TETTE VAN DER LENDE

IMPACT OF EARLY PREGNANCY ON PRENATAL DEVELOPMENT IN THE PIG

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Proefschrift

ter verkrijging van de graad van

doctor in de landbouwwetenschappen,

op gezag van de rector magnificus,

dr. H.C. van der Plas,

in het openbaar te verdedigen

op woensdag 11 januari 1989

des namiddags te vier uur in de aula

van de Landbouwuniversiteit te Wageningen

STELLINGEN

1. De bij even oude, sferische varkensblastocysten gevonden variatie in diameter levert slechts beperkte informatie op over variatie in ontwikkeling.
   Kronnie, G. te, Boerjan, M.L. en Leen, T., 1988. J. Reprod. Fert., Abstract Series 1: 59.

2. Bij het varken wordt de aard van de verdeling van geboorte-gewichten in het merendeel van de tomen gedurende de eerste 35 dagen van de dracht bepaald.
   Dit proefschrift.

3. Zeugen die opnieuw berigheidsverschijnselen vertonen rond dag 28 na inseminatie zijn ten minste 12 dagen drachtig geweest.
   Meulen, J.v.d., Helmond, F.A. en Oudenaarden, C.P.J., 1988. J. Reprod. Fert., 84:157-162.

4. De door Murray et al. in twee onafhankelijke experimenten gevonden positieve invloed van uteriene presensibilisatie tegen sperma-antigenen op de worpgrootte bij het varken, rechtvaardigt nader onderzoek onder nederlandse praktijk-omstandigheden.
   Murray, F.A., Grifo, A.P. en Parker, C.F., 1983. J. Anim. Sci., 56: 895-900.
   Murray, F.A. en Grifo, A.P., 1986. J. Anim. Sci., 62: 187-190.

5. Bij het analyseren van onderzoeksresultaten gaat informatie verloren omdat veelal onvoldoende in gedachte wordt gehouden dat een meting die sterk afwijkt van de overigen in een reeks pas als uitbijter mag worden aangeduid als is komen vast te staan dat er geen aanwijsbare oorzaak voor deze afwijking is.

6. De ontwikkeling van nieuwe voortplantingstechnieken gecombineerd met een verruiming van de wetgeving ten aanzien van ouderschap zal onherroepelijk leiden tot een verzakelijking van de humane procreatie.

7. Het gebruik van de kreet "de aalparasiet" in plaats van de term "zwemblaasnematode van aal" is meer een reflexie van de stand van zaken bij het parasitologisch onderzoek van aal dan van het belang van deze nematode voor de aalproductie.

8. De stelling dat een proefdier dat in het laboratorium wordt onderworpen aan het ergste, meest vervelende experiment nog altijd beter af is dan een soortgenoot in de natuur, getuigt van een gebrek aan kennis van de experimenten die worden uitgevoerd of van een vertekend beeld van de natuur.
   Rörsch, A.,1988. Advances in animal breeding:proceedings of the world symposium in honour of professor R.D. Politiek.

9. In het licht van de achtergrond en betekenis van de schaap-geit chimaera ("scheit" of "gaap") is het verwijzen naar deze chimaera teneinde daarmee de dierlijke biotechnologie in diskrediet te brengen, onterecht.

10. Struisvogelpolitiek ten aanzien van bodemvervuiling kan ons de kop kosten.

11. In tegenstelling tot scharrelkippen scharrelen scharrelvarkens niet.

T. van der Lende.
Impact of early pregnancy on prenatal development in the pig.
11 januari 1989.

VOORWOORD

Dit proefschrift is tot stand gekomen dankzij een bijdrage van velen. Op deze plaats wil ik hiervoor een woord van dank uitbrengen.

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CONTENTS

INTRODUCTION

In the pig on average 20-40% of all embryos dies before day 35 of pregnancy (for a review, see Pope and First, 1985). Embryonic loss reduces sow productivity through its effect on pregnancy rate and litter size, and thus on number of piglets born per sow per year. This has been recognized for many decades and has initiated numerous studies to determine the factors which influence the extent of embryonic mortality and the mechanism(s) underlying this loss. As far as our knowledge about the latter is concerned little progress has been made. However, these studies have largely contributed to our knowledge concerning the regulation and mechanism of early pregnancy in the pig.

There is some evidence that the development of day 28 conceptuses (embryos and their extra-embryonic membranes) is related to the extent of embryonic loss during the first four weeks of pregnancy (Lutter et al., 1981). This indicates that factors which are associated with embryonic mortality might also be associated with embryonic development. The uterus and its secretion products might have this role since embryos depend on uterine secretion products for their development and they can only survive if the uterine environment develops synchronous with their own development (Dziuk, 1987; Roberts and Bazer, 1988). Whether the development of conceptuses during the foetal stage is also related to the embryonic mortality rate has not been investigated.

