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Piglet mortality: the impact of induction of farrowing using prostaglandins and oxytocin

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Abstract

Induction is usually carried out by administering prostaglandins (prostaglandin $F_{2\alpha}$ or a synthetic analogue). Other hormones, most commonly oxytocin, may also be given. The primary objective is to increase the synchrony of farrowing. This facilitates farrowing supervision, early fostering and 'all in, all out' management of the farrowing house, all of which have the potential to decrease piglet mortality. However, there are also risks, including decreased piglet viability when farrowing is induced too early and an increased probability of dystocia associated with oxytocin use. What are the effects of induction procedures on mortality in pigs? With respect to prostaglandins, studies show that the date of induction and the level of supervision provided are important factors affecting piglet mortality. We recommend administering prostaglandins no earlier than 2 d before the expected farrowing date for the herd. Some studies have reported that prostaglandin induction decreases stillbirth and live-born mortality, but this is probably due to increased farrowing supervision. The incidence of postpartum dysgalactia syndrome is also decreased in herds with a high prevalence of this condition. Inconsistent effects on the progress of farrowing are reported following the routine administration of oxytocin 20-24 h after prostaglandin. Although there is generally no effect on stillbirth rate, dystocia may increase. Earlier administration of low doses may decrease stillbirths, but this requires further research. Carbetocin, a long-acting analogue of oxytocin, is a possible alternative. We recommend that prostaglandin induction be used in conjunction with skilled farrowing supervision to decrease piglet mortality.

Keywords: pig; farrowing; induction; mortality; oxytocin; prostaglandin

1. Introduction

Management strategies can reduce piglet mortality. Many reviewers conclude that mortality can be substantially decreased by supervising farrowings, providing assistance for dystocic sows and caring for piglets, including early fostering and procedures to improve the vitality of piglets that are small or weak (English and Wilkinson, 1982; England, 1986; Kingston, 1989; Hughes, 1992; Vaillancourt and Tubbs, 1992; English, 1993; Muirhead and Alexander, 1997; Cutler et al., 2006; Kirkden et al., in press).

The induction of farrowing is usually carried out by administering the natural hormone prostaglandin $F_{2\alpha}$ ($PGF_{2\alpha}$), or a synthetic analogue such as cloprostenol, collectively referred to here as prostaglandins, prior to the expected date of farrowing. Other hormones, most commonly oxytocin, may also be given. Induction can be a means to facilitate farrowing supervision (Sprecher et al., 1974; Dial, 1984; Vaillancourt and Tubbs, 1992; Kirkwood, 1999; Lawlor and Lynch, 2005). This is because induction increases the synchrony of farrowing, making it more economical to provide continual supervision and making early fostering easier. Induction also has several other potential benefits for the efficiency of farrowing house management and piglet health, described below. However, there are also risks associated with parturition induction. For example, it is widely recognised that if prostaglandins are administered too early in gestation the piglets will be born prematurely and may have reduced viability. Perhaps less widely

known in the industry is the risk of dystocia associated with using oxytocin to further increase the synchrony of farrowing following prostaglandin treatment (Gilbert, 1999; Kirkwood, 1999), with negative effects for the welfare of the sow and the viability of the piglets. In this review, we discuss the details of prostaglandin and oxytocin administration procedures and consider the evidence that farrowing induction can have a beneficial effect on piglet survival.

The date of prostaglandin administration is generally determined with reference to the expected farrowing date, which is calculated from the average gestation length of the herd, because mean gestation length varies between herds, ranging from 113 d to 117 d (Kirkwood, 2010). Unfortunately, most experimental studies have reported the timing of induction in terms of a specified day of gestation, rather than as a given number of days prior the herd's expected farrowing date, and some have not provided the necessary information to convert from one to the other. In order to include as many studies as possible, we compared studies using the day of gestation on which induction occurred. However, when drawing conclusions concerning the optimal timing of induction, we have re-expressed this as a number of days prior to the expected farrowing date, by means of an estimation procedure. This involved taking an average of the natural mean gestation lengths of the herds or control groups in the 37 studies which reported this information. Mean gestation lengths ranged from 113.4 to 117.0 d, with an overall mean 115.2 d and a median 115.3 d, so we used a herd gestation length of 115 d to convert from day of gestation to number of days prior to farrowing.

2. Increasing the synchrony of farrowing

The primary objective of induction is to increase the synchrony of farrowing. Because sows vary in the interval between weaning and oestrus and in the length of gestation, the natural farrowing times within a batch of sows are typically spread over a period of about 10 d (King et al., 1979). The synchronisation of mating or artificial insemination decreases this variability but, because gestation length varies among individuals (Cox, 1964; Sasaki and Koketsu, 2007; Rydhmer et al., 2008), the induction of parturition can further increase farrowing synchrony (Cowart, 2007). An additional problem is that the farrowing times of individual sows are difficult to predict and parturition often occurs at night when staff are not present (Hammond and Matty, 1980). Attempts have been made to increase the proportion of daytime farrowings by using prostaglandins, or by using a combination of prostaglandins and other agents.

