle, differences in e.g. IgG content can be observed (Pritchett et al., 1991; Meganck et al., 2012). This dilution effect is important when developing strategies to increase CY. Insufficient CY as such is not a problem but insufficient provision of colostral components to the piglets is. During the neonatal period, especially nutrients are important to optimize piglet performance while Ig become more important when piglets survive the first days/weeks of life (Le Dividich *et al.*, 2005a). This was confirmed in our studies. When CI in piglets was lower, a higher proportion of colostral protein was used as energy source and Ig intake had only limited effect on

performance during lactation (**chapter 3.4.**). CY was not correlated with the concentration of colostral components in our studies and thus, total output of nutrient and IgG increased when CY increased (**chapter 3.1., and 3.3.**). We were able to increase CY with a high peripartal feeding strategy and this increase in CY was concomitant with an increase in total output of colostral components (**chapter 3.2.**). Our results showed that CY was not negatively related to colostrum composition but when implementing long-term strategies to improve CY potential, the possibility of a dilution effect as seen in cattle, should always be kept in mind.

3. PIGLET FEATURES: IMPROVING COLOSTRUM YIELD AND INTAKE

As explained before, the sow and not the piglets is considered as the limiting factor for CY (Le Dividich *et al.*, 1997; Le Dividich *et al.*, 2005a). Therefore, piglet characteristics at birth are likely less important than sow characteristics for improving CY. Neonatal piglet characteristics are, however, important for the uptake of colostrum by these piglets. Approximately 30% of sows does not produce sufficient colostrum for her litter (**chapter 3.1.**, Foisnet *et al.*, 2010a), based on a threshold value of minimum required CI per piglet of 160 g/kg BW_B (Le Dividich *et al.*, 2005a). Colostrum intake within a litter is heterogeneous (**chapter 3.4.**) and, therefore, even when a sow produces on average sufficient colostrum for her litter, there will be piglets with an insufficient CI. Indeed, the percentage of piglets with insufficient CI was approximately 40% (**chapter 3.1.**). Devillers *et al.* (2007) showed that piglets with splayleg and indications of hypoxia had a reduced CI, that BW_B was positively correlated with CI, but within-litter BW_B variation affected CI negatively. Three factors thus seem important to optimize the piglets' possibility to consume colostrum: optimizing piglet vitality, optimizing piglet BW_B, and reducing within-litter BW_B variation.

3.1. Improving piglet vitality

A good vitality at birth offers the piglets a fair chance of reaching the mammary gland and start suckling. A long duration of the expulsive phase of farrowing and dystocia is a major risk factor for intrapartum asphyxia (Herpin *et al.*, 1996). Therefore, minimizing the duration of farrowing might be important. Several risk factors for an increased farrowing duration have been described such as a crate pen design, BF levels above 17 mm, and constipation (Oliviero *et al.*, 2010), small litter size (Knol *et al.*, 2002; Canario *et al.*, 2006a), selection for high number of total born piglets (Canario *et al.*, 2006b), decreased gestation length (van Dijk *et al.*, 2005), and increased fear levels for humans (Thodberg *et al.*, 2002; Janczak *et al.*, 2003; Mosnier *et al.*, 2009). Farrowing duration can be decreased by farrowing induction using

oxytocin (Mota-Rojas *et al.*, 2002; van Dijk *et al.*, 2005) although other studies could not confirm this (Cassar *et al.*, 2004; Wherend *et al.*, 2005; Kaeoket *et al.*, 2006). The use of carbetocin, a long-acting oxytocin derivative, decreased farrowing duration (Gheller *et al.*, 2009). Close supervision of farrowing generally leads to less stillborn piglets and a lower neonatal mortality due to the timely provided farrowing assistance when dystocia occurs and so reducing the risk of dystocia (Holyoake *et al.*, 1995; White *et al.*, 1996). Supplementation of the sow's diet during gestation with n-3-long chain polyunsaturated fatty acids also increased piglet vitality at birth (Lauritzen *et al.*, 2001; Edwards, 2002; Rooke *et al.*, 2001a; Adeleye *et al.*, 2014) due to the docosahexaenoic acid (Rooke *et al.*, 2001b; Li *et al.*, 2009) which results in better organ maturation (Innis, 2005) and brain development (Innis, 2007) but not all studies showed this effect (Tanghe and De Smet, 2013). Piglet vitality is positively correlated with piglet BW_B (Canario *et al.*, 2006a). Nonetheless, genetic factors not related to BW_B might affect piglet vitality, as Meishan piglets are very small at birth but have an exceptionally high vitality (van der Steen *et al.*, 1992; Canario *et al.*, 2009). A better placental vascularization in the Meishan breed could partially explain this high vitality even when birth weights are rather low within this breed due to uterine crowding (Biensen *et al.*, 1998; Wilson *et al.*, 1998). Arginine supplementation in the gestation diet of the sow improves placental vascularization by enhancing placental angiogenesis (Hazeleger *et al.*, 2007) although not all studies found positive effects of arginine supplementation. The key features thus are creating the conditions for a smooth farrowing, diminishing the risk of hypoxia by appropriate farrowing intervention, being present at farrowing to help piglets at risk, and already start preparing piglets prenatally for the postnatal life.

