



Intrinsic challenges of neonatal adaptation in swine

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Abstract. The losses of piglets in commercial pig farming remain at concerning levels and need to be addressed through the implementation of new sustainable breeding and management strategies. In fact, piglets are especially at risk in the first days of life. Both genetics and the farrowing process have been shown to impact piglet vitality. In addition, knowledge of the animal-intrinsic responses in adapting to extra-uterine life is particularly important but is scarcely described in the scientific literature. In this review, the three phases that constitute neonatal adaptation in the pig are systematically presented. The first phase of early adaptation involves primarily the development of cardiorespiratory function (within the first 10 min of life) as well as thermoregulatory processes and acid–base balance (up to 24 h of life). In the second phase, homeostasis is established, and organ maturation takes place (up to 14 d post natum). The final third phase aims at the development of neurological, immunological and muscular features (up to 28 d of life). The involvement of aggravating and ameliorating factors such as dystocia, low colostrum yield and heat supply is key to the development of strategies to reduce piglet losses and increase vitality. The insights are of particular value in addressing current concerns in pig farming and to further improve animal welfare in pig production across different management types.

1 Introduction

High piglet losses up to weaning are an ethical as well as economic challenge in various housing and management systems. In fact, the mortality currently remains around 15 %–25 %, which is equivalent to three to five piglets per litter in absolute terms given current litter sizes (Schild et al., 2020; Rootwelt, 2013). Furthermore, stillborn piglets account for another 6 % loss of total piglets born (Gourley et al., 2020). Consequently, the industry is obliged to further improve animal welfare aspects due to increased public perception.

It was observed that most losses happen within 3 d after parturition (Svendsen et al., 1991). A significant number of total losses already happen during the first 24 h after birth (Tuchscherer et al., 2000; Pandolfi et al., 2017; Devillers et al., 2011), and low-birth-weight piglets are overrepresented (Le Dividich et al., 2017). Most of these losses can be attributed to the “crushing” complex, which is associated with postnatal hypothermia and hypoglycemia (Tuchscherer et al.,

2000). Modern hybrid lines in particular often produce litters with a high birth weight variation (i.e., a greater dispersion of birth weights), thus also producing light piglets with an increased risk of being crushed (Schild et al., 2020). In addition, colostrum production and litter size are not correlated in pigs, reducing nutrient intake per piglet and increasing the risk of crushing of individual piglets (Devillers et al., 2007). In this context, there are risks due to teat competition and the associated variation in the amount of colostrum available per piglet and therefore nutrient supply, which further increases the risk of crushing individual piglets (Mersmann, 1974; Devillers et al., 2007). Furthermore, in an investigation of 69 litters of hyper-prolific db.Viktoria sows, dystocia positively correlated with the risk of crushing her offspring (Blim, 2020; Lehn, 2020).

Taking into account the negative correlation of birth weight with pre-weaning death (Tuchscherer et al., 2000), it is necessary to elucidate the deficits of normally developed but lightweight piglets. Although neonatal pigs are born

precocial, modern sow lines are thought to deliver a higher number of immature piglets (Mersmann, 1974; Fainberg et al., 2012; Schild et al., 2020). This immaturity might be one of the possible reasons for the lower viability and low birth weight of piglets, which is partly attributed to poorer placental supply (Mersmann, 1974; Fainberg et al., 2012; König et al., 2021). Management measures have been proposed to counteract the negative effects and associated increased piglet mortality, including genetic selection of breeding sows with regard to maternity behaviour, sow feeding, housing conditions at farrowing, hygiene and early individual care for at-risk neonates (Quesnel et al., 2008; Rutherford et al., 2013; Baxter et al., 2013).

The end of gestation and onset of birth are mediated by fetal cortisol. Although multiple authors conclude cortisol is not the single mediator of parturition in swine, the exact pathways inducing birth are not known yet (Silver, 1990; Nagel et al., 2019). Studies into this showed that lack of cortisol in hypophysectomized fetuses leads to a delayed parturition, but the injection of dexamethasone does not lead to the induction of birth as it does in ruminants (Randall, 1987). The adrenal function and uncoupling of hypothalamic–pituitary–adrenal feedback lead to high cortisol concentrations in late fetal development and ensure maturation of the lung as well as, in most species, leading to luteolysis and subsequently birth (Brooks et al., 1996).

Conflicting data exist on large litters and gestational length. It is conceivable that parturition occurs earlier because more fetuses contribute to cortisol secretion in larger litters, and a supposed threshold of cortisol concentration is reached sooner (Sasaki and Koketsu, 2007). On the other hand, Pietruszka et al. (2020) showed no difference of gestational length in large litters. An investigation into the corresponding gestational length is necessary, as there is an evident lack of knowledge about the stability of birth in modern highly prolific sows and the influence of shortened gestation due to hormonal administration at birth induction. It remains unclear as to whether high-prolific sows exhibit “birth stability”, i.e., whether physiological farrowing can occur consistently without physical intervention or administration of obstetric drugs.

The release of (stress) hormones during parturition induces a “kick start” in the piglet’s metabolism, as is shown by a surge of thyroxine, catecholamines and cortisol. The mostly inactive, oxygen-deprived fetus with a low metabolism rate rapidly changes to a vigorous, active neonate with a high metabolism rate to ensure gain of temperature and locomotion to the sow’s teats. The stress of birth is considered fundamental, as can be seen by (human) fetuses, which have decreased lung compliance when delivered by caesarean section (Gerten et al., 2005). Notably, sows show only passive maternal care (e.g., warmth, protection) during parturition and do not attend to their offspring to the same degree as uniparous mammals do (e.g., licking of the newborns, assistance in cutting the umbilical cord).

Multiple studies on pigs show a significant role of a prematurely ruptured umbilical cord in reduced viability. This is explained by a stronger acidosis and possibly plays a role in as much as 57 % of neonatal losses (Langendijk and Plush, 2019; Gourley et al., 2020; Rootwelt, 2013). A correlation between length of parturition and the condition of umbilical cord was shown (Gourley et al., 2020; Rootwelt, 2013). Nevertheless, some studies do not show an influence of the umbilical cord’s status on weight gain, indicating that piglets are able to reconcile (Nuntapaitoon et al., 2018).

These survival-related factors, i.e., litter size, gestational length, birth induction, and umbilical cord status, form the basis of the pig’s neonatal adaptation. As for all mammals, the latter is categorized into three phases, which are distinguished by specific functional, metabolic and endocrine characteristics. This review on porcine neonates focuses on these individual factors of the offspring. Based on the clinical classification of neonatal adaptation in multiparous (canine) species, the authors propose the usage of the following classification for neonatal piglet adaptation to characterize associated disorders (Bostedt, 2016).

2 Time course of neonatal adaptation in swine

The first phase of neonatal adaptation in piglets extends from birth to 24 h of life and is further subdivided. Establishment of cardiorespiratory function is the first challenge and is the characterizing event of the first subphase. It lasts about 10 min in swine. In the fetus, a bypass by the foramen ovale and ductus arteriosus exists, directing venous blood to the left atrium and aorta respectively, thereby circumventing the lung. After birth, those shunts close due to changing pressures. While the foramen ovale closes quickly after birth, the ductus arteriosus persists for a couple of days, enabling a left–right shunt (e.g., blood from the aorta flowing into the arteria pulmonalis). The neonate is solely dependent on heart rate to adapt cardiac output per minute with normal frequencies > 200 beats per minute (bpm). This mechanism alone is not sufficient to regulate circulation in stressful situations. An unstable blood pressure and low stress tolerance result.

The same as cardiac function, respiratory function is, to a degree, impaired after birth, and high breathing frequencies result. Due to the soft ribs, which complicate passive inspiration, the diaphragm is the motor of respiration. All of this leads to a physiological weakness of compensatory capacity. Not least, the start of respiratory function is possible only when alveolar ventilation is ensured by adequate surfactant and lung maturity.

Within the first few hours of life, the neonatal piglet needs to take up colostrum in order to gain passive immunity and meet energy demands. To enable location of the teats, concepts of “the udder” are inherited, and the piglet searches for a vertical plane (i.e., the lying sow). This is quite different to other (farm) animals where the mother stands, and a hori-

zontal surface is imprinted (Walser and Bostedt, 2008). The neonates spent the remaining hours of the first phase with accommodation to the new environment and building a relationship with the sow and their littermates. The closure of the intestinal barrier for globulins within the first 24 h should be discussed as the endpoint of the first phase in pigs.