Increasing the synchrony of farrowing has many potential advantages, both for piglet survival and management efficiency. By reducing the number of days over which farrowing occurs in a batch of sows, there can be more efficient planning, use of labour and use of the farrowing house (King et al., 1979; Dial, 1984; Pressing, 1992; Muirhead and Alexander, 1997). Increased labour efficiency is due to the concentration of management tasks into shorter time periods. This makes the continual supervision of farrowing more economically realistic (Holyoake et al., 1995), which means that assistance can be given more frequently to dystocic sows and to vulnerable piglets. More

116 efficient use of the farrowing house is possible because each batch of sows occupies the
117 house for a shorter time. An ‘all in, all out’ system of management is facilitated by
118 simultaneous departure of all sows in a batch. It may also allow more time for cleaning
119 and disinfection of the house between batches. The synchrony of farrowing facilitates
120 early fostering and also results in a more uniform time of weaning.
121
122 When prostaglandins are administered on a single day between d 111 and d 114 of
123 gestation, they usually cause an earlier mean onset of farrowing (Ehnvall et al., 1977;
124 Hühn et al., 1977; Lynch and Langley, 1977; Walker, 1977; Hansen, 1979; King et al.,
125 1979; Boland and Herlihy, 1982; Holtz et al., 1983; Martin et al., 1985; Chantaraprateep
126 et al., 1986; Dial et al., 1987; Gall and Day, 1987; Ko et al., 1989; Holyoake et al. 1995;
127 Alexopoulos et al., 1998; Sellier et al., 1999; Gunvaldsen et al., 2007; Sabuncu et al.,
128 2008; Olson et al., 2009; Gheller et al., 2011; but not: Hansen and Jacobsen, 1976; Diehl
129 et al., 1977; Butler and Boyd, 1983) and a much reduced variation in time to onset
130 (Hansen and Jacobsen, 1976; Hansen, 1979; Butler and Boyd, 1983; Welp and Holtz,
131 1985; Dial et al., 1987; Gall and Day, 1987) compared with sows which are allowed to
132 farrow naturally. However, the natural variation in gestation length means that not all
133 individuals are successfully induced. Those with a naturally short gestation still farrow
134 early, before the treatment is administered or has had time to take effect; while the
135 prostaglandin treatment may occur too early to induce parturition in some sows which
136 have a naturally long gestation (Hansen, 1979). A compromise that has been shown to be
137 effective on commercial farms is a ‘partial induction’ programme, in which prostaglandin
138 administration is delayed until d 114 so that sows with a naturally short gestation period

139 are allowed to farrow spontaneously, while individuals with a long gestation period are
140 induced to farrow early (Leike and Hühn, 1992).
141
142 Another objective of farrowing induction is to increase the proportion of births that occur
143 during normal working hours. Ideally, induction would allow farrowing to be
144 synchronised with enough precision to cause most sows to farrow within working hours
145 on a single day. This would reduce the need for supervision at night and thus further
146 increase the feasibility of continual supervision. In reality, while the administration of
147 prostaglandins at the start of the working day often results in a substantial proportion of
148 sows farrowing during working hours on the following day, the percentage of sows that
149 do so varies greatly and is frequently not enough to eliminate the need for night-time
150 supervision. When the treatment is administered on d 111-114 of gestation, the
151 proportion of sows farrowing during the next 8-12 h working day varies from about 40%
152 to >90% (Bosc et al., 1975; Downey et al., 1976; Hühn et al., 1977; Lynch and Langley,
153 1977; Walker, 1977; Černe, 1978; Boland et al., 1979; Hansen, 1979; Humke et al., 1979;
154 King et al., 1979; Hammond and Matty, 1980; Jainudeen and Brandenburg, 1980; Černe
155 and Jöchle, 1981; Einarsson et al., 1981; Arbeiter et al., 1982; Boland and Herlihy, 1982;
156 Smith et al., 1982; Martin et al., 1985; Gall and Day, 1987; Holyoake et al., 1995;
157 Kirkwood et al., 1996; Alexopoulos et al., 1998; Kirkwood and Aherne, 1998; Balogh
158 and Bilkei, 2003; Cassar et al., 2005; Kaeoket, 2006; Gunvaldsen et al., 2007; Straw et
159 al., 2008). Various factors can affect the degree of synchronisation achieved, including
160 the day of injection (d 111 may be too early: Robertson et al., 1978; Hansen, 1979;
161 Alexopoulos et al., 1998; but not Welp and Holtz, 1985) and the number of doses

administered (2 injections, 6 h apart, may be better than 1 injection: Kirkwood and Aherne, 1998; Cassar et al., 2005). The timing of farm management routines such as feeding and cleaning might also affect the onset of parturition, by causing disturbances that delay farrowing (Welp and Holtz, 1985).