3.2. Improving piglet birth weight

Increasing the energy content of the sow's gestation diet during the last third of gestation could not increase litter BW_B (Coffey *et al.*, 1987; Seerley *et al.*, 1974; Clowes *et al.*, 2003;

Quiniou *et al.*, 2008) although some studies were successful (Coffey *et al.*, 1994; Papadopoulos *et al.*, 2009) but more recent research is lacking despite the continuous improvement in sow productivity. Increasing the feed intake during the last third of gestation increased piglet BW_B (Cromwell *et al.*, 1989) but in most studies, no effect was observed (Dwyer *et al.* 1994; Nissen *et al.*, 2003; Rehfeldt *et al.*, 2006). Also, there was no effect of low energy supply in the sow's gestation diet on piglet's BW_B (Bee, 2004; Lawlor *et al.*, 2007). Protein content in the sow's gestation diet seems more important as low levels (0.5-8.5%) as well as very high levels (30%) decreased piglet BW_B (Atinmo *et al.*, 1974; Mahan *et al.*, 1977; Schoknecht *et al.*, 1993; Kusina *et al.*, 1999; Lang *et al.*, 2008; Rehfeldt *et al.*, 2011). Arginine supplementation during gestation increased number of liveborn piglets and litter BW_B (Ramaekers *et al.*, 2006; Mateo *et al.*, 2007; Wu *et al.*, 2010) and the same was observed with supplementation of glutamine, a precursor of arginine (Wu *et al.*, 2011). Supplementation of L-carnitine also positively affected piglet BW_B (Musser *et al.*, 1999; Eder *et al.*, 2001; Ramanau *et al.*, 2008). We should keep in mind that the minimal needed amount of CI is 160 g/kg BW_B. An increase in BW_B leads to a higher need for CI (Devillers *et al.*, 2007) but it is not known whether an increase in litter BW_B also improves CI of all piglets within the litter.

3.3. Improving within-litter birth weight homogeneity

Genetic selection for increased litter size increased within-litter piglet BW_B variation (Milligan *et al.*, 2002; Quiniou *et al.*, 2002; Quesnel *et al.*, 2008a). Birth weight heterogeneity was lowest in first and second parity sows and increased progressively with increasing parity, and heterogeneity was also positively related to BF gain during gestation but these could only explain 20% of the BW_B variation (Quesnel *et al.*, 2008a). There are no indications that feed intake during gestation can affect litter BW_B homogeneity (Cassar *et al.*, 1994; Musser *et al.* 2004, Cerisuelo *et al.*, 2008; Quesnel *et al.*, 2010) except for a study by Kim *et al.* (2009) who

showed that a diet with an adjusted AA profile at the end of gestation (arginine and leucine as more important AA) increased litter BW_B homogeneity compared to a control diet according to NRC standards. Within-litter variation of BW_B is already established as soon as 30 – 35 days of gestation (van der Lende *et al.*, 1990; Wise *et al.*, 1997; Finch *et al.*, 2002). Indeed, fetal growth, and with it piglet BW_B, is largely determined by placental size (Biensen *et al.*, 1999; Town *et al.*, 2005; Foxcroft *et al.*, 2009; Vallet *et al.*, 2009). The placental size is determined by the available uterine space, and this is fixed at d 35 of gestation after which newly available uterine space cannot be used by the piglets (Vonnahme *et al.*, 2002, Vallet *et al.*, 2009, Vallet *et al.*, 2011). This implies that nutrition and management during the first month of gestation are determinant for the within-litter BW_B homogeneity (Wientjes, 2013). There is also a breed effect for litter BW_B homogeneity. Homogeneity is higher in Meishan sows compared to other breeds (Finch *et al.*, 2002; Canario *et al.*, 2009) and genetic selection could be used to improve homogeneity (Damgaard *et al.*, 2003).