The following second phase spans over the first 2 weeks of the piglets' life. Now the parenchymal organs mature, with the intestines and pancreas experiencing the highest relative growth (Walser and Bostedt, 2008). The ribs harden, and heart rate declines. Amongst other mechanisms, the peripheral vasoconstriction matures, enabling improved circulatory and blood pressure regulation. Further, the ductus arteriosus closes, marking an important step in postnatal development of the heart. Hepatic function matures, and the liver ensures the synthesis of proteins. In addition, kidney function reaches physiological levels, and homeostasis of plasma molarity and volume can be maintained. As pigs are born with mature neurological and locomotor function, the second phase focuses on the metabolism and further strengthening of homeostasis.

The third phase lasts until 4 weeks after birth and is characterized by ethological development, further muscular growth and neurological improvement. As maternal immunoglobulin G (IgG) begins to decline in the first week of life, their concentration is surpassed by piglet-produced IgG around the fourth to fifth week of life. Consequently the intestinal immunoglobulin A (IgA) system develops, and their own IgG is built in the liver (Walser and Bostedt, 2008). While the maternal immunoglobulins decline, and the piglet's immunocompetence is still developing, a window of immunological weakness arises, which ranges from day 28 to about day 56 of life (Juul-Madsen et al., 2010).

For a successful neonatal adaptation, the series of events must proceed in order. Most complaints in neonatal pigs can be thematically assigned to acid–base balance, thermoregulation and energy allocation. Their systemic significance during the temporal course of the phase model is described below.

3 Acid–base balance and blood gases

The fetus is able to develop despite low oxygen tension, once coined as “Everest in utero” (Eastmann, 1954). Comline and Silver (1974) described partial oxygen pressure (pO_2) around 60 mm Hg in the maternal and 20–30 mm Hg in the fetal artery in pigs. This is a far wider pO_2 gap than in horses, as a species with the most similarity in terms of placentation (Wooding and Burton, 2008). A gap also exists in pH, with fetal values in swine being 0.1 lower than maternal ones. To attenuate the effects of hypoxia in utero, three major mechanisms have developed. First, the oxygen binding capacity is elevated in the fetus. This is mainly reached by a reduction of 50 % in concentration of 2,3-bisphosphoglyceric acid (2,3-BPG) (Comline and Silver, 1974), as there is no

hemoglobin-isoform. Despite the allometry of energy need, as defined in Kleiber's law, demanding a high energy need in fetuses, the actual demand is similar to their mother's (Dawes and Mott, 1959). Amongst others, this is possible because no thermoregulation is needed in utero. In addition, high-demand organs (e.g., brain, liver) of the fetus have a lower energy need than in the newborn, decreasing the total energy demand in utero. It is supposed that the underlying mechanism in the brain is a reduced membrane leakiness, saving energy normally needed for upholding the membrane potential (Hansen, 1977; Xia and Haddad, 1994). The lower oxygen consumption also enables a deeper tissue oxygenation at low tensions (Krogh, 1919). While the main energy is required for growth and development, it seems plausible that the fetus can slow the growth to save energy. Thirdly and auxiliary to these general adjustments, a diving reflex like behavior in temporary shortened oxygen supply exists. Here hypoxic events are answered by bradycardia, slowing blood flow and centralization, limiting anaerobiosis to peripheral, non-essential tissue (Snyder, 1983). The accumulating lactate is, when the oxygen demand is met again, metabolized in the liver. The enhanced hypoxia resistance of neonatal hearts supports the transport due to stable heart function throughout the hypoxic events (Bove and Stammers, 1986). All this is to some degree still active in neonatal mammals and contributes to an upholding of hypoxia resistance within the first phase of early adaptation of life (Dawes and Mott, 1959). One should keep in mind the relative advanced neurological maturity in porcine neonates, compared to other precocial mammals, making them more sensitive to perinatal oxygen deprivation (Mellor and Lentle, 2015).

Because of ante- and intrapartum uterine contractions, neonates experience certain degrees of hypoxia, rendering the outlined mechanisms indispensable to marginalize the impact (Randall, 1971; Taverne et al., 1979). Until 15 min before the onset of birth, oxygen levels remain largely stable, and negative influences are reduced by centralization and slowing of blood circulation (i.e., diving reflex) as well as a reduction of movement (Randall, 1992). Uterine contractions along with compromised blood flow in the umbilical cord lower the available oxygen for the fetus, inducing an anaerobic milieu in the muscle and, if compensatory capacity is exceeded, subsequently in vital organs.

A certain amount of perinatal stress is normal, and catecholamine has vital functions in managing extra uterine life. When particularly strong perinatal distress is present, the rise in catecholamines has a fundamental impact on the metabolism, resulting in activation of glycolysis and hyperglycemia. This is accompanied by a negative prognosis (Tuchscherer et al., 2000; Mota-Rojas et al., 2011), since a higher metabolic rate further increases oxygen debt and degree of acidosis. It will be discussed later how this stress response further affects neonatal adaptation.

With leaving the birth canal, the first breath of the neonate usually occurs within 15 s and is mediated by central and

peripheral chemoreceptors detecting hypercapnia (Randall, 1992). In order to establish breathing, the lung has to be ventilated for the first time. To accomplish this, the fetus “practices” breathing in utero, and muscular function is gained prior to birth (Koos and Rajae, 2014). Furthermore, adrenaline released during birth stops secretion in the lung and enables absorption of fluids. A delay in onset of respiration can originate from a lack of surfactant, especially in immature piglets. More commonly, it is the result of intra-partum asphyxia, which can be caused by a depressant effect of acidosis on respiration (Alonso-Spilsbury et al., 2005). In contrast, big piglets seem to have problems passing the birth canal, resulting in deeper acidosis, probably when uterine weakness is present (Trujillo-Ortega et al., 2011; Pandolfi et al., 2017). Yet it has not been discussed explicitly why and if the big piglets are able to recover better from low pH values than low-birth-weight piglets.

Although in early adaptation, the newborn pig has higher O₂ affinity compared with the adult post natum, the amount of 2,3-BPG and subsequently oxygen affinity declines (Comline and Silver, 1974). Oxygen concentration quickly rises after onset of respiration (Herpin et al., 1996) and is around 75%–80% within a few seconds (Casellas et al., 2004; Panzardi et al., 2013). Nuntapaitoon et al. (2018) measured *p*O₂ at around 5 min after birth, achieving similar values to those measured after 1 or 24 h, leading to the conclusion that only a few minutes is necessary to establish sufficient oxygen saturations in viable piglets (Rootwelt, 2013; Panzardi et al., 2013). Thus, establishment of oxygen saturation marks the end of the first phase of early adaptation. However, oxygen levels measured post natum have a low prognostic value for neonatal viability. In contrast, concentrations of carbon dioxide or lactate are of high prognostic value (Gourley et al., 2020; Trujillo-Ortega et al., 2011; Singer, 1999). This can be explained by the well-established negative influence of metabolic–respiratory acidosis on piglet viability (Herpin et al., 1996; Tuchscherer et al., 2000). Hence, a disturbed acid–base balance can be discussed as one of the main contributors to perinatal death.

Nevertheless, neonatal acidosis is to a degree physiological, and neonates are able to endure the low pH values after parturition without detrimental effects on further life (Randall, 1971). In the adult mammal, pH is kept in between 7.21–7.59, and small deviations have detrimental effects. A pH value of 6.9–7.0 seems to be a cutoff in the neonate below which consecutive negative effects become apparent (Randall, 1971; Zaleski and Hacker, 1993).

With the start of normal respiratory function, the peripheral tissue is oxygenated, and lactate, which was produced in the muscle during birth, is set free in the first 15–30 min and leads to a post natum acid high (Walser and Bostedt, 2008). Subsequently pH correction is accomplished within 2 h of life (Wehrend et al., 2005), which is an important step in early adaptation. Three mechanisms, descending from fastest to slowest, are responsible for acid–base balance: buffer sys-

tems (bicarbonate, phosphate and proteins) in the blood, the respiratory rate for CO₂ regulation and the renal change of carbonic anhydrase activity to regulate the secretion of bicarbonate.

Animal-intrinsic efforts to maintain homeostasis, within the first phase of neonatal adaptation, are further strengthened. They are dependent on renal function and tissue integrity. Kidney development in pigs is completed in the third phase of neonatal adaptation around the 21st day (Frazier, 2017). In mammals with delayed acquisition of adult glomerular filtration rate (GFR), a thinner juvenile cortex with “fetal” glomeruli morphology can persist until around 8 weeks post natum in the pig (Bergelin and Karlsson, 1975; Friis, 1980).