Various agents have been employed in conjunction with prostaglandins in order to control the timing of farrowing more precisely. The most widely used in commercial practice is oxytocin, typically administered 20-24 h after prostaglandin injection to stimulate uterine contraction. However, experimental studies have shown that it is not always effective. Doses of 5-30 IU have been variously reported to cause an earlier onset of farrowing (Welp et al., 1984, 20-30 IU; Chantaraprateep et al., 1986, 10-20 IU; Dial et al., 1987, 30 IU; Kirkwood and Thacker, 1995, 10 IU; Hernandez et al., 2009, 20-30 IU), or a later onset (Dial et al., 1987, 5-20 IU), or to have no effect (Holtz et al, 1983, 30 IU; Welp et al., 1984, 5-10 IU; Chantaraprateep et al., 1986, 30 IU; Gall and Day, 1987, 40 IU; Alexopoulos et al., 1998, 10 IU; Cassar et al., 2005, 20 IU; Kaeoket, 2006, 10 IU; Hernandez et al., 2009, 10 IU; Gheller et al., 2011, 10 IU), with no consistent dose-response pattern. They are also reported to either decrease the variation in farrowing time (Holtz et al., 1983; Gall and Day, 1987; Balogh and Bilkei, 2003; Cassar et al., 2005), or show a numerical tendency to decrease variation that cannot be evaluated due to a lack of statistical analysis (Welp et al., 1984, 20-30 IU; Chantaraprateep et al., 1986, 10-20 IU), or have no effect (Chantaraprateep et al., 1986, 30 IU; Dial et al., 1987; Alexopoulos et al., 1998). Some authors have observed that higher doses are more effective (Welp et al., 1984; Dial et al., 1987), while others have found that lower doses work better

(Chantaraprateep et al., 1986). The reason is that oxytocin administration before farrowing can precipitate uterine inertia (see below).

Alternative methods to increase the synchrony of farrowing are reviewed by Guthrie (1985) and Cutler et al. (2006). They include parasympathomimetic drugs that stimulate uterine contraction, e.g. β-blockers and acetylcholine analogues, and drugs that delay parturition, including progestagens and prostaglandin synthesis inhibitors. Progestin antagonists have also been used to induce farrowing as an alternative to prostaglandins (Keister, 1989; Gaynor and Mann, 2004). Several agents may be given in combination, for example a prostaglandin may be administered at 0900 h to induce farrowing on the next day, followed by a progestagen at 1600 h to prevent overnight farrowing and then a combination of oxytocin and a β-blocker in the morning to stimulate parturition (Cutler et al., 2006).

3. Prostaglandin induction and piglet mortality

3.1. Intrapartum stillbirth

Intrapartum stillbirths are mostly caused by asphyxia (Randall and Penny, 1967 and 1968; Mota-Rojas et al., 2006a). Signs of perinatal asphyxia include increased pCO_2, glucose and lactic acid concentrations in the blood, decreased blood pH, and meconium

208 staining on the skin. Meconium staining occurs when hypoxia *in utero* increases
209 intestinal peristalsis and relaxes the anal sphincter causing the expulsion of meconium
210 into the amniotic fluid (Randall and Penny, 1967). Asphyxia also causes reduced viability
211 and vitality in piglets that survive the birth process (Randall, 1971; Herpin et al., 1996;
212 Trujillo-Ortega et al., 2007; Kammersgaard et al., 2011) and is responsible for a high
213 proportion of the deaths that occur shortly after birth (Randall, 1972). Dystocia is an
214 important risk factor for stillbirth (Jackson, 1975), so farrowing supervision is widely
215 recommended as a means to decrease the rate of stillbirth and improve piglet vitality
216 (Hughes, 1992; Zaleski and Hacker, 1993; Herpin et al., 1996; Lucia et al., 2002; Cutler
217 et al., 2006; Fangman and Amass, 2007).
218
219 Most studies have reported no effect of prostaglandins on farrowing duration (Bosc et al.,
220 1975; Hühn et al., 1977; Lynch and Langley, 1977; Černe, 1978; Humke et al., 1979;
221 Jainudeen and Brandenburg, 1980; Arbeiter et al., 1982, experiment 1; Butler and Boyd,
222 1983; Martin et al., 1985; Gall and Day, 1987; Stephens et al., 1988; Ko et al., 1989;
223 Hühn and Gey, 1999; Kaeoket, 2006; Sabuncu et al., 2008), but increased (Smith et al.,
224 1982) and decreased (Arbeiter et al., 1982, experiment 2) durations are occasionally
225 reported. The proportion of sows requiring farrowing assistance is not reported to be
226 affected (Dial et al., 1987; Holyoake et al., 1995; Alexopoulos et al., 1998; Gheller et al.,
227 2011), but there have been contradictory findings with respect to the frequency of
228 intrapartum asphyxia. Kaeoket (2006) observed no effect of prostaglandin administration
229 on d 113-114, 1-2 d before the expected farrowing date, on the degree of meconium
230 staining or umbilical cord morphology; but Sánchez-Aparicio et al. (2009) reported an