Apart from the reproductive losses during pregnancy, considerable losses are due to preweaning piglet mortality. The variation in birthweight within litters is an important determinant of the preweaning death risk, especially in litters with a relatively low average birthweight (English and Smith, 1975). One component of the variation in birthweight within a litter might be the within-litter weight distribution. Although it is generally assumed that the within-litter weight distribution is normal (Gaussian), Royston et al. (1982) have provided evidence, later confirmed by Wootton et al. (1983), that a discrete subpopulation of one or more intrauterine growth retarded piglets

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can be found in approximately one-third of all litters. There is also evidence that the within-litter variation in developmental stage of embryos already exists during the preimplantation stage of pregnancy (Anderson, 1978; Wright and Grammer, 1980; Wright et al., 1983; Richter and Elze, 1986; Elze et al., 1987; Papaioannou and Ebert, 1988; Te Kronnie et al., 1988). This variation can probably be reduced through a mechanism of selective mortality of the less developed embryos which operates in the uterus at the time of maternal recognition of pregnancy (Pope et al., 1982a; Pope et al., 1986a, 1986b; Morgan et al., 1987a, 1987b). These results elicit the question whether the within-litter weight distribution at birth is determined during early pregnancy. If so, it might be associated with embryonic mortality.

The aims of the present study were to investigate:

1. the possibility to create a model in order to study the role of the uterus and its secretion products as determinants of embryonic mortality and embryonic development and to use this model to study the relationship between embryonic mortality and prenatal development,

2. the relationship between the embryonic mortality rate and development of the surviving conceptuses at the end of the embryonic stage of pregnancy (day 35) and during the subsequent foetal stage of pregnancy, and

3. the relationship between the within-litter weight distribution and the embryonic mortality rate as well as the consequences of the within-litter weight distribution for post-natal piglet survival and growth until weaning.

A brief review of the literature concerning early pregnancy in the pig is given in chapter 2. In chapter 3 an experiment is described in which it was attempted to create a model to study the role of the uterus and its secretion products as determinants of embryonic mortality and embryonic development. In chapter 4 the relationship between conceptus development and uterine development on day 35 of pregnancy and embryonic mortality during the first 35 days of pregnancy is described. A comparable study concerning the foetal and placental development in relation to prenatal mortality is described in chapter 5. Chapter 6 contains the results of a study concerning the within-

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litter weight distribution at the early foetal stage of pregnancy and at birth as well as its relationship with prenatal mortality. The consequences of the within-litter weight distribution for the death risk and growth rate of piglets during the suckling period are described in chapter 7. Chapter 8 is a general discussion of the results and contains the conclusions.

CHAPTER 2

EARLY PREGNANCY IN THE PIG: A REVIEW OF THE LITERATURE

2.1 Chronological description of the early pregnancy in the pig

Porcine ova are fertilized in the ampulla of the oviduct, near the
ampullary-isthmic junction (Hunter, 1977). The embryos enter the uterus
within 2 or 3 days after fertilization, which is relatively rapid in
comparison to other species (Pomeroy, 1955; Perry and Rowlands, 1962;
Oxenreider and Day, 1965). By this time they have reached the 3 or 4 cell-
stage, but they might even be in the 8 cell-stage (Perry and Rowlands,
1962; Oxenreider and Day, 1965). On day 6 of pregnancy the embryos, which
are by this time in the early blastocyst stage, hatch from the zona
pellucida (Perry and Rowlands, 1962; Hunter 1977). The latter is a complex
extracellular glycoprotein matrix that is formed around each oocyte during
follicular development (Dunbar and Bundman, 1987).

Between day 7 and day 12 after fertilization the embryos migrate from
the oviductal to the cervical end of the uterine horns to redistribute
themselves subsequently over the full length of both horns (Dhindsa et al.,
1967; Dziuk, 1985). This process of spacing is often accompanied by trans-
uterine migration, even if the distribution of ovulations over both ovaries
has been equal (Dziuk et al., 1964). According to Pope et al. (1982b) both
oestradiol-17ß and histamine are involved in intrauterine migration of
embryos.