Neonatal anemia is common in piglets, and the occurrence increases in big litters (Steinhardt et al., 1984). This is an important factor, since hemoglobin serves as important buffer and is essential for oxygen transport (Bünger et al., 1988). The anemic piglet experiences all phases of a manifest iron deficiency in the first 72 h of life (Lemacher and Bostedt, 1995, 1994). This has an impairing effect on early adaptation, with consequences for erythropoiesis and iron-dependent enzymes. They showed a recourse on liver stored iron at the end of the first phase of adaptation. The usual supplementation of iron takes place later in a piglet’s life and does not extenuate the effects completely, which can develop to a significant handicap (Lemacher and Bostedt, 1995, 1994). It should also be mentioned that neonatal anemia worsens thermotolerance, most likely due to lack of oxygenation (Mayfield et al., 1987).

4 Thermoregulation

The loss of ambient temperature after expulsion decreases body temperature of neonates by up to 3.5 °C (Vande Pol et al., 2020) and is, after establishment of (i) respiration and (ii) homeostasis, the third problem in early adaptation (Herpin et al., 1996, 2002). Farm animal species differ in several aspects considering environment (e.g., seasonal differences or outdoor housing) and individual disposition (e.g., lack of fur). The drop in body temperature is increased by evaporation, attributable to the amniotic fluid (Vande Pol et al., 2020).

In the porcine species the lack of hair, the body proportions with a relatively large body surface area and only scarce adipose tissue result in a temperature around 34 °C needed for thermoneutrality (Malmkvist et al., 2006; Mount, 1959). This temperature is partly lowered by the effect of social huddling to 25–30 °C (Mount, 1968).

With temperature in farms being around 21 °C, the neonates have to activate compensatory mechanisms. One of those, present in adult mammals, is reduction of peripheral blood flow by vasoconstriction, which probably is deficient in neonatal piglets (Lossec et al., 1999), although in older studies a calculatory influence was shown (Mount, 1963). In

terms of insulation, piglets can multiply their scarce subcutaneous body fat at birth by tripling it within 48 h (Elliot and Lodge, 1977). This is possible because the high alimentary fat intake is primarily used to increase body fat (Theil et al., 2014). Combined with a maturation of the adipocytes from multi- to unilocular, as described in the review by Loveau et al. (Louveau et al., 2016), the heat loss is reduced. Still the improved thermal homeostasis is mainly influenced by increased heat production (Mount, 1959, 1963).

Berthon et al. (1994) and Herpin et al. (2002) concluded an overall absence of non-shivering thermogenesis (NST) in pigs. Studies show that Suidae ancestors lost the ability to express uncoupling protein (UCP)-1 20 million years ago, and it is accepted that therefore they lack brown adipose tissue (BAT) (Fyda et al., 2020). Thus, pigs were thought to exclusively rely on shivering thermogenesis, with authors ascribing up to 97 % of heat production on shivering (Herpin et al., 2002). Herpin et al. (2002) suggested an increase of efficiency mediated by increased myofibril mass, blood supply and triad proliferation to compensate the disadvantage.

Most species of Suidae and other classes lacking BAT occupy tropical climate zones (Gaudry et al., 2017; Fyda et al., 2020). In contrast, wild boars (*Sus scrofa*) live in cold to moderate climate and have had to develop additional mechanisms to mitigate heat loss in offspring. This is accomplished by huddling and nest building (Berg et al., 2006). Although this behavior is also expressed in domesticated pigs, especially nest building is considerably compromised in modern pig production due to lack of nest building material and restricted space. The alternatively offered heat lamps in conventional stables bear low attraction to the piglets, and they tend to stay with each other or in the sow's proximity for the first couple of days (Hrupka et al., 2000). In particular, piglets with lower viability express this behavior longer (Weary et al., 1996). Low temperatures are thought to affect the survival of low-viability piglets (Pandolfi et al., 2017; Pedersen et al., 2011). In this context, a recent study on mechanisms of thermoregulation is noteworthy, as it suggests a muscle-derived form of non-shivering thermogenesis (NST) exists in wild boar (Nowack et al., 2019). The NST is mediated by the sarco-/endoplasmic reticulum Ca^{2+} -ATPase (SERCA) and regulated by sarcolipin. The underlying mechanism and its contribution to heat tolerance in BAT-ablated mice have been described previously (Bal et al., 2016, 2012). Briefly, sarcolipin is able to mediate the uncoupling of SERCA in order to increase heat production and ATP hydrolysis. It seems plausible that this mechanism persists in domestic pig, which could explain the aforementioned increase of thermoregulatory efficiency. Further, mainly lipids seem to be used for muscular heat production, creating an interesting perspective on intramuscular fat (Herpin et al., 2004).

The observed resistance to cold temperatures in outdoor farms, where straw is readily provided and hut temperatures can get near freezing, is explained by the aforementioned be-

havioral strategies (Schild et al., 2019). Multiple studies (Kilbride et al., 2012; Baxter et al., 2012; Rangstrup-Christensen et al., 2018b; Leeb et al., 2019) have shown no increase of early piglet mortality in outdoor housing conditions compared to indoor housing. Schild et al. (2019) emphasize the importance of hut insulation in outdoor housing, and Algers and Jensen (1990) showed no influence of temperatures as low as -17°C . It is indicated that heat in summer does have an effect on stillborn rate due to maternal stress (Schild et al., 2020; Rangstrup-Christensen et al., 2018a). Analysis of seasonal effects has to be done carefully, since multiple effects (e.g., straw bedding, air-conditioning in indoor warms, huts, light) can have an impact, and it is difficult to differentiate those. Research into this is in demand due to growing interest in organic produced food and animal welfare.

A genetic contribution to the phenotypic variation in thermal capacity is likely, as differences between Asian and European breeds, but also between closely related European commercial lines, have been described. Schild et al. (2020) highlighted the influence of breed, which was also described between traditional Asian domestic pigs and commercial European lines (Herpin et al., 1993).

Despite being described separately, it is most important to realize the connection between acid–base balance and body temperature. Acidotic piglets are less viable, thus complicating postnatal adaptation and ultimately increasing the risk to die from a crushing complex (Randall, 1971; Zaleski and Hacker, 1993). As will be explained below, the piglet has few endogenous resources and is highly dependent on early colostrum uptake. Herpin et al. (1996) showed that lactate concentrations at birth correlate with thermal resistance and death within 21 d of life. Therefore, a hypothermia–hypoglycemia crushing relationship was established.

5 Energy demand

As described above, normothermia is usually developed at the end of early adaptation, and the piglet exerts maximal metabolic efforts in reaching and keeping this temperature (Xiong et al., 2018; Malmkvist et al., 2006; Herpin et al., 2002). Coldness slows growth as energy necessary for anabolism is diverted to thermoregulation (Berthon et al., 1996). A negative impact on survival was shown by Pedersen et al. (2011), who observed a relation between low body temperature 2 h after birth and a risk of crushing. Thyroxine plays an important role as a postnatal surge of active thyroid hormones is followed by an increase of heat production (Ślebodziński, 1965, 1979; Mount, 1959). The utilization rate of thyroxine differs between species and is exceptionally high in neonatal pigs (Mount, 1959). Mostyn et al. (2006) found differences in thyroxine levels between pig breeds. While thyroid hormones mediate the calorogenic effect, Kaciuba-Uścilko (1971) and LeBlanc and Mount (1968) suggest a complementary role for adrenalin. To understand the initial

situation porcine newborns face, it is important to understand the energy metabolism and available resources. Supposedly, these resources can enable homeostasis for up to 12 h (Mellor and Cockburn, 1986; Mccance and Widdowson, 1959).

The piglet's first external source of energy is colostrum. The amount of ingested colostrum correlates with heat production. This is hardly explainable by gastro-intestinal heat production alone, which accounts for about 10 % (Herpin et al., 2002). Trujillo-Ortega et al. (2011) have shown the dysregulation in thermoregulation following insufficient or absent colostrum intake. It is essential that colostrum be taken in soon after birth. Nevertheless, it should be kept in mind that in the first day of life, colostrum itself is not sufficient to sustain metabolism, and glycogen stores are necessary (Theil et al., 2014; Szymeczko et al., 2008). In addition, Le Dividich et al. (2017) and Devillers et al. (2011) showed that the minimal amount of 180 g colostrum needed by each piglet cannot necessarily be provided in hyper-prolific sows (Quesnel et al., 2012). The subsequent lack of energy and immunoglobulins is a particular problem for small and weak piglets.

Pathways of energy provision are insufficient at birth and hinder efficient use of the scarce resources, but most develop within hours of adaptation in the neonate (Mersmann, 1974). This metabolic immaturity is in contrast to the relative neurological maturity and can result in a theoretical imbalance in energy demand and supply if certain factors are off. It should be taken into consideration that maternal stress in late fetal development (e.g., third trimester) seems to affect the fetus' HPA axis (Schwerin et al., 2005). The implications for piglet viability are yet unknown.