231 increased frequency of meconium staining, increased blood lactate and glucose
232 concentrations and a decreased mean viability score when prostaglandin was
233 administered 3 d before the expected farrowing date. The negative findings of Sánchez-
234 Aparicio et al. (2009) appear to be atypical and are probably due to a lack of farrowing
235 assistance (see below), since the great majority of studies that administered
236 prostaglandins between d 111 and d 114 have observed no effect of induction on the
237 number or proportion of stillbirths (Downey et al., 1976; Ehnvall et al., 1977; Lynch and
238 Langley, 1977; Walker, 1977; Boland et al., 1979; Jainudeen and Brandenburg, 1980;
239 Černe and Jöchle, 1981; Boland and Herlihy, 1982; Smith et al., 1982; Butler and Boyd,
240 1983; Martin et al., 1985; Dial et al., 1987; Gall and Day, 1987; Stephens et al., 1988,
241 experiments 2 and 3; Ko et al., 1989; Sellier et al., 1999; Le Cozler et al., 2002; Borges et
242 al., 2005; Kaeoket, 2006; Gunvaldsen et al., 2007; Straw et al., 2008; Sánchez-Aparicio
243 et al., 2009; Vanderhaeghe et al., 2010a and 2010b; Gheller et al., 2011), while a few
244 studies have reported a reduced stillbirth rate (Hammond and Matty, 1980; Černe and
245 Jöchle, 1981; Stephens et al., 1988, experiment 1). Alexopoulos et al. (1998) found that
246 farrowing duration and stillbirth rate were increased following administration on d 111,
247 but not when prostaglandin was given on d 112 or 113 (control sows farrowed naturally
248 on d 115).
249
250 In a large-scale survey of sows farrowing naturally with a mean herd gestation length of
251 115.4 d, an increased risk of stillbirth was observed when farrowing occurred on d 109-
252 111, or d 112-113, compared with farrowing on d 114-117 (Vanderhaeghe et al., 2011).
253 Other surveys also show that early natural farrowing is associated with an increased risk

of stillbirth (Zaleski and Hacker, 1993), particularly prior to about d 114 (Leenhouwers et al., 1999; mean herd gestation length 114.6 d) or d 115 (Sasaki and Koketsu, 2007; mean herd gestation length 115.3 d). Hence, although there is no evidence that induction *per se* increases the incidence of stillbirth, it is inadvisable to administer prostaglandins before d 113, causing farrowing to occur before d 114.

3.2. Birthweight

Low birthweight substantially increases the risk of pre-weaning mortality. Both absolute birthweight and birthweight relative to littermates are important (Le Dividich, 1999). Low absolute birthweight is associated with a poor thermoregulatory ability, due to increased heat loss, and with reduced vitality; while a low relative birthweight impairs the piglet's ability to compete at the udder. When a litter is born early, this risks a uniform reduction in the birthweights of the piglets.

The effect of prostaglandin induction on birthweight is variable. The day on which farrowing is induced is an important factor, with several studies showing that prostaglandin administration on d 110 (Jainudeen and Brandenburg, 1980), d 111 (Downey et al., 1976; Hansen, 1979; but not Martin et al., 1985), or d 113 (Straw et al., 2008) can reduce birthweight compared with a later induction date. This suggests that administration on d 110 or 111 may be too early to achieve a normal birthweight. The majority of studies in which prostaglandin was administered on d 110-111 have reported

277 a reduced birthweight compared with non-induced controls (Bosc et al., 1975; Downey et
278 al., 1976; Jainudeen and Brandenburg, 1980; but not Lynch and Langley, 1977), whereas
279 studies that gave the treatment on d 111-114 have more often reported no effect (Downey
280 et al., 1976; Lynch and Langley, 1977; Černe, 1978; Hühn et al., 1980, experiment 1;
281 Jainudeen and Brandenburg, 1980; Boland and Herlihy, 1982; Smith et al., 1982; Butler
282 and Boyd, 1983; Martin et al., 1985; Gall and Day, 1987; Gunvaldsen et al., 2007,
283 intramuscular injection) than a reduction in birthweight (Walker, 1977; Hühn et al., 1980,
284 experiment 2; Welp and Holtz, 1985; Gunvaldsen et al., 2007, vulvomucosal injection;
285 Olson et al., 2009).
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287
288 ***3.3. Live-born mortality***
289
290 The effect on live-born mortality is also variable, but most studies have reported either a
291 reduction in mortality (Downey et al., 1976; Hammond and Matty, 1980; Jainudeen and
292 Brandenburg, 1980, d 110; Černe and Jöchle, 1981), or no effect (Ehnvall et al., 1977;
293 Lynch and Langley, 1977; Černe, 1978; Boland et al., 1979; Hansen, 1979; Hühn et al.,
294 1980; Jainudeen and Brandenburg, 1980, d 112-113; Boland and Herlihy, 1982; Smith et
295 al., 1982; Butler and Boyd, 1983; Ko et al., 1989; Bilkei et al., 1995; Holyoake et al.,
296 1995; Ravel et al., 1996; Gunvaldsen et al., 2007). Sellier et al. (1999) observed
297 decreased mortality in Large White sows induced to farrow on average 0.8 d before their
298 expected date, but not in Piétrain sows induced to farrow 2.6 d early. Where an increase
299 in mortality was reported, prostaglandin treatment was mostly on d 110 or 111 (Bosc et

al., 1975; Lynch and Langley, 1977; Hansen, 1979; but not Walker, 1977). Decreased birthweight is likely to be a contributing factor when increased mortality occurs, as suggested by Walker (1977), but a relationship between these variables is not always apparent because there are other factors affecting the risk of mortality, particularly the extent to which farrowings are supervised.