4. PERSPECTIVES FOR FUTURE RESEARCH

- The use of body reserves cannot completely compensate for insufficient nutrient intake through the feed during lactation. Feeding strategies and management of BC should be optimised. This is a major challenge as sows during gestation are group-housed and often no individual feeding strategies can be applied and solutions for this should be investigated.
- Colostrum yield can be improved by peripartal feeding strategies, without negatively altering colostrum composition. Colostrum yield thus can be managed relatively easily. It is important to understand that we increased the level of feed intake, without altering the feed composition. It might be important to elucidate which nutrients are more important for this effect. Then, this information should be used to fine-tune peripartal feeds.
- Mammogenesis can be managed and might offer a strategy to improve CY. The indications of an association between CY and amount of functional mammary tissue should be established by specially developed study designs.
- Protein metabolism during the peripartal period seems important but contradictory results were described, probably due to differences in energy balance. This should be elucidated.
- Insufficient CY and insufficient CI are not uncommon. The high variability in CI warrants research to improve homogeneity of CI within a litter.
- The indirect methods to estimate colostrum yield is a major limitation and the development of an easy, reliable and direct method could stimulate this area of research. The development of medical imaging techniques could allow measuring the amount of functional mammary tissue real-time (and when correlated with CY serving as an estimate of CY) or closure of the mammary gland barrier might deliver lacteal components in the blood of the sow that perhaps could be used as an estimate of CY.

5. CONCLUSIONS

- Colostrum yield and intake are highly variable between sows and piglets.
- One third of the sows / piglets have an insufficient CY / CI.
- The use of body energy reserves during late gestation is correlated with CY. Colostrum yield was negatively correlated with the BF change between d 85 and 108 of gestation, and positively correlated with the BF change during the last week of gestation.
- A negative energy balance during the last week of gestation should be avoided. A high peripartal feed intake resulted in a higher CY.
- Management of sow BC is important. Sows should enter the farrowing unit in moderate BC. This was defined as 17-23 mm BF in our studies, but this range cannot be extrapolated *as such* to other breeds.
- Colostrum yield is not correlated with colostrum composition and thus a higher CY is concomitant with a higher output of colostral nutrients.
- The maternal metabolism is heavily challenged in the peripartal period and an imbalance at the citric acid cycle might lead to suboptimal performance. This should be supported by proper feeding strategies.
- Mammogenesis might be important in determining CY whereas insulin sensitivity seems to have no effect.
- Protein metabolism in the peripartal period is related to CY but the mechanisms are not clear yet.
- Colostrum intake by the piglets determines piglet survival rate and daily weight gain until weaning.
- When CI is low, the piglet starts to use colostral protein as an energy source.

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SUMMARY

Piglets are born with limited energy reserves, agammaglobulinemic and with an immature gastro-intestinal tract. Colostrum is the sole external nutrient resource for piglets after birth, provides the piglets with maternal immunity and also contains several factors that stimulate the development of the gastro-intestinal tract and other organs (**chapter 1**). Colostrum thus has important functions and insufficient CI is a major cause of pre-weaning mortality and reduced daily weight gain (**chapter 3.4.**), both causing major economic losses in modern sow herds. Approximately 30% of sows do not produce sufficient colostrum for their litter (**chapter 3.1.**) and the CY is independent of litter size (**chapter 3.4.**). Consequently, insufficient CY in sows is a major problem and becomes even more pronounced in high-prolific sows.

Research on CY in sows is scarce and mainly focused on the hormonal regulation (**chapter 1**). Very limited information is available on how the sow's use of energy and protein derived from the feed or body reserves affects CY. The general aim of this thesis was to investigate the use of energy and protein from feed or body reserves during gestation in relation to CY in sows.