One of those deficient pathways is found in the carbohydrate metabolism. As in most fetuses, fructose is the preferred substrate of the porcine fetus, the deficiency of fructokinase after birth marks the change of substrate for carbohydrate metabolism. The ability to metabolize fructose via fructokinase is not regained until day 9 (Bird and Hartmann, 1996). Thus, fructose is thought to be a marker for immaturity in neonates as it is quickly eliminated after birth and higher in less viable piglets. In the neonate, glucose is the main substrate pre-colostrum, especially if stressed by cold (Mellor and Cockburn, 1986). Steele et al. (1971) have shown a dysregulated glucose homeostatic response of newborn swine. A colostrum-induced maturation of glucoregulatory mechanism is likely and explains the adverse glucagon response in fasted individuals (Lepine et al., 1989).

Glycogen stores, created in late fetal development, are readily available at birth (Elliot and Lodge, 1977). Being mainly stored in liver and muscle, it is used subsequent to birth, reaching minimum values 12–24 and 24–36 h after birth respectively. Gluconeogenic capacity is probably attenuated in early adaptation, as is shown in an *in vitro* study by Mersmann and Phinney (1973). Mellor and Cockburn (1986) estimated liver glycogen being sufficient to sustain homeothermia for 2 h, while in fact the fasted piglet develops hypothermia after 12 h. The muscle glycogen used for

shivering plausibly explains the postponed developing hypothermia. In this context, it is once again important to point out the limited possibilities of hypoxic piglets, which cannot use those supplies.

Studies observing the respiratory quotient (RQ) suggest a change in substrate to lipids at around 6–12 h post natum, indicated by a decrease of the RQ (Mount, 1969). In the pig, lipid metabolism is hindered by an immature carnitine palmitoyltransferase 1 (CPT-1) and low pancreas lipase activity (Fainberg et al., 2012). CPT-1 is necessary to transport the long chain fatty acids, found in colostrum, into the mitochondria, hence beta-oxidation being less efficient. In contrast to other species, piglets do not develop a neonatal hyperketonemia as ketogenesis is slowly developed (Adams and Odle, 1993). Nevertheless, swine have to deal with the low-carbohydrate and high-fat content of colostrum. It is hypothesized that acetate production via CoA release is a consequence of an oversaturated citrate cycle and necessary to sustain thiolase function of beta-oxidation (Adams et al., 1997; Adams and Odle, 1993). This is further supported by 10- to 100-fold higher plasma concentrations ($311 \pm 18 \mu\text{molL}^{-1}$ in newborns) of acetate than beta-hydroxybutyrate ($6 \pm 1 \mu\text{molL}^{-1}$ in newborns) as described by Adams and Odle (1998). This values increase after suckling. Lin et al. (2010) showed in an *in vitro* study, that acetogenesis takes place in the mitochondria and therefore is proportional to CPT-1 activity. An increase with piglet age is observed and is one of the steps in maturation of the lipid metabolism. The reason behind this is a change in sensitivity of CPT-1 to the inhibitory effect of malonyl-CoA (Lepine et al., 1989). Furthermore, a positive relation of acetogenic activity with non-esterified fatty acid (NEFA) availability is observed, when fasted and fed individuals are compared. It can be concluded that acetate is the primary product of mitochondrial oxidation in pig; consequently the preferred substrate in porcine liver, brain and intestine and early regulation is brought about by kinetic CPT-1 inhibition (Steele et al., 1984; Darcy-Vrillon et al., 1996).

Boyd et al. (1982) showed different patterns for NEFA oxidation. Oleic acid (18 : 1) was the most pronounced and stearic acid (18 : 0) the least pronounced fatty acid. From the results of Theil et al. (2014) and Herpin et al. (2002), it can be concluded that the liver can oxidize long- and medium-chain fatty acids (LCFAs and MCFAs), while only LCFAs are a suitable substrate for muscular lipid metabolism and thus can contribute to heat production. Interestingly, in Chinese Meishan pig, the newborn animals are able to metabolize stearic acid to omega-9 forms (e.g., 18 : 1, 20 : 1), enabling a faster oxidation of them or synthesis of triglycerides (TGs) (Fainberg et al., 2012). Fatty acid patterns change later to mirror adult Meishan, becoming comparable to commercial European lines' patterns.

Lepine et al. (1989) showed a 6-fold increase in NEFAs during ad libitum colostrum intake. This also indicates a relation of beta-oxidation and gluconeogenesis with glycerol-3-

phosphate dehydrogenase (GPDH) and pyruvate carboxylase (PC). GPDH is necessary to activate acyl-CoA and nicotinamide adenine dinucleotide hydrogen (NADH), while PC provides ATP for the gluconeogenesis. Cholesterol steadily increases during the first 21 d (Kabalin et al., 2017). This is explained by a high fat diet and improved lipid utilization via upregulated bile acid synthesis (Lewis et al., 2000). In contrast, TGs are twice as high on day 1 compared to day 7 to 21, respectively. The decrease in TGs can be explained in adipocyte maturation and lipogenesis (Kabalin et al., 2017; Louveau et al., 2016). An additional part of 4%–8% of heat production is due to protein metabolism (Mellor and Cockburn, 1986). The piglet has a low protein oxidation capacity, and amino acids are mainly used for protein biosynthesis (De Vos et al., 2015). Nevertheless, protein catabolism will occur in cold-stressed or starving piglets if energy demand cannot be met (McCance and Widdowson, 1959).

The hepatic capability of producing insulin-like growth factor-1 (IGF-1) is impaired in neonatal swine. The growth hormone receptors have a low binding capacity, and low levels of IGF-1 are observed (Louveau et al., 2000). Therefore, the main source of IGF-1 is the colostrum. As lactogenic IGF-1 is not absorbed, an influence on gut maturation and growth is discussed (Burrin et al., 1997; Louveau et al., 2000). A stimulatory response of IGF-1 secretion to pig growth hormone (GH) can be seen, and the weaning weight increases if additional IGF-1 is supplemented (Wester et al., 1998). This leads to the conclusion that the somatotrophic axis, albeit functional, is not a relevant factor in (early) neonatal adaptation (Louveau et al., 2000).

6 Remarks on the current situation in conventional farming

Further remarks on the influence of common conventional farming and recent breeding seem necessary, since they interfere with parturition and aggravate the challenges.

Longer birth durations have been reported in modern breeds (Björkman et al., 2017; Van Dijk et al., 2005). Van Dijk et al. (2006, 2005) and Panzardi et al. (2013) have shown a cumulative effect of farrowing duration for later born piglets so that they were less viable, but only a little effect of the individual birth duration was observed. The cumulative effect is explained by repeated episodes of contraction, resulting in momentary asphyxia. The asphyxia leads to an oxygen deficit at birth, which increases the debt to be overcome in the first adaptation processes. An additional effect of contraction strength was seen in the higher mortality of piglets when uterotonics are used (Zaremba et al., 2019). Higher individual birth intervals are related to stillborn piglets, but it remains unclear as to whether they die sub partu or ante partum (Devillers et al., 2011).

Birth induction possibly interferes negatively with the biology of birth and gestation. It is clear that treatment with

oxytocin can increase the risk of stillbirth and is increased in high dosages (Muro et al., 2020). A disrupted uterine blood flow due to increased myometrium contraction is often discussed as responsible. In other polytocous species, evidence also points to the negative influence of longer birth intervals (Groppetti et al., 2010). In one study (Taverne et al., 1979) an electromyogram during spontaneous birth was done and showed simultaneous contractions over multiple parts. This indicates whole-muscular uterine contractions, which could affect the piglets born later. Langendijk et al. (2018) showed that if dystocia can be detected as early as the fourth piglet, it points to sow-related problems (e.g., lack of oxytocin). On the other side, a positive effect of carbetocin in reducing piglet hypoxia is seen due to shorter birth intervals, as well as a positive effect due to shorter birth durations (Wähler and Hühn, 2001; Ward et al., 2019). However, the use of carbetocin might have a negative effect on colostrum yield (Boonraungrod et al., 2018; Vongsariyanich et al., 2021).

Although it is often discussed, an effect on piglet viability of a shorter gestation length due to a prostaglandin $F_{2\alpha}$ use has not been proven (Kirkden et al., 2013). With regard to neonates, artificially shortened gestation possibly impairs fetal adaptation prior to birth (e.g., in lung development and energy metabolism). To the best of our knowledge, an explicit evaluation of the possible effects on the phases of early adaptation is not published yet.