3.4. Importance of supervision

The extent and quality of farrowing supervision is likely to be an important factor influencing the effect that induction has on the frequency of stillbirth and live-born mortality. The level of supervision provided may have affected the results of a number of studies. At one extreme, Hammond and Matty (1980) provided continual supervision during an 18 h period and timed the induction treatment to maximise the rate of night-time farrowing, when staff were employed to focus exclusively on assisting sows and piglets. They achieved a reduction in both stillbirths and live-born pre-weaning mortality, with a particularly large decrease in the frequency of crushing. At the opposite extreme, Sánchez-Aparicio et al. (2009) did not intervene at all in the birth process and obtained no improvement in the rate of stillbirths, while also reporting an increased frequency of intrapartum hypoxia and decreased vitality in surviving piglets. In more typical studies, additional personnel were not employed to supervise farrowings, but the usual farrowing house staff provided some level of assistance during normal working hours. Insofar as prostaglandin induction increased the proportion of farrowings that occurred during these

323 hours, the frequency of supervision would have tended to increase, although the quantity
324 and quality of supervision will have depended on the stockperson's other daytime duties.
325 Thus, where decreased mortality has been achieved, this has sometimes been attributed to
326 more farrowings occurring during working hours (Černe, 1978; Sellier et al., 1999).
327 Conversely, where there has been no improvement in mortality, this may have been due
328 to lack of attention by farrowing house staff (Straw et al., 2008). Welp and Holtz (1985)
329 observed that the frequency of stillbirths was decreased on one farm where farrowings
330 were carefully supervised, but increased on three other farms where they were not
331 (prostaglandin was administered on d 111-113; expected farrowing date not specified).
332 This means that parturition induction should be regarded primarily as a means to
333 facilitate the supervision of farrowing, rather than as a technique that can be used alone to
334 improve piglet survival. Further research is required to ascertain the level of supervision
335 that is necessary and to investigate whether farrowing can be safely induced on an earlier
336 date when careful supervision is provided.
337
338
339 ***3.5. Postpartum dysgalactia syndrome***
340
341 Postpartum dysgalactia syndrome (PDS or PPDS), formerly known as the mastitis-
342 metritis-agalactia (MMA) complex, is a common cause of hypogalactia (decreased
343 colostrum or milk production) in some herds. It usually develops within the first 3 d after
344 farrowing (Martineau et al., 1992; Jackson and Cockroft, 2007, p. 164) and may result in
345 significant piglet mortality if measures are not rapidly taken to provide the litter with

346 supplementary milk, either by giving the sow oxytocin injections to stimulate milk
347 ejection, by artificial feeding, or by fostering (English and Wilkinson, 1982; Martineau et
348 al., 1992).
349
350 A number of studies have reported that prostaglandin induction decreases the incidence
351 of MMA (Einarsson et al., 1975; Černe and Jöchle, 1981; Arbeiter et al., 1982; Smith et
352 al., 1982; Hühn, 1992; Hühn and Gey, 1999, experiment 1), or clinical signs predictive of
353 MMA (Hühn et al., 1980, experiment 1; Welp and Holtz, 1985). Others have reported no
354 effect, but the background incidence of MMA in the herd was low (Ehnvall et al., 1977;
355 Hühn et al., 1980, experiment 2; Boland and Herlihy, 1982; Alexopoulos et al., 1998;
356 Hühn and Gey, 1999, experiment 2). An exception is Hansen and Jacobsen (1976), who
357 observed no reduction in MMA in a herd with a high prevalence of the condition. A few
358 studies have reported an increased incidence of hypogalactia, but the validity of these
359 findings may be questionable: Ash and Heap (1973) made only a qualitative observation
360 that some treated sows developed hypogalactia; Papadopoulos et al. (2010) observed a
361 positive correlation between farrowing induction and the incidence of PDS in a survey of
362 farms, but indicated that this could have been because farms with PDS problems were
363 attempting to use induction as a preventive measure; and Devillers et al. (2007) reported
364 a decreased colostrum yield, but suggested that induction may have been confounded
365 with gestation length since only sows farrowing after d 114 were induced. The
366 mechanism by which prostaglandin administration reduces the prevalence of MMA or
367 PDS is not understood, but prostaglandin injection is known to stimulate colostrum
368 production (Diehl et al., 1974).

3.6. Piglet disease

Most studies indicate that the ability of piglets to obtain adequate passive immunity from colostrum is not impaired by induction. Milon et al. (1983) reported that prostaglandin administration on d 109 had no effect on piglets' serum IgG, IgA, or IgM concentrations on d 4, 12 or 42, despite a reduced colostrum intake, because the induced piglets tended to retain in their blood a greater proportion of the immunoglobulins that they ingested. The herd's average gestation length was not stated, but the farrowing dates for non-induced control sows ranged from d 111 to d 114, suggesting that prostaglandin was administered approximately 3-4 d prior to the expected farrowing date. Similarly, Olson et al. (2009) reported that treatment on d 113 or 114, 2 d prior to the expected farrowing date, had no effect on piglets' serum IgG concentrations at 24 h, faecal *Clostridium perfringens* levels at 24 h, or the risk of pre-weaning veterinary treatment; while Lynch and Langley (1977) found no effect of induction treatment on d 111-112, approximately 3 d prior to the expected farrowing date, on the number of scour days per litter, or on the severity of scouring. However, when Gunvaldsen et al. (2007) administered prostaglandin on d 114, 3 d prior to the average farrowing date of control sows, there was an increased risk of veterinary treatment, mainly for diarrhoea, arthritis and trauma. The authors suggested that induced piglets may have been less vigorous due to immaturity and hence may have ingested less colostrum but this explanation is not consistent with the findings of Milon et al. (1983).