In a first study (**chapter 3.1.**), we identified 2 periods in late gestation during which the use of body energy reserves was correlated with CY. The BF change between d 85 and 108 of gestation was negatively correlated with CY (r = -0.346, P = 0.032) whereas the BF change the week prior to farrowing was positively correlated with CY (r = 0.391, P = 0.017). In this study, we also collected sow serum samples 3-4 days before farrowing and at d 1 of lactation and blood analyses confirmed that the use of body energy and protein reserves just prior to farrowing was negatively correlated with CY. This study also showed that there was no correlation between CY and colostrum composition, which is interesting as this suggests that improving CY should not be at cost of the colostrum composition. Causal relationships

between CY and the change of body reserves could not be established with this study design. Therefore, the 2 identified periods of interest were further investigated.

In the second study (**chapter 3.2.**), we focused on the positive correlation between CY and the BF change 1 week before farrowing. Sows were randomly divided into 2 treatment groups at d 108 of gestation. The first group (L, n = 28) received 1.5 kg feed per day, the second group (H, n = 22) received 3 times 1.5 kg feed per day until farrowing. Based on BF at d 108, sows were divided into 3 BC groups: skinny (< 17 mm, n = 15), moderate (17 to 23 mm, n = 21), fat (> 23 mm, n = 14). The H-group tended to have a greater total CY (P = 0.074) and had a greater CY per kg liveborn piglet (P = 0.018) than the L-group. Compared to sows in moderate BC, fat sows had a lower total CY (P = 0.044), and a lower CY per kg liveborn piglet (P = 0.005). The H-group had a greater concentration of lactose (P = 0.009) and n-3 PUFA (P < 0.001) but a lower concentration of protein (P = 0.040) in colostrum than the L-group. The concentration of IgG and IgA did not differ between treatment and BC groups. The H-group mobilized less body fat (NEFA: P = 0.002) and protein (creatinine: P < 0.001, C4: P = 0.016) reserves but had a greater ratio urea:NEFA (P < 0.001) and less ketone bodies (3-OH-C4: P < 0.001) compared to the L-group before farrowing. This indicates a more balanced entry of metabolites in the citric acid cycle and thus a better support of the maternal peripartal metabolism in the H-group. This study showed that both CY and composition can be influenced by the peripartal feeding strategy and BC. Management of the peripartal feeding strategy and BC thus offer short-term strategies to improve the CY and composition.

In the third study (**chapter 3.3.**), we tried to unravel the negative correlation between CY and the BF change between d 85 and 108 of gestation. We proposed 2 hypotheses based on literature (**chapter 1**) 1) the BF change was an indicator of energy use for mammogenesis and a BF loss thus indicated more gestational mammogenesis resulting in a higher CY during the observed period, and 2) the BF change was correlated with the sow's insulin sensitivity and as

such might affect the direction of glucose towards the mammary gland. At d 85 of gestation, 47 sows were stratified for BF and parity, and randomly divided into 6 groups differing in daily feed allowance between d 85 and 108 of gestation. Group 1 was allowed 1.8 kg feed per sow per day. Feed allowance for each next group increased with 300 g feed per sow per day and reached 3.3 kg feed per sow per day in group 6. From d 108 of gestation until weaning, all sows were managed and fed similarly. The CY was correlated with BF change between d 85 and 108 of gestation (r = -0.446, P = 0.002) but not with daily feed allowance between d 85 and 108 of gestation (r = -0.156, P = 0.312). We found 3 indications to support the hypothesis of mammogenesis: 1) gestational mammogenesis occurs between d 85 and 108 of gestation. A BF loss between d 85 and 108 of gestation might partially evolve from an increased mammogenesis; 2) colostrum composition was not correlated with CY or BF change between d 85 and 108 of gestation (P > 0.10) which is indicative for more functional mammary tissue; 3) piglets' daily weight gain was correlated with BF change between d 85 and 108 of gestation up to d 3 of lactation (r = -0.359, P = 0.019) which is right before the start of lactational mammogenesis. Although BF change between d 85 and 108 of gestation and daily feed allowance between d 85 and 108 of gestation affected the glucose and insulin metabolism, CY was not correlated with the changes in insulin (r = 0.025, P = 0.876) and glucose (r = -0.149, P = 0.359) between d 85 and 108 of gestation which makes this hypothesis less evident. Improving mammogenesis in sows thus seems promising as a long term strategy to increase CY in sows.