Until day 11 or 12 the embryos are spherical. Their diameter increases
during this period up to 10 mm (Stroband et al., 1984). Subsequently the
embryos start to elongate (Perry and Rowlands, 1962; Anderson, 1978). This
elongation is mainly due to cell reorganization and not to hyperplasia
(Geisert et al., 1982b). Almost simultaneously with the elongation the
embryos start to synthesize and secrete oestrogens (Heap et al., 1979;
Gadsby et al., 1980; Bazer et al., 1982; Geisert et al., 1982a). These
oestrogens are thought to be important for the maintenance of the corpora
lutea and thus the continuation of progesterone secretion (Bazer and

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Thatcher, 1977; Flint, 1981; Flint et al., 1983). Because luteal progesterone is essential during the whole period of pregnancy, this embryo mediated prolongation of the lifespan of the corpora lutea, also called maternal recognition of pregnancy, is essential for continuation of pregnancy. Besides this, embryonic oestrogens are also important because they stimulate the secretion of proteins from the endometrium (Geisert et al., 1982a).

During or shortly after elongation the embryos start to attach to the luminal epithelium of the endometrium. The blastocysts, each with a length of up to 100 cm by the end of elongation (day 14), follow the endometrial folds. Each blastocyst occupies only a relatively short length of the uterus (Perry and Rowlands, 1962).

The allantois first appears at about day 14 of pregnancy and grows rapidly in size, ultimately filling the majority of space within the chorion (trophoblastic ectoderm and mesoderm). The amnion is formed from dorsal folds of the somatopleure (ectoderm and mesoderm). Its formation is complete by day 18 of pregnancy when these folds have fused over the dorsal surface of the embryonic disc (Steven, 1975). By this time the embryo contains five to six pairs of somites (Perry and Rowlands, 1962). After the first contact between the vascular mesoderm covering of the allantois and the chorion at approximately day 19 of pregnancy, the chorion becomes extensively vascularised by allantoic blood vessels. The vascularization is maximal by day 30 of pregnancy (Steven, 1975). During the time of vascularization of the chorion the areolae start to develop on the chorion opposite the orifices of uterine glands, but only after intimate contact between allantois and chorion has been established. The areolae are fully differentiated by day 35 of pregnancy (Brambel, 1933).

2.2 Embryonic mortality

2.2.1 Incidence

In the pig the loss of fertilized oocytes during the first 30 to 40 days of pregnancy is referred to as embryonic mortality. It is well documented that on average approximately 30% of the potential embryos are lost during this period (Hanly, 1961; Hughes and Varley, 1980; Flint et al., 1982; Pope

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and First, 1985; Bolet, 1986). This is almost similar to the embryonic mortality rate found for sheep (Bolet, 1986) and cattle (Sreenan and Diskin, 1986).

Several genetic and environmental factors have been associated with the incidence of embryonic mortality. It has long been assumed that embryonic mortality is mainly due to embryonic genetic abberations. This was promoted by a publication by Bishop (1964) in which it was hypothesized that embryonic mortality must be due to chromosomal mutations during gametogenesis, fertilization or the first cleavage divisions of the fertilized oocyte. Recent cytogenetic analyses of day 3 and day 4 morulae (Van der Hoeven et al., 1985) and day 10 embryos (McFeely, 1967; Dolch and Chrisman, 1981; Long and Williams, 1982) have shown that lethal chromosomal mutations like polyploidy (e.g. 3N) and aneuploidy (e.g. 2N-1 or 2N+1) hardly occur in the pig. According to Bolet (1986) identifiable genetic factors (chromosonal abnormalities and genes with a major effect or playing a role as markers) do not fundamentally account for the basal loss, although they may lead to a considerable increase in embryonic mortality in some cases.

Breed differences in embryonic mortality rate have been reported (Young et al., 1976; Bolet, 1986; Bolet et al., 1986). Within a breed the embryonic mortality rate can be influenced by the boar (Swierstra and Dyck, 1976; Martin and Dziuk, 1977), the length of the period between parturition and insemination (Svajgr et al., 1974; Varley and Cole, 1976), the time of insemination relative to the time of ovulation (Hunter, 1967; Helmond et al., 1986), the feeding level during early pregnancy (Gossett and Sorensen, 1959; Haines et al., 1959; Goode et al., 1965; Tassell, 1967; den Hartog and van Kempen, 1980; Cole, 1982) and the occurrence of stress during early pregnancy (Schnurrbusch and Elze, 1981).