392

393 An increased incidence of splayleg in litters treated on d 112 of gestation, but not on d
394 113 or 114, was described by Bölcskei et al. (1996; expected farrowing date not
395 specified), but Walker (1977) and Sellier et al. (1999) found no effect of prostaglandin
396 induction on d 111-113. It has been suggested that immaturity at birth could be the reason
397 (Ward, 1978; Bölcskei et al., 1996; Sellier et al., 1999), since litters affected by splayleg
398 have been found to have a shorter gestation period than unaffected litters (Sellier and
399 Ollivier, 1982).

400

401

402 ***3.7. Periparturient sow behaviour***

403

404 In addition to inducing parturition, $PGF_{2\alpha}$ administration triggers pre-farrowing nest-
405 building behaviour in sows (Gilbert, 2001). When sows are provided with adequate space
406 and access to straw, the behaviours observed resemble natural nest-building activities,
407 including locomotion, rooting, pawing the ground and carrying and arranging straw
408 (Widowski and Curtis, 1989; Widowski et al., 1990; Boulton et al., 1997; Burne et al.,
409 2000; Gilbert et al., 2000; Walton et al., 2002). In more confined housing systems,
410 restlessness, chewing, rooting and pawing are frequently reported (Diehl et al., 1974;
411 Robertson et al., 1978; Einarsson et al., 1981; Blackshaw and Blackshaw, 1982;
412 Widowski et al., 1990; Boulton et al., 1997). Some synthetic prostaglandin analogues
413 have an effect on sow behaviour that is similar to natural $PGF_{2\alpha}$ (Ash and Heap, 1973;
414 Downey et al., 1976), whereas others, such as cloprostenol, have a much reduced or

415 delayed effect (Holtz et al., 1979; Jainudeen and Brandenburg, 1980; Einarsson et al.,
416 1981; Silver et al., 1983; Widowski et al., 1990; Walton et al., 2002; Kaeoket, 2006). The
417 restlessness and related behaviours that are observed when $PGF_{2\alpha}$ is administered to
418 induce farrowing are short-lived (Ash and Heap, 1973), lasting from <1 h to several hours
419 (Downey et al., 1976; Robertson et al., 1978; Widowski and Curtis, 1989; Widowski et
420 al., 1990). A second bout of nest-building activity may occur closer to the time of
421 farrowing, coinciding with the normal peak of behaviour that is observed in untreated
422 sows (Widowski and Curtis, 1989; Widowski et al., 1990), but there are no reports that
423 nest-building persists during or after farrowing when it might be hazardous to the piglets.
424 $PGF_{2\alpha}$ has been found to have no effect on the sow's behaviour toward newborn piglets
425 (Gilbert et al., 2001, testing pseudopregnant gilts), or on crushing mortality (Walker,
426 1977; Jainudeen and Brandenburg, 1980).
427
428 A few authors have observed signs of abdominal discomfort in preparturient sows
429 following prostaglandin administration, such as arching of the back (Robertson et al.,
430 1978) or occasional vomiting (Downey et al., 1976), but these effects lasted <1 h and
431 other studies have reported that such behaviours did not occur (Einarsson et al., 1981;
432 Widowski and Curtis, 1989). Abdominal discomfort is more prevalent when $PGF_{2\alpha}$ is
433 experimentally administered to non-pregnant sows and young pigs than to sows due to
434 farrow (Blackshaw and Blackshaw, 1982; Widowski and Curtis, 1989).
435
436
437 ***3.8. Summary***

Overall, the induction of farrowing using prostaglandins may make piglets somewhat more vulnerable around the time of parturition, due to reduced maturity, but this effect is offset by an increased opportunity for farrowing supervision and perhaps a decreased risk of hypogalactia. The frequencies of stillbirth and live-born pre-weaning mortality are shown by most studies to be unaffected or decreased. Important factors affecting the level of mortality include the date of induction and the degree of supervision provided. We recommend administering prostaglandin no earlier than d 113. Given that the average natural gestation length in the studies cited was 115 d, d 113 corresponds to 2 d prior to the expected date of farrowing. Some studies have achieved good results with earlier induction, particularly when farrowing was carefully supervised (e.g. Holyoake et al. 1995), but the effect of supervision on the optimal date for induction has not been investigated. Several authors have emphasised the importance of keeping accurate gestation records to ensure that individual sows within the herd are not induced too early (Jainudeen and Brandenburg, 1980; Pressing, 1992; Cutler et al. 2006), as well as the importance of supervision (Dial et al., 1987; Pressing, 1992). In North America, commercial prostaglandin products are licensed for administration 2 or 3 d prior to the expected farrowing date (Gunvaldsen et al., 2007; Olson et al., 2009), which corresponds to d 112-113 in many herds.