In the fourth study (**chapter 3.4.**) we investigated the effects of CI on piglet performance (survival and daily weight gain) during lactation. All piglets born to 37 PIC sows were observed until weaning and 4 piglets per litter were randomly selected for serum collection 24-30 h after birth. The daily weight gain was positively correlated with BW_B and CI/kg BW_B, and negatively with time between birth and first suckle until d 3 of lactation (R^2 = 0.39,

P < 0.001), d 7 of lactation (R^2 = 0.26, *P* < 0.001) and weaning (R^2 = 0.18, *P* < 0.001). The pre-weaning mortality rate was higher for piglets with a BW_B < 1 kg (*P* < 0.001), a CI/kg BW_B < 160g (*P* < 0.001) and a time between birth and first suckle > 60 min (*P* < 0.01). The CI/kg BW_B was negatively correlated with urea (*P* = 0.002), positively to some free AA (*P* < 0.05) but not to creatinine, NEFA, IgG and IgA in piglets' serum. The daily weight gain was negatively correlated with urea and positively to leucine until d 3 of lactation (R^2 = 0.19, *P* < 0.001), until d 7 of lactation (R^2 = 0.13, *P* < 0.001) and until weaning (R^2 = 0.08, *P* < 0.001). A lower CI/kg BW_B was accompanied by a higher catabolism of protein that did not seem to originate from the piglets' body reserves. It seems that piglets with a lower CI/kg BW_B use a larger proportion of colostral protein as a substrate for energy production rather than for other purposes such as lean growth, as there was a negative correlation between parameters indicating protein catabolism and daily weight gain at least until weaning. Sufficient CI is thus essential for piglet performance at least until weaning. This underlines the importance of improving CY in sows and distribution of the available CY within a litter.

In conclusion, this thesis showed that CY in sows and CI in piglets are highly variable and also insufficient for a considerable number of the animals. The results also documented the importance of sufficient CI for piglet's performance during the entire lactation period. Next to elucidating the importance of insufficient CY and intake, the thesis also showed that the use of body reserves during late gestation is correlated with CY. A negative energy balance the week prior to farrowing should be avoided. A high peripartal feeding strategy the week prior to farrowing resulted in decreased negative energy balance, less imbalance at the entry of the citric acid cycle and a higher CY. The use of body energy reserves between d 85 and 108 of gestation was negatively correlated with CY and several indications were presented showing that this correlation might be due to better gestational mammogenesis. The thesis provided opportunities for both short-term and long-term strategies to improve CY in sows.

SAMENVATTING

Biggen worden geboren met een minimale hoeveelheid energiereserves, agammaglobulinemisch en met een immatuur gastro-intestinaal stelsel. Colostrum is de belangrijkste bron van energie; passieve, maternale immuniteit en componenten die de ontwikkeling van het gastro-intestinaal stelsel stimuleren voor biggen (**hoofdstuk 1**). Colostrum heeft dus belangrijke functies en onvoldoende colostrumopname is een belangrijke oorzaak van sterfte en beperkte dagelijkse groei tijdens de lactatie (**hoofdstuk 3.4.**), beide belangrijke economische verliesposten in de moderne zeugenhouderij. Ongeveer 30% van de zeugen produceert onvoldoende colostrum voor haar biggen (**hoofdstuk 3.1.**) en de geproduceerde colostrumhoeveelheid is onafhankelijk van de nestgrootte (**hoofdstuk 3.4.**). Als gevolg hiervan is onvoldoende colostrumproductie een groot probleem en dit wordt nog relatief belangrijker bij hoog-productieve zeugen.

Onderzoek over colostrumproductie bij zeugen is beperkt en richtte zich tot nog toe hoofdzakelijk op de hormonale controle (**hoofdstuk 1**). Er is zeer weinig informatie beschikbaar over hoe de colostrumproductie beïnvloed wordt door de zeug haar gebruik van energie en eiwit afkomstig van voeder of de lichaamsreserves. De algemene doelstelling van deze thesis was om te onderzoeken hoe het gebruik van energie en eiwit, afkomstig van het voeder of de lichaamsreserves, de colostrumhoeveelheid kon beïnvloeden.