Although conventional farming offers heat lamps for providing adequate ambient temperature, they come with limitations as piglets tend to stay with the sow. Straw bedding keeps temperature as well as thermotolerance, therefore enabling more energy for maturation and growth. Furthermore, nest-building behavior is expressed by sows and, if not satisfied (e.g., lack of material to manipulate), can lead to stress. It has been shown that cortisol interferes with oxytocin binding, and stress-induced cortisol elevation could lead to dystocia (Nagel et al., 2019; Edwards et al., 2019; Yun et al., 2013). In addition, Edwards et al. (2019) describe a positive impact of nest-building material even after parturition, while Yun et al. (2013) observed a more careful behavior of the sows.

Beside the high litter sizes in modern high-performance pig production, there seems to be evidence that conventional farrowing crates can have an additional negative influence on birth under the current conditions. Greater prolongation and less capability to compensate dystocia are observable in fixed sows (Blim, 2020; Lehn, 2020). This does not appear true for sows allowed to farrow freely, although the overall losses might be the same. The relationship of piglet and sow is impaired by conventional crates (Thodberg et al., 1999). In aspects of environment, the piglet vitality appeared better in group farrowing or free farrowing than in farrowing crates, while the observed crushing risk was lower in farrowing crates (Damm et al., 2005; Lohmeier et al., 2020).

7 Conclusion

The characterization of neonatal adaptation is important to determine causes for piglet loss and possible follow-up intervention. This should focus on the introduced phases of adaptation and respective processes. Although there is sufficient knowledge about the neonatal metabolism in general, studies are needed which take genetic differences in breeds into account. In addition, the social demand for new husbandry systems must be addressed. Particular emphasis on low-birth-weight piglets is needed, including the evaluation of pathophysiological findings. This could be important to elaborate strategies in breeding or management to increase piglet vitality and animal welfare.

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References

Adams, S. H. and Odle, J.: Plasma beta-hydroxybutyrate after octanoate challenge: attenuated ketogenic capacity in neonatal swine, *Am. J. Physiol.-Reg. I.*, 265, 761–765, 1993.

Adams, S. H. and Odle, J.: Acetogenesis does not replace ketogenesis in fasting piglets infused with hexanoate, *Am. J. Physiol.-Endoc. M.*, 274, 963–970, 1998.

Adams, S. H., Lin, X., Yu, X. X., Odle, J., and Drackley, J. K.: Hepatic fatty acid metabolism in pigs and rats: major differences in endproducts, O₂ uptake, and beta-oxidation, *Am. J. Physiol.-Reg. I.*, 272, 1641–1646, 1997.

Algers, B. and Jensen, P.: Thermal microclimate in winter farrowing nests of free-ranging domestic pigs, *Livest. Prod. Sci.*, 25, 177–181, 1990.

Alonso-Spilsbury, M., Mota-Rojas, D., Villanueva-Garcia, D., Martinez-Burnes, J., Orozco, H., Ramirez-Necoechea, R., Mayagoitia, A. L., and Trujillo, M. E.: Perinatal asphyxia pathophysiology in pig and human: a review, *Anim. Reprod. Sci.*, 90, 1–30, <https://doi.org/10.1016/j.anireprosci.2005.01.007>, 2005.

Bal, N. C., Maurya, S. K., Sopariwala, D. H., Sahoo, S. K., Gupta, S. C., Shaikh, S. A., Pant, M., Rowland, L. A., Bombardier, E., and Goonasekera, S. A.: Sarcolipin is a newly identified regulator of muscle-based thermogenesis in mammals, *Nat. Med.*, 18, 1575–1579, 2012.

Bal, N. C., Maurya, S. K., Singh, S., Wehrens, X. H., and Periasamy, M.: Increased reliance on muscle-based thermogenesis upon acute minimization of brown adipose tissue function, *J. Biol. Chem.*, 291, 17247–17257, 2016.

Baxter, E. M., Lawrence, A. B., and Edwards, S. A.: Alternative farrowing accommodation: welfare and economic aspects of existing farrowing and lactation systems for pigs, *Animal*, 6, 96–117, 2012.

Baxter, E. M., Rutherford, K. M. D., D'earth, R. B., Arnott, G., Turner, S. P., Sandøe, P., Moustsen, V. A., Thorup, F., Edwards, S. A., and Lawrence, A. B.: The welfare implications of large litter size in the domestic pig II: management factors, *Anim. Welfare*, 22, 219–238, 2013.

Berg, F., Gustafson, U., and Andersson, L.: The uncoupling protein 1 gene (UCP1) is disrupted in the pig lineage: a genetic explanation for poor thermoregulation in piglets, *PLoS Genet.*, 2, 1178–1181, 2006.

Bergelin, I. and Karlsson, B.: Functional structure of the glomerular filtration barrier and the proximal tubuli in the developing foetal and neonatal pig kidney, *Anat. Embryol.*, 148, 223–234, 1975.

Berthon, D., Herpin, P., and Le Dividich, J.: Shivering thermogenesis in the neonatal pig, *J. Therm. Biol.*, 19, 413–418, 1994.

Berthon, D., Herpin, P., Le Dividich, J., and Dauncey, M.: Interactive effects of thermal environment and energy intake on thyroid hormone metabolism in newborn pigs, *Neonatology*, 69, 51–59, 1996.

Bird, P. and Hartmann, P.: Changes in the concentration of fructose in the blood of piglets of different ages after doses of fructose, fructose plus glucose, and sucrose, *Brit. J. Nutr.*, 76, 399–407, 1996.

Björkman, S., Oliviero, C., Rajala-Schultz, P. J., Soede, N. M., and Peltoniemi, O. A. T.: The effect of litter size, parity and farrowing duration on placenta expulsion and retention in sows, *Theriogenology*, 92, 36–44, <https://doi.org/10.1016/j.theriogenology.2017.01.003>, 2017.

Blim, S. M.: Über das Geburtsgeschehen bei Schweinen einer hochproliferativen Linie unter verschiedenen Haltungsbedingungen: Quantifizierung der partusrelevanten Belastung anhand klinischer, stoffwechselbezogener und ethologischer Parameter, Universitätsbibliothek Gießen, <http://geb.uni-giessen.de/geb/volltexte/2020/15523/> (last access: 20 December 2021), ISBN/ISSN 978-3-86345-551-4, 2020.

Boonraungrod, N., Sutthiya, N., Kumwan, P., Tossakui, P., Nuntapaitoon, M., Muns, R., and Tummaruk, P.: Control of parturition in swine using PGF₂α in combination with carbetocin, *Livest. Sci.*, 214, 1–8, 2018.