4. Oxytocin administration and piglet mortality

461 The administration of oxytocin 20-24 h after prostaglandin is intended to bring about a
462 prompt onset of parturition and thereby increase the proportion of farrowings that occur
463 during normal working hours. However, as stated above, its effects on the timing of
464 parturition are inconsistent. It also has unpredictable and sometimes negative effects on
465 the progress of farrowing. Some studies have observed that the use of oxytocin can
466 substantially increase the proportion of sows that require assistance (Welp et al., 1984;
467 Chantaraprateep et al., 1986), while others have found no effect (Dial et al., 1987;
468 Alexopoulos et al., 1998; Cassar et al., 2005; Gheller et al., 2011) and there is no
469 consistent effect of dose (Welp et al., 1984; Chantaraprateep et al., 1986; Dial et al.,
470 1987). The frequency of intervention can be very high, ranging from 10% to 52% of
471 farrowings in these studies.
472
473 Despite the fact that oxytocin stimulates uterine contraction, few studies have reported a
474 reduction in the duration of farrowing when it is administered prior to parturition (only
475 Stephens et al., 1988), most having found no effect (Holtz et al., 1983 and 1990; Bilkei
476 and Krüger, 1993; Bilkei Papp, 1994; Alexopoulos et al., 1998; Cassar et al., 2005;
477 Kaeoket, 2006; Gheller et al., 2011). Kirkwood and Thacker (1995) reported that
478 oxytocin decreased the time to birth of the first piglet compared with controls that
479 received prostaglandin only, but increased the mean birth interval due to the development
480 of dystocia in several sows. Welp et al. (1984) also observed that sows given oxytocin
481 often experienced a delay after of the birth of their first or second piglet and they
482 suggested that this might be due to uterine spasm. Dial et al. (1987) noted that some sows

483 which developed uterine inertia after oxytocin treatment required repeated doses of
484 oxytocin to expel a series of retained piglets.
485
486 Gilbert (1999) has argued that the most probable reason for this unpredictable occurrence
487 of dystocia is that the injection of oxytocin sometimes occurs before the cervix has
488 completely dilated. Individual sows differ in the rate at which they respond to
489 prostaglandin treatment and hence may also vary in the state of their cervix when
490 oxytocin is administered. Those with an open cervix will show accelerated birth, but
491 those with incomplete opening will experience dystocia. Delivery of the first piglet may
492 not be possible. If it does occur, this will be painful and might cause release of
493 adrenaline, inhibiting further uterine contractions (Cassar et al., 2005). When oxytocin
494 administration is delayed until after birth of the first piglet, by which time cervical
495 dilation is presumably complete, dystocia may be avoided (Mota-Rojas et al., 2002),
496 although some studies still report an increased risk of dystocia, perhaps due to the
497 saturation of uterine oxytocin receptors (Alonso-Spilsbury et al., 2004; Mota-Rojas et al.,
498 2006b).
499
500 Surprisingly, most studies have reported no adverse effect of oxytocin administration
501 prior to farrowing on the frequency of stillbirths (Holtz et al., 1983; Chantaraprateep et
502 al., 1986; Dial et al., 1987; Gall and Day, 1987; Stephens et al., 1988; Bilkei Papp, 1994;
503 Kirkwood and Thacker, 1995; Alexopoulos et al., 1998; Cassar et al., 2005; Kaeoket,
504 2006; Gheller et al., 2011), the incidence of intrapartum asphyxia (Wehrend et al., 2005;
505 Kaeoket, 2006). This might be due to a high level of farrowing supervision. Hernandez et

al. (2009) reported a numerical reduction in the frequency of stillbirths, whose veracity cannot be established in the absence of statistical analysis, and attributed this tendency to an 'optimum staffing rate'. Some authors have argued that manual assistance or additional oxytocin treatments are required to avoid an increased risk of stillbirth (Dial, 1984) and that oxytocin should not be used in induction programmes unless sows can be continually supervised (Kirkwood and Aherne, 1998; Kirkwood, 1999). Others have recommended the use of low dosages to reduce the risk of dystocia (Cowart, 2007), but the advantage of using a low dose (5-10 IU) is not very clear (Welp et al., 1984; Chantaraprateep et al., 1986). Bilkei and Krüger (1993) achieved reductions in stillbirths and early postnatal mortality using low doses (2-10 IU), but did not compare these with higher doses. Clark and Bilkei (2002) have proposed that oxytocin should be administered earlier than the normal 20-24 h after prostaglandin and in repeated low doses, to stimulate increased endogenous prostaglandin synthesis. They found that the administration of 10 IU oxytocin either 6 h, 6 and 12 h, or 6, 12 and 18 h after prostaglandin injection decreased farrowing duration and stillbirth rate, while increasing the synchrony of farrowing, compared with prostaglandin treatment alone.