In de eerste studie (**hoofdstuk 3.1.**) werden 2 periodes tijdens de late dracht geïdentificeerd waarin het gebruik van de vetreserves gecorreleerd was met de colostrumhoeveelheid. De spekdikteverandering tussen dag 85 en 108 van de dracht was negatief gecorreleerd met de colostrumhoeveelheid ($r = -0.346$, $P = 0.032$) terwijl de spekdikteverandering de week voor werpen positief gecorreleerd was met de colostrumhoeveelheid ($r = 0.391$, $P = 0.017$). Er werd ook serum van de zeugen verzameld 3 - 4 dagen voor werpen en op dag 1 van de lactatie en analyse bevestigde dat het gebruik van energie- en eiwitreserves de week voor werpen negatief gecorreleerd was met de colostrumhoeveelheid. De studie toonde ook aan dat er geen

verband was tussen de colostrumhoeveelheid en de colostrumsamenstelling wat impliceert dat het verhogen van de colostrumhoeveelheid niet per se ten koste van de colostrumsamenstelling hoeft te gaan. Oorzakelijke verbanden tussen de colostrumhoeveelheid en de verandering in lichaamsreserves konden met de gegevens uit deze studie echter niet getrokken worden. Daarom werden de twee interessante periodes in volgende studies verder onderzocht.

In de tweede studie (**hoofdstuk 3.2.**) werd de positieve correlatie tussen de colostrumhoeveelheid en de spekdikteverandering de week voor werpen verder onderzocht. Op dag 108 van de dracht werden de zeugen at random verdeeld over 2 proefgroepen. De eerste behandelingsgroep (L, n = 28) kreeg 1.5 kg voeder per dag tot aan de partus. De tweede behandelingsgroep (H, n = 22) kreeg 3 maal 1.5 kg voeder per dag tot aan de partus. De zeugen werden ingedeeld in 3 conditiegroepen op basis van hun spekdikte op dag 108 van de dracht: mager (< 17 mm, n = 15), matig (17 – 23 mm, n = 21), vet (> 23 mm, n = 14). De H-groep toonde een tendens voor een hogere colostrumhoeveelheid (P = 0.074) en had meer colostrum per kg levend geboren big (P = 0.018) dan de L-groep. Vette zeugen hadden een lagere colostrumhoeveelheid (P = 0.044) en een lagere colostrumhoeveelheid per kg levend geboren big (P = 0.005) dan zeugen in matige conditie. De H-groep had een hogere concentratie lactose (P = 0.009) en n-3 PUFA (P < 0.001) maar een lagere concentratie eiwit (P = 0.040) in colostrum dan de L-groep. De concentratie van IgG en IgA in colostrum verschilde niet tussen de verschillende conditie en behandelingsgroepen. De H-groep mobiliseerde minder vetreserves (NEFA: P = 0.002) en eiwitreserves (creatinine: P < 0.001, C4: P = 0.016) maar had een hogere verhouding ureum:NEFA (P < 0.001) and minder ketonlichamen (3-OH-C4: P < 0.001) dan de L-groep. Dit wijst op een betere balans ter hoogte van de Krebscyclus en dus een betere ondersteuning van het maternale peripartale metabolisme in de H-groep. Deze studie toonde aan dat zowel colostrumhoeveelheid als

colostrumsamenstelling beïnvloed kunnen worden via peripartale voederstrategieën en lichaamsconditie. Management van de peripartale voederstrategie en lichaamsconditie vormen dus kortetermijn strategieën om colostrumhoeveelheid en colostrumsamenstelling te optimaliseren.

De negatieve correlatie tussen de colostrumhoeveelheid en de spekdikteverandering tussen dag 85 en 108 van de dracht werd verder onderzocht in de derde studie (**hoofdstuk 3.1.**). Op basis van literatuurgegevens (**hoofdstuk 1**) werden 2 hypotheses vooropgesteld: 1) de spekdikteverandering was een indicator voor het gebruik van energiereserves voor mammogenese. Spekdikteverlies wees dan op meer mammogenese tijdens de dracht wat zou leiden tot een hogere colostrumhoeveelheid; 2) de spekdikteverandering was een indicator voor de verandering in de zeug haar insulinegevoeligheid en beïnvloedde op die manier de glucosetoevoer naar de melkklier. Op dag 85 van de dracht werden 47 zeugen gestratificeerd voor spekdikte en pariteit en at random verdeeld in 6 groepen met een verschillende dagelijkse voedergift tussen dag 85 en 108 van de dracht. Groep 1 kreeg 1.8 kg voeder per zeug per dag. De voedergift voor elke volgende groep steeg met 300 g per zeug per dag en bereikte 3.3 kg voeder per zeug per dag in groep 6. Tussen dag 108 van de dracht en spenen werden alle zeugen op dezelfde manier gevoederd en gemanaged. De colostrumhoeveelheid was gecorreleerd met de spekdikteverandering tussen dag 85 en 108 van de dracht ($r = -0.446$, $P = 0.002$) maar niet met de dagelijkse voedergift tussen dag 85 en 108 van de dracht ($r = -0.156$, $P = 0.312$). Er werden 3 indicaties gevonden die de hypothese van mammogenese ondersteunen: 1) mammogenese tijdens de dracht vindt plaats vanaf dag 85 van de dracht. Spekdikteverlies tussen dag 85 en 108 van de dracht kan deels te wijten zijn aan een verhoogde mammogenese; 2) de colostrumsamenstelling was niet gecorreleerd met de colostrumhoeveelheid of de spekdikteverandering tussen dag 85 en 108 van de dracht ($P > 0.10$) wat indicatief is voor meer functioneel melkklierweefsel; 3) de dagelijkse groei van