- Bostedt, H.: Klinische Einteilung der postnatalen Entwicklung, in: Reproduktionsmedizin und Neonatologie von Hund und Katze, edited by: Günzel-Apel, A.-R. and Bostedt, H., Schattauer Verlag, Stuttgart, 542–544, ISBN 978-3-7945-2249-1, 2016.
- Bove, E. L. and Stammers, A. H.: Recovery of left ventricular function after hypothermic global ischemia: age-related differences in the isolated working rabbit heart, *J. Thorac. Cardio. Sur.*, 91, 115–122, 1986.
- Boyd, R., Britton, R., Knoche, H., Moser, B., Peo, Jr., E., and Johnson, R.: Oxidation rates of major fatty acids in fasting neonatal pigs, *J. Anim. Sci.*, 55, 95–100, 1982.
- Brooks, A., Hagan, D., and Howe, D.: Neuroendocrine regulation of pituitary–adrenal function during fetal life, *Eur. J. Endocrinol.*, 135, 153–165, 1996.
- Bünger, B., Bünger, U., and Lemke, E.: Verhaltensbiologische Vitalitätseinschätzung von Ferkeln mit hoch- und mittelgradiger konnataler Eisenmangelanämie, *Monatsh. Veterinarmed.*, 43, 583–587, 1988.
- Burrin, D., Davis, T., Fiorotto, M., and Reeds, P.: Role of milk-borne vs. endogenous insulin-like growth factor I in neonatal growth, *J. Anim. Sci.*, 75, 2739–2743, 1997.
- Casellas, J., Noguera, J., Varona, L., Sánchez, A., Arqué, M., and Piedrafita, J.: Viability of Iberian × Meishan F2 newborn pigs. II. Survival analysis up to weaning, *J. Anim. Sci.*, 82, 1925–1930, 2004.
- Comline, R. and Silver, M.: A comparative study of blood gas tensions, oxygen affinity and red cell 2, 3 DPG concentrations in foetal and maternal blood in the mare, cow and sow, *J. Physiol.*, 242, 805–826, 1974.
- Damm, B. I., Forkman, B., and Pedersen, L. J.: Lying down and rolling behaviour in sows in relation to piglet crushing, *Appl. Anim. Behav. Sci.*, 90, 3–20, 2005.
- Darcy-Vrillon, B., Cherbuy, C., Morel, M.-T., Durand, M., and Duée, P.-H.: Short chain fatty acid and glucose metabolism in isolated pig colonocytes: modulation by NH_4^+ , *Mol. Cell Biochem.*, 156, 145–151, 1996.
- Dawes, G. and Mott, J. C.: The increase in oxygen consumption in the lamb after birth, *J. Physiol.*, 146, 295–315, 1959.
- De Vos, M., Huygelen, V., Hesta, M., Willems, S. A., Franssen, E., Casteleyn, C., Van Cruyten, S., and Van Ginneken, C.: Birth-weight has no influence on chemical body composition and muscle energy stores in suckling piglets, *Anim. Prod. Sci.*, 56, 844–849, 2015.
- Devillers, N., Farmer, C., Le Dividich, J., and Prunier, A.: Variability of colostrum yield and colostrum intake in pigs, *Animal*, 1, 1033–1041, 2007.
- Devillers, N., Le Dividich, J., and Prunier, A.: Influence of colostrum intake on piglet survival and immunity, *Animal*, 5, 1605–1612, 2011.
- Eastmann, N.: Mount Everest in utero, *Am. J. Obstet. Gynecol.*, 67, 701–711, 1954.
- Edwards, L. E., Plush, K. J., Ralph, C. R., Morrison, R. S., Acharya, R. Y., and Doyle, R. E.: Enrichment with lucerne hay improves sow maternal behaviour and improves piglet survival, *Animals*, 9, 558, 2019.
- Elliot, J. and Lodge, G.: Body composition and glycogen reserves in the neonatal pig during the first 96 hours postpartum, *Can. J. Anim. Sci.*, 57, 141–150, 1977.
- Fainberg, H. P., Bodley, K., Bacardit, J., Li, D., Wessely, F., Mongan, N. P., Symonds, M. E., Clarke, L., and Mostyn, A.: Reduced neonatal mortality in Meishan piglets: a role for hepatic fatty acids?, *PLoS One*, 7, e49101, <https://doi.org/10.1371/journal.pone.0049101>, 2012.
- Frazier, K. S.: Species differences in renal development and associated developmental nephrotoxicity, *Birth Defects Res.*, 109, 1243–1256, 2017.
- Friis, C.: Postnatal development of the pig kidney: ultrastructure of the glomerulus and the proximal tubule, *J. Anat.*, 130, 513–526, 1980.
- Fyda, T. J., Spencer, C., Jastroch, M., and Gaudry, M. J.: Disruption of thermogenic UCPI predated the divergence of pigs and peccaries, *J. Exp. Biol.*, 223, <https://doi.org/10.1242/jeb.223974>, 2020.
- Gaudry, M. J., Jastroch, M., Treberg, J. R., Hofreiter, M., Paijmans, J. L., Starrett, J., Wales, N., Signore, A. V., Springer, M. S., and Campbell, K. L.: Inactivation of thermogenic UCPI as a historical contingency in multiple placental mammal clades, *Sci. Adv.*, 3, e1602878, <https://doi.org/10.1126/sciadv.1602878>, 2017.
- Gerten, K. A., Coonrod, D. V., Bay, R. C., and Chambliss, L. R.: Cesarean delivery and respiratory distress syndrome: does labor make a difference?, *Am. J. Obstet. Gynecol.*, 193, 1061–1064, 2005.
- Gourley, K. M., DeRouchey, J. M., Tokach, M. D., Dritz, S. S., Goodband, R. D., and Woodworth, J. C.: Associations between piglet umbilical blood hematological criteria, birth order, birth interval, colostrum intake, and piglet survival, *J. Anim. Sci.*, 98, 1–8, 2020.
- Groppetti, D., Pecile, A., Del Carro, A., Copley, K., Minero, M., and Cremonesi, F.: Evaluation of newborn canine viability by means of umbilical vein lactate measurement, apgar score and uterine tocodynamometry, *Theriogenology*, 74, 1187–1196, 2010.
- Hansen, A. J.: Extracellular potassium concentration in juvenile and adult rat brain cortex during anoxia, *Acta Physiol. Scand.*, 99, 412–420, 1977.
- Herpin, P., Le Dividich, J., and Amaral, N.: Effect of selection for lean tissue growth on body composition and physiological state of the pig at birth, *J. Anim. Sci.*, 71, 2645–2653, 1993.
- Herpin, P., Le Dividich, J., Hulin, J. C., Fillaut, M., De Marco, F., and Bertin, R.: Effects of the level of asphyxia during delivery on viability at birth and early postnatal vitality of newborn pigs, *J. Anim. Sci.*, 74, 2067–2075, 1996.
- Herpin, P., Damon, M., and Le Dividich, J.: Development of thermoregulation and neonatal survival in pigs, *Livest. Prod. Sci.*, 78, 25–45, 2002.
- Herpin, P., Vincent, A., and Damon, M.: Effect of breed and body weight on thermoregulatory abilities of European (Piétrain × (Landrace × Large White)) and Chinese (Meishan) piglets at birth, *Livest. Prod. Sci.*, 88, 17–26, <https://doi.org/10.1016/j.livprodsci.2003.11.006>, 2004.
- Hrupka, B., Leibbrandt, V., Crenshaw, T., and Benevenga, N.: The effect of thermal environment and age on neonatal pig behavior, *J. Anim. Sci.*, 78, 583–591, 2000.
- Juul-Madsen, H. R., Jensen, K. H., Nielsen, J., and Damgaard, B. M.: Ontogeny and characterization of blood leukocyte subsets and serum proteins in piglets before and after weaning, *Vet. Immunol. Immunop.*, 133, 95–108, 2010.