Kirkwood et al. (1996) and Gilbert (1999) have proposed that oxytocin should not be used for the induction of farrowing, but reserved for treating cases of dystocia once farrowing has begun. However, it might be that certain treatment regimens, such as the one proposed by Clark and Bilkei (2002), are safe and effective. Further research is needed to follow up this approach.

529 Oxytocin administration prior to farrowing has been found to have no effect on the
530 incidence of MMA in sows (Alexopoulos et al., 1998). Nor does it influence pre-
531 farrowing nest-building behaviour (Kaeoket, 2006).
532
533 Several studies have investigated the use of carbetocin, a longer-acting synthetic
534 analogue of oxytocin, as a safer and more effective alternative to oxytocin. Routine
535 administration of carbetocin 24 h after prostaglandin treatment has been reported to cause
536 farrowing to occur sooner than oxytocin (Gericke and Hühn, 1990) and to decrease
537 farrowing duration (Gericke and Hühn, 1990, in multiparous sows but not in gilts;
538 Gheller et al., 2011), while having no adverse effect on the frequency of farrowing
539 assistance required (Gheller et al., 2011), or on piglet blood pH as an indicator of
540 asphyxia (Wehrend et al., 2005). It has had inconsistent effects on piglet survival, with
541 Udluft and Bostedt (2004) reporting a decreased stillbirth rate (not clear that it was
542 statistically significant), but Gheller et al. (2011) finding no effect on the frequency of
543 stillbirth compared with oxytocin. Comparing the administration of carbetocin 24 h after
544 prostaglandin treatment with the use of prostaglandin alone, carbetocin has been reported
545 to cause farrowing to occur sooner (Leike and Hühn, 1992) and to either reduce (Leike
546 and Hühn, 1992) or have no effect on (Hühn and Gey, 1999) farrowing duration, while
547 having no effect on the frequency of manual assistance required or the stillbirth rate
548 (Leike and Hühn, 1992). It has been found to synchronise farrowing sufficiently to
549 eliminate the need for supervision on weekends (Leike and Hühn, 1992). Carbetocin
550 therefore appears to be a promising alternative to oxytocin.
551

552

553 5. Conclusions

554

555 Induction of farrowing with prostaglandins on d 111-114 increases the synchrony of
556 farrowing, facilitating farrowing supervision, early fostering and 'all in, all out'
557 management of the farrowing house. Prostaglandin administration on d 112-114
558 generally has no adverse effects on farrowing duration, frequency of dystocia, stillbirth
559 rate, birthweight, live-born mortality, PDS, piglet serum immunoglobulin levels, or piglet
560 morbidity; and administration on d 113-114 has no effect on the prevalence of splayleg.

561

562 Administration on d 111 can lead to adverse effects on stillbirth rate, birthweight and
563 live-born mortality, while administration on d 112 may increase the prevalence of
564 splayleg. Moreover, in view of the increased risk of stillbirth when sows farrow naturally
565 before d 114, it is generally advisable not to administer prostaglandins before d 113.
566 Hence, prostaglandin induction may be considered to be a low risk procedure when
567 treatment occurs on d 113 or later. Farrowing supervision is likely to be important to
568 reduce the levels of stillbirth and live-born mortality. Because the average herd gestation
569 length in the studies cited was 115 d, we therefore recommend that prostaglandin should
570 be administered no earlier than 2 d prior to the expected farrowing date. It is possible to
571 achieve good results with an earlier induction date, particularly if farrowings are carefully
572 supervised, but further research is required to ascertain the level of supervision that is
573 needed and to establish how much earlier farrowing can safely be induced.

574

575 Some studies have reported a beneficial effect of prostaglandin induction on stillbirth and
576 live-born mortality. This is probably due to an increased level of farrowing supervision.
577 Moreover, the incidence of PDS is decreased in herds with a high prevalence of this
578 condition.
579
580 The routine administration of oxytocin 20-24 h after prostaglandin treatment is intended
581 to further increase the synchrony of farrowing, but has had inconsistent effects. Some
582 studies have reported an increased incidence of dystocia, which might be due to the
583 stimulation of contractions before the cervix has fully dilated, or uterine fatigue. Stillbirth
584 rate is generally unaffected. Several studies suggest that low doses, or earlier
585 administration, may be effective at decreasing stillbirth rate, but more research is required
586 before the use of oxytocin prior to parturition can be recommended. Carbetocin, a long-
587 acting analogue of oxytocin, appears to be a promising alternative.
588
589 Prostaglandin induction has been used successfully in commercial practice for many
590 decades (English and Wilkinson, 1982). It may be used routinely for all sows in the herd,
591 or selectively for those which have not farrowed by a certain date. The latter approach
592 reduces the risk of inducing some sows too early (Pressing, 1992; Lawlor and Lynch,
593 2005), whilst at the same time preventing overly long gestation periods that may be
594 associated with an increased risk of PDS (Hühn, 1992; Hühn and Gey, 1999). We
595 recommend that prostaglandin induction is used in conjunction with a programme of
596 farrowing supervision, where a skilled attendant is continually present to assist dystocic

sows and provide care for small and weak piglets, because a combination of induction and supervision can substantially decrease piglet mortality (Kirkden et al., in press).

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