biggen was gecorreleerd met de spekdiktеverandering tussen dag 85 en 108 van de dracht tot en met dag 3 van de lactatie (r = -0.359, *P* = 0.019), dus tot net voor de start van de melkklierontwikkeling tijdens de lactatie. De spekdiktеverandering en de voedergift tussen dag 85 en 108 van de dracht beïnvloedden het glucose- en insulinemetabolisme, maar de colostrumhoeveelheid was niet gecorreleerd met veranderingen in insuline (r = 0.025, *P* = 0.876) en glucose (r = -0.149, *P* = 0.359) tussen dag 85 en 108 van de dracht. Dit maakt de hypothese over de invloed van de insulinegevoeligheid minder waarschijnlijk. Het verbeteren van de mammogenese bij zeugen lijkt dus veelbelovend als een langetermijn strategie om de colostrumhoeveelheid bij zeugen te optimaliseren.

De invloed van colostrumopname op bigprestaties (overleving en dagelijkse gewichtstoename) tijdens de lactatie werd onderzocht in de vierde studie (**hoofdstuk 3.4.**). Alle biggen van 37 PIC zeugen werden geobserveerd tijdens de lactatie en van 4 at random geselecteerde biggen per nest werd serum verzameld 24-30 uur na geboorte. De dagelijkse gewichtstoename was positief gecorreleerd met geboortegewicht en colostrumopname per kg geboortegewicht, en negatief met tijd tussen geboorte en eerste drinkbeurt tot dag 3 van de lactatie (R^2 = 0.39, *P* < 0.001), dag 7 van de lactatie (R^2 = 0.26, *P* < 0.001) en tot spenen (R^2 = 0.18, *P* < 0.001). De sterfte tijdens de lactatie was hoger voor biggen met een geboortegewicht lager dan 1 kg (*P* < 0.001), een colostrumopname per kg geboortegewicht lager dan 160 g (*P* < 0.001) en een tijd tussen geboorte en eerste drinkbeurt van meer dan 60 min (*P* < 0.01). De colostrumopname per kg geboortegewicht was negatief gecorreleerd met ureum (*P* = 0.002), positief gecorreleerd met enkele vrije aminozuren (*P* < 0.05) maar niet gecorreleerd met creatinine, NEFA, IgG en IgA in het serum van de biggen. De dagelijkse gewichtstoename was negatief gecorreleerd met ureum en positief gecorreleerd met leucine tot dag 3 van de lactatie (R^2 = 0.19, *P* < 0.001), dag 7 van de lactatie (R^2 = 0.13, *P* < 0.001), en tot spenen (R^2 = 0.08, *P* < 0.001). Een lage colostrumopname ging gepaard met meer

eiwitkatabolieten die niet afkomstig bleken te zijn van de lichaamsreserves van de big. Biggen met een lage colostrumopname per kg geboortegewicht gebruiken een groter deel van het eiwit in colostrum als energiebron in plaats van het gebruik voor andere doeleinden zoals spieraanzet, aangezien een negatieve correlatie werd vastgesteld tussen dagelijkse gewichtstoename en de hoeveelheid eiwitkatabolieten op z'n minst tot het einde van de lactatie. Een voldoende colostrumopname is dus essentieel voor goede bigprestaties tot op het einde van de lactatie. Dit benadrukt het belang van het optimaliseren van de colostrumhoeveelheid en het homogeniseren van de verdeling van het beschikbare colostrum binnen een nest.