- Kabalin, A. E., Balenović, T., Šperanda, M., Milinković-Tur, S., Štoković, I., Menčik, S., Maurić, M., and Pavičić, Ž.: Serum biochemical parameters in suckling piglets with low and average birth mass, *Vet. Arhiv*, 87, 171–184, 2017.
- Kaciuba-Uściłko, H.: The effect of previous thyroxine administration on the metabolic response to adrenaline in new-born pigs, *Neonatology*, 19, 220–226, 1971.
- KilBride, A., Mendl, M., Statham, P., Held, S., Harris, M., Cooper, S., and Green, L.: A cohort study of preweaning piglet mortality and farrowing accommodation on 112 commercial pig farms in England, *Prev. Vet. Med.*, 104, 281–291, 2012.
- Kirkden, R., Broom, D., and Andersen, I.: Piglet mortality: the impact of induction of farrowing using prostaglandins and oxytocin, *Anim. Reprod. Sci.*, 138, 14–24, 2013.
- König, N. L., Wähner, M., Seeger, J., Sigmarsson, H. L., and Kaufold, J.: An investigation into uterine capacity based on litter and placental characteristics in two sow lines with different prolificacy (Danish Landrace × Danish Yorkshire versus German Saddleback), *Reprod. Domest. Anim.*, 56, 34–45, 2021.
- Koos, B. J. and Rajae, A.: Fetal Breathing Movements and Changes at Birth, in: *Advances in Fetal and Neonatal Physiology. Advances in Experimental Medicine and Biology*, vol. 814, edited by: Zhang L. and Ducsay C., Springer, New York, NY, https://doi.org/10.1007/978-1-4939-1031-1_8, 2014.
- Krogh, A.: The number and distribution of capillaries in muscles with calculations of the oxygen pressure head necessary for supplying the tissue, *J. Physiol.*, 52, 409–415, 1919.
- Langendijk, P. and Plush, K.: Parturition and its relationship with stillbirths and asphyxiated piglets, *Animals*, 9, 885, 2019.
- Langendijk, P., Fleuren, M., van Hees, H., and van Kempen, T.: The Course of Parturition Affects Piglet Condition at Birth and Survival and Growth through the Nursery Phase, *Animals*, 8, 60, <https://doi.org/10.3390/ani8050060>, 2018.
- Le Dividich, J., Charneca, R., and Thomas, F.: Relationship between birth order, birth weight, colostrum intake, acquisition of passive immunity and pre-weaning mortality of piglets, *Span. J. Agric. Res.*, 15, e0603, <https://doi.org/10.5424/sjar/2017152-9921>, 2017.
- LeBlanc, J. and Mount, L.: Effects of noradrenaline and adrenaline on oxygen consumption rate and arterial blood pressure in the newborn pig, *Nature*, 217, 77–78, 1968.
- Leeb, C., Rudolph, G., Bochicchio, D., Edwards, S., Früh, B., Holinger, M., Holmes, D., Illmann, G., Knop, D., Prunier, A., Rousing, T., Winckler, C., and Dippel, S.: Effects of three husbandry systems on health, welfare and productivity of organic pigs, *Animal*, 13, 2025–2033, 2019.
- Lehn, D.: Untersuchungen zum Ablauf der peripartalen Periode des Schweines in verschiedenen Haltungsbedingungen unter besonderer Berücksichtigung des endokrinen Status und ethologischer Merkmale, *Universitätsbibliothek Gießen*, <https://doi.org/10.22029/jlupub-544>, 2020.
- Lemacher, S. and Bostedt, H.: The development of plasma iron concentration and hemoglobin content in piglets in the first three days of life and the significance of prenatal anemia, *Tierarztl. Prax.*, 22, 39–45, 1994.
- Lemacher, S. and Bostedt, H.: Development of the iron supply in suckling pigs under variable iron supplementation with regard to environmental conditions, *Tierarztl. Prax.*, 23, 457–464, 1995.
- Lepine, A., Boyd, R., and Welch, J.: Effect of colostrum intake on plasma glucose, non-esterified fatty acid and glucoregulatory hormone patterns in the neonatal pig, *Domest. Anim. Endocrin.*, 6, 231–241, 1989.
- Lewis, D., Oren, S., Wang, X., Moyer, M., Beitz, D., Knight, T., and Mott, G.: Developmental changes in cholesterol 7 α - and 27-hydroxylases in the piglet, *J. Anim. Sci.*, 78, 943–951, 2000.
- Lin, X., Shim, K., and Odle, J.: Carnitine palmitoyltransferase I control of acetogenesis, the major pathway of fatty acid β -oxidation in liver of neonatal swine, *Am. J. Physiol.-Reg. I.*, 298, 1435–1443, 2010.
- Lohmeier, R. Y., Grimberg-Henrici, C. G. E., Büttner, K., Burfeind, O., and Krieter, J.: Farrowing pens used with and without short-term fixation impact on reproductive traits of sows, *Livest. Sci.*, 231, 103889, <https://doi.org/10.1016/j.livsci.2019.103889>, 2020.
- Lossec, G., Duchamp, C., Lebreton, Y., and Herpin, P.: Postnatal changes in regional blood flow during cold-induced shivering in sow-reared piglets, *Can. J. Physiol. Pharm.*, 77, 414–421, 1999.
- Louveau, I., Dauncey, M., and Le Dividich, J.: Regulation of development by nutrition and by the somatotrophic and thyroid axes in the neonatal pig, *Livest. Prod. Sci.*, 66, 121–131, 2000.
- Louveau, I., Perruchot, M.-H., Bonnet, M., and Gondret, F.: Invited review: Pre- and postnatal adipose tissue development in farm animals: from stem cells to adipocyte physiology, *Animal*, 10, 1839–1847, 2016.
- Malmkvist, J., Pedersen, L. J., Damgaard, B. M., Thodberg, K., Jørgensen, E., and Labouriau, R.: Does floor heating around parturition affect the vitality of piglets born to loose housed sows?, *Appl. Anim. Behav. Sci.*, 99, 88–105, <https://doi.org/10.1016/j.applanim.2005.10.007>, 2006.
- Mayfield, S. R., Shaul, P. W., Oh, W., and Stonestreet, B. S.: Anemia blunts the thermogenic response to environmental cold stress in newborn piglets, *Pediatr. Res.*, 21, 482–486, 1987.
- McCance, R. and Widdowson, E. M.: The effect of lowering the ambient temperature on the metabolism of the new-born pig, *J. Physiol.*, 147, 124, 1959.
- Mellor, D. and Cockburn, F.: A comparison of energy metabolism in the new-born infant, piglet and lamb, *Q. J. Exp. Physiol.*, 71, 361–379, 1986.
- Mellor, D. and Lentle, R. G.: Survival implications of the development of behavioural responsiveness and awareness in different groups of mammalian young, *New Zeal. Vet. J.*, 63, 131–140, 2015.
- Mersmann, H.: Metabolic patterns in the neonatal swine, *J. Anim. Sci.*, 38, 1022–1030, 1974.
- Mersmann, H. and Phinney, G.: Glycerokinase activity in liver and adipose tissue of developing swine (*Sus domesticus*), *Int. J. Biochem.*, 4, 575–579, 1973.
- Mostyn, A., Sebert, S., Litten, J. C., Perkins, K. S., Laws, J., Symonds, M. E., and Clarke, L.: Influence of porcine genotype on the abundance of thyroid hormones and leptin in sow milk and its impact on growth, metabolism and expression of key adipose tissue genes in offspring, *J. Endocrinol.*, 190, 631–639, 2006.
- Mota-Rojas, D., Orozco-Gregorio, H., Villanueva-Garcia, D., Bonilla-Jaime, H., Suarez-Bonilla, X., Hernandez-Gonzalez, R., Roldan-Santiago, P., and Trujillo-Ortega, M.: Foetal and neonatal energy metabolism in pigs and humans: a review, *Vet. Med. (Praha)*, 56, 215–225, 2011.

- Mount, L.: The metabolic rate of the new-born pig in relation to environmental temperature and to age, *J. Physiol.*, 147, 333–345, 1959.
- Mount, L.: The thermal insulation of the new-born pig, *J. Physiol.*, 168, 698–705, 1963.
- Mount, L.: The respiratory quotient in the newborn pig, *Brit. J. Nutr.*, 23, 407–413, 1969.
- Mount, L. E.: The climatic physiology of the pig, *The Climatic Physiology of the Pig*, ISBN 9780713141405, 0713141409, 1968.
- Muro, B. B., Carnevale, R. F., Andretta, I., Leal, D. F., Monteiro, M. S., Poor, A. P., Almond, G. W., and Garbossa, C. A.: Effects of uterotronics on farrowing traits and piglet vitality: a systematic review and meta-analysis, *Theriogenology*, 161, 151–160, 2020.
- Nagel, C., Aurich, C., and Aurich, J.: Stress effects on the regulation of parturition in different domestic animal species, *Anim. Reprod. Sci.*, 207, 153–161, 2019.
- Nowack, J., Vetter, S. G., Stalder, G., Painer, J., Kral, M., Smith, S., Le, M. H., Jurcevic, P., Bieber, C., and Arnold, W.: Muscle nonshivering thermogenesis in a feral mammal, *Sci. Rep.-UK*, 9, 1–10, 2019.
- Nuntapaitoon, M., Muns, R., and Tummaruk, P.: Newborn traits associated with pre-weaning growth and survival in piglets, *Asian Austral. J. Anim.*, 31, 237–244, 2018.
- Pandolfi, F., Edwards, S., Robert, F., and Kyriazakis, I.: Risk factors associated with the different categories of piglet perinatal mortality in French farms, *Prev. Vet. Med.*, 137, 1–12, 2017.
- Panzardi, A., Bernardi, M., Mellagi, A., Bierhals, T., Bortolozzo, F., and Wentz, I.: Newborn piglet traits associated with survival and growth performance until weaning, *Prev. Vet. Med.*, 110, 206–213, 2013.
- Pedersen, L., Berg, P., Jørgensen, G., and Andersen, I.: Neonatal piglet traits of importance for survival in crates and indoor pens, *J. Anim. Sci.*, 89, 1207–1218, 2011.
- Pietruszka, A., Der, A., and Matysiak, B.: Analysis of gestation length and its influence on the reproductive performance of crossbred sows kept on a large-scale pig farm, *Sci. Ann. Polish Soc. Anim. Prod.*, 16, 29–36, 2020.
- Quesnel, H., Brossard, L., Valancogne, A., and Quiniou, N.: Influence of some sow characteristics on within-litter variation of piglet birth weight, *Animal*, 2, 1842–1849, 2008.
- Quesnel, H., Farmer, C., and Devillers, N.: Colostrum intake: Influence on piglet performance and factors of variation, *Livest. Sci.*, 146, 105–114, 2012.
- Randall, G.: The relationship of arterial blood pH and pCO₂ to the viability of the newborn piglet, *Can. J. Comp. Med.*, 35, 141–146, 1971.
- Randall, G.: Influence of fetal numbers and hypophysectomy on the length of gestation in the pig, *Can. J. Anim. Sci.*, 67, 1125–1127, 1987.
- Randall, G. C.: Perinatal adaptation in animals, *Anim. Reprod. Sci.*, 28, 309–318, 1992.
- Rangstrup-Christensen, L., Krogh, M. A., Pedersen, L., and Sørensen, J. T.: Sow level risk factors for early piglet mortality and crushing in organic outdoor production, *Animal*, 12, 810–818, 2018a.
- Rangstrup-Christensen, L., Schild, S.-L. A., Pedersen, L. J., and Sørensen, J. T.: Causes of preweaning mortality in organic outdoor sow herds, *Res. Vet. Sci.*, 118, 171–180, 2018b.
- Rootwelt, V.: Postpartum deaths: Piglet, placental and umbilical characteristics, *J. Anim. Sci.*, 91, 2647–2656, <https://doi.org/10.2527/jas.2012-5531>, 2013.
- Sasaki, Y. and Koketsu, Y.: Variability and repeatability in gestation length related to litter performance in female pigs on commercial farms, *Theriogenology*, 68, 123–127, 2007.
- Schild, S.-L., Foldager, L., Bonde, M., Andersen, H.-L., and Pedersen, L.: Does hut climate matter for piglet survival in organic production?, *Animal*, 13, 826–834, 2019.
- Schild, S.-L. A., Foldager, L., Rangstrup-Christensen, L., and Pedersen, L. J.: Characteristics of piglets born by two highly prolific sow hybrids, *Front. Vet. Sci.*, 7, 355, 2020.
- Schwerin, M., Kanitz, E., Tuchscherer, M., Brussow, K. P., Nurnberg, G., and Otten, W.: Stress-related gene expression in brain and adrenal gland of porcine fetuses and neonates, *Theriogenology*, 63, 1220–1234, 2005.
- Silver, M.: Prenatal maturation, the timing of birth and how it may be regulated in domestic animals, *Exp. Physiol.*, 75, 285–307, 1990.
- Singer, D.: Neonatal tolerance to hypoxia: a comparative-physiological approach, *Comp. Biochem. Phys. A*, 123, 221–234, 1999.
- Ślebodziński, A.: Interaction between thyroid hormone and thyroxine-binding proteins in the early neonatal period, *J. Endocrinol.*, 32, 45–57, 1965.
- Ślebodziński, A.: Metabolic response to thyroxine in the newborn pig, *Neonatology*, 36, 198–205, 1979.
- Snyder, G. K.: Respiratory adaptations in diving mammals, *Resp. Physiol.*, 54, 269–294, 1983.
- Steele, N., Frobish, L., Miller, L., and Young, E.: Certain aspects on the utilization of carbohydrates by the neonatal pig, *J. Anim. Sci.*, 33, 983–986, 1971.
- Steele, N., Rosebrough, R., and McMurtry, J.: Fetal hepatic and neural substrate utilization as affected by induced nutritional ketosis in swine, *J. Anim. Sci.*, 58, 1388–1395, 1984.
- Steinhardt, M., Bünger, U., and Furcht, G.: Zum Eisenbedarf des Schweines in den ersten 2 Lebensmonaten, *Arch. Exp. Vet. Med.*, 38, 472–482, 1984.
- Svendsen, L., Weström, B., Svendsen, J., Olsson, A.-C., and Karlsson, B.: Blood serum characteristics of newborn pigs: Comparison of unaffected pigs with pigs belonging to five mortality groups, *Acta Vet. Scand.*, 32, 287–299, 1991.
- Szymeczko, R., Kapelański, W., Piotrowska, A., Dybała, J., Bogusławska-Tryk, M., Burlikowska, K., Hertig, I., Sassek, M., Pruszyńska-Oszmałek, E., and Maćkowiak, P.: Changes in the content of major proteins and selected hormones in the blood serum of piglets during the early postnatal period, *Folia Biol.-Prague*, 57, 97–103, 2008.
- Taverne, M., Naaktgeboren, C., Elsaesser, F., Forsling, M., Van der Weyden, G., Ellendorff, F., and Smidt, D.: Myometrial electrical activity and plasma concentrations of progesterone, estrogens and oxytocin during late pregnancy and parturition in the miniature pig, *Biol. Reprod.*, 21, 1125–1134, 1979.
- Theil, P. K., Lauridsen, C., and Quesnel, H.: Neonatal piglet survival: impact of sow nutrition around parturition on fetal glycogen deposition and production and composition of colostrum and transient milk, *Animal*, 8, 1021–1030, 2014.
- Thodberg, K., Jensen, K. H., Herskin, M. S., and Jørgensen, E.: Influence of environmental stimuli on nest building and farrowing

- behaviour in domestic sows, *Appl. Anim. Behav. Sci.*, 63, 131–144, 1999.
- Trujillo-Ortega, M., Mota-Rojas, D., Juarez, O., Villanueva-Garcia, D., Roldan-Santiago, P., Becerril-Herrera, M., Hernandez-Gonzalez, R., Mora-Medina, P., Alonso-Spilsbury, M., and Rosales, A.: Porcine neonates failing vitality score: physio-metabolic profile and latency to the first teat contact, *Czech J. Anim. Sci.*, 56, 499–508, 2011.
- Tuchscherer, M., Puppe, B., Tuchscherer, A., and Tiemann, U.: Early identification of neonates at risk: traits of newborn piglets with respect to survival, *Theriogenology*, 54, 371–388, 2000.
- van Dijk, A. J., van Rens, B. T., van der Lende, T., and Taverne, M. A.: Factors affecting duration of the expulsive stage of parturition and piglet birth intervals in sows with uncomplicated, spontaneous farrowings, *Theriogenology*, 64, 1573–1590, <https://doi.org/10.1016/j.theriogenology.2005.03.017>, 2005.
- van Dijk, A. J., van der Lende, T., and Taverne, M. A.: Acid-base balance of umbilical artery blood of liveborn piglets at birth and its relation with factors affecting delivery of individual piglets, *Theriogenology*, 66, 1824–1833, <https://doi.org/10.1016/j.theriogenology.2006.04.035>, 2006.
- Vande Pol, K. D., Tolosa, A. F., Shull, C. M., Brown, C. B., Alencar, S. A., and Ellis, M.: Effect of drying and warming piglets at birth on preweaning mortality, *Transl. Anim. Sci.*, 4, 1–12, 2020.
- Vongsariyanich, S., Soontornpornnawin, P., Sakulsirajit, R., Suriyapornchaikul, C., Therarachatamongkol, S., Boonraungrod, N., Pearodwong, P., and Tummaruk, P.: Effect of carbetocin administration during the mid-period of parturition on farrowing duration, newborn piglet characteristics, colostrum yield and milk yield in hyperprolific sows, *Theriogenology*, 172, 150–159, 2021.
- Wähner, M. and Hühn, U.: Control of parturition in sows by using a combined treatment with Cloprostenol plus Depotocin[®], *Arch. Tierzucht*, 44, 151–154, 2001.
- Walsler, K. and Bostedt, H.: *Neugeborenen- und Säuglingskunde der Tiere*, Enke Verlag, Stuttgart, ISBN: 3432983816, 2008.
- Ward, S. A., Kirkwood, R., and Plush, K.: Effects of oxytocin and carbetocin on farrowing performance, *Anim. Reprod. Sci.*, 205, 88–93, 2019.
- Weary, D. M., Pajor, E. A., Thompson, B. K., and Fraser, D.: Risky behaviour by piglets: a trade off between feeding and risk of mortality by maternal crushing?, *Anim. Behav.*, 51, 619–624, 1996.
- Wehrend, A., Stratmann, N., Failing, K., and Bostedt, H.: Influence of partus induction on the pH value in the blood of newborn piglets, *J. Vet. Med. A*, 52, 472–473, 2005.
- Wester, T. J., Davis, T. A., Fiorotto, M. L., and Burrin, D. G.: Exogenous growth hormone stimulates somatotrophic axis function and growth in neonatal pigs, *Am. J. Physiol.-Endoc. M.*, 274, E29–E37, 1998.
- Wooding, P. and Burton, G.: 5 Eutheria: Epitheliochorial Placentation Pig and Horse, in: *Comparative Placentation: Structures, Functions and Evolution*, edited by: Wooding, P. and Burton, G., Springer Science & Business Media, ISBN: 978-3-540-78797-6, 2008.
- Xia, Y. and Haddad, G. G.: Postnatal development of voltage sensitive Na⁺ channels in rat brain, *J. Comp. Neurol.*, 345, 279–287, 1994.
- Xiong, Y., Gates, R. S., Cooper, N. C., and Ellis, M.: Neonatal piglet core body temperature model from surface temperature and environment measurements, 10th International Livestock Environment Symposium (ILES X), 1, 2018.
- Yun, J., Swan, K.-M., Vienola, K., Farmer, C., Oliviero, C., Peltoniemi, O., and Valros, A.: Nest-building in sows: effects of farrowing housing on hormonal modulation of maternal characteristics, *Appl. Anim. Behav. Sci.*, 148, 77–84, 2013.
- Zaleski, H. M. and Hacker, R. R.: Comparison of viability scoring and blood gas analysis as measures of piglet viability, *Can. J. Anim. Sci.*, 73, 649–653, 1993.
- Zaremba, W., Udluft, T., Failing, K., and Bostedt, H.: Analysis of the course of birth and the early postpartal period in pigs after hormonal partus induction with special consideration of complication rate, *Anim. Vet. Sci.*, 7, 29–39, <https://doi.org/10.11648/j.avs.20190702.11>, 2019.