Deze thesis heeft aangetoond dat colostrumhoeveelheid bij zeugen en colostrumopname bij biggen zeer variabel is en onvoldoende voor een aanzienlijk aantal dieren. De resultaten tonen ook belang van voldoende colostrumopname aan voor goede bigprestaties gedurende de volledige lactatieperiode. De thesis toont ook verbanden aan tussen de colostrumhoeveelheid en het gebruik van lichaamsreserves tijdens de dracht. Een negatieve energiebalans de week voor werpen moet vermeden worden. Een hoge peripartale voederstrategie zorgde voor een gereduceerde negatieve energiebalans, een beter evenwicht in de Krebscyclus en een hogere colostrumhoeveelheid. Het gebruik van vetreserves tussen dag 85 en 108 van de dracht was negatief gecorreleerd met de colostrumhoeveelheid en er werden verschillende argumenten gevonden om te ondersteunen dat mammogenese tijdens de dracht een belangrijke oorzaak zou kunnen zijn. De thesis presenteerde belangrijke opportuniteiten om zowel op korte als op lange termijn de colostrumhoeveelheid bij zeugen te verhogen.

CURRICULUM VITAE

Ruben Decaluwé was born on the 24th of January 1986 in Bruges. He graduated from high school (Sint-Leocollege, Bruges, Science and Mathematics) in 2004 and started his studies of Veterinary Medicine at the Faculty of Veterinary Medicine of Ghent University the same year. He obtained his Bachelor degree in 2007 with great distinction and his Master degree in 2010 (option pig, poultry and rabbit) with great distinction.

In December 2010, he obtained an IWT doctoral scholarship for strategic basic research. He started as a doctoral student in 2011 at the Laboratory of Animal Nutrition (Department of Nutrition, Genetics and Ethology) and the Unit of Porcine Health Management (Department of Reproduction, Obstetrics and Herd Health). For 4 years, he performed research on the peripartal period of the sow, mainly focusing at colostrum and farrowing induction. He was responsible for herd health management at several pig farms, helped with 2nd-line clinical work, cooperated with the practical education of the last year students (option pig, poultry and rabbit), and assisted with numerous experiments on both departments. He obtained the degree of 'vakdierenarts Varken' in 2013 at the faculty of Veterinary Medicine, Ghent University.

Ruben Decaluwé is author or co-author of multiple scientific articles in international journals and presented at several national and international symposia and conferences.

Ruben Decaluwé werd geboren op 24 januari 1986 te Brugge. In 2004 behaalde hij zijn middelbaar diploma (Wetenschappen-Wiskunde) aan het Sint-Leocollege te Brugge. Hetzelfde jaar startte hij de opleiding Diergeneeskunde aan de faculteit Diergeneeskunde van de universiteit Gent. Hij behaalde het Bachelorsdiploma in 2007 met grote onderscheiding en het Masterdiploma in 2010 met grote onderscheiding (optie varken, pluimvee en konijn).

In december 2010 behaalde hij een IWT doctoraatsbeurs voor strategisch basisonderzoek. In 2011 begon hij als doctoraatsstudent aan de faculteit Diergeneeskunde aan het labo Diervoeding (Vakgroep Voeding, Genetica en Ethologie) en de eenheid gezondheidszorg varken (Vakgroep Voortplanting, Verloskunde en Bedrijfsdiergeneeskunde). Hij voerde 4 jaar onderzoek uit over de peripartale periode bij de zeug waarbij hij zich hoofdzakelijk toespitste op colostrum en partusinductie. Hij was ook verantwoordelijk voor de bedrijfsbegeleiding op verschillende varkensbedrijven, hielp met de 2de-lijns diergeneeskunde in het kader van Veepeiler varken, stond mee in voor de praktische opleiding van de laatstejaarsstudenten optie varken, pluimvee en konijn, en assisteerde bij tal van proeven op beide vakgroepen. In 2013 behaalde hij het diploma ‘Vakdierenarts Varken’ aan de faculteit Diergeneeskunde, Universiteit Gent.

Ruben Decaluwé is auteur of coauteur van meerdere wetenschappelijke publicaties in internationale tijdschriften en presenteerde op verschillende nationale en internationale congressen.

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A pessimist sees the difficulty in every opportunity,

an optimist sees the opportunity in every difficulty.

Winston Churchill

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