2.2.2 Within-litter variation in early embryonic development as a cause of embryonic mortality

In the pig within-litter variation in developmental stage of embryos is already evident during the preimplantation period (Anderson, 1978; Wright and Grammer, 1980; Wright et al., 1983; Richter and Elze, 1986; Elze et al. 1987; Papaioannou and Ebert, 1988; Te Kronnie et al., 1988). During this

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period and the subsequent period of implantation the histomorphology of the endometrium and the amount and composition of the uterine secretion products change almost continuously (Knight et al., 1973; Johnson et al., 1988; Van der Lende et al., 1988). As early pregnancy progresses the embryos become more dependent on the uterine environment (Heap et al., 1979), each embryonic developmental stage allowing only a relatively small deviation from the required uterine stage (Wilmut et al., 1985; Dziuk, 1987). If the within-litter variation in developmental stage exceeds a certain limit, the asynchrony of some embryos with the prevailing uterine stage will be too large to allow a normal development, resulting in embryonic death (Wilmut et al., 1985; Pope et al., 1986a, 1986b; Richter and Elze, 1986). Although this mechanism might operate throughout early pregnancy, the tolerable asynchrony might vary during early pregnancy. Evidence for this comes from the work of Pope et al. (1982a) in which day 5 and day 7 embryos were transferred together into day 6 non-pregnant recipients. The recipients were slaughtered on day 11 or between day 60 and 70 of pregnancy. No difference in survival rate was found on day 11, but between day 60 and 70 more foetuses from day 7 embryos than from day 5 embryos were found. These results were substantiated by Pope et al. (1986b) in an experiment in which day 6 embryos were transferred into day 7 recipients and day 7 embryos into day 6 recipients. The recipients were slaughtered either on day 12 or 13 or on day 30. No difference in survival rate was found on day 12 or 13, but the variation in development was much higher in the day 7 recipients with day 6 embryos than in the other group. This increased variation resulted in an increased embryonic mortality between day 12/13 and day 30. Pope et al. (1982a) suggested that the more developed embryos start to synthesize oestrogens earlier than less developed embryos, thus inducing a uterine environment which might be embryocidic for the retarded embryos. Evidence to substantiate this hypothesis has been presented by Pope et al. (1986a) and Morgan et al. (1987a, 1987b). The results of the latter authors indicate that the mortality of the retarded embryos most probably occur between day 12 and day 16 of pregnancy, i.e. at the onset of implantation.

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CHAPTER 3

EFFECT OF GROWTH RETARDATION EARLY IN LIFE ON THE EMBRYONIC DEVELOPMENT AND EMBRYONIC MORTALITY RATE DURING FIRST PREGNANCY

3.1 Introduction

The role of the uterus and its secretions as determinants of embryonic development and embryonic mortality are poorly understood. If the development of the uterus of gilts could be influenced in such a way that these gilts subsequently have increased embryonic mortality rates and/or embryos which develop abnormal, then a model will be available to study this role. The same model can also be used to study the impact of early pregnancy on subsequent prenatal development.

The porcine uterus is largely undifferentiated at birth. The differentiation, which is accompanied by various well described histomorphological changes, takes place during the first 12 weeks after birth (Hadek and Getty, 1959; Bal and Getty, 1970; Erices and Schnurrbusch, 1979; Schnurrbusch et al., 1980; Dyck and Swierstra, 1983). The uterine glands, which are absent at birth, appear within two weeks after birth (Hadek and Getty, 1959; Bal and Getty, 1970; Erices and Schnurrbusch, 1979; Schnurrbusch et al., 1980) and are fully developed by 12 weeks after birth (Bal and Getty, 1970).

The purpose of the present experiment is to investigate the possibility to influence the uterine development in gilts in order to create a model as mentioned before. The effect of a severe growth retardation early in life on the early post-natal uterine development and its consequences for the embryonic mortality rate and embryonic development are described.

3.2 Materials and methods

The experiment was conducted with three experimental groups, which differed as far as treatment during the first 80 days after birth are

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concerned. The piglets of two groups were weaned early and fed either unrestricted or restricted. The piglets of the third group remained with the sow together with their male littermates until they were weaned on day 35 after birth. These groups will be refered to as unrestricted fed group, restricted fed group and control group, respectively.

3.2.1 Animals

For the unrestricted fed group and restricted fed group 69 female piglets from 13 Dutch Landrace litters were weaned between 15 and 40 hours after birth. Before weaning the piglets were allowed to ingest colostrum. Littermate piglets were randomly allotted to an unrestricted or restricted feeding scheme. The number of piglets in these two groups was 35 and 34, respectively. The control group consisted of 38 female piglets from 9 Dutch Landrace litters.

At an age of 80 days 8 piglets from the unrestricted fed group, 8 piglets from the restricted fed group and 10 piglets from the control group were slaughtered. The piglets from the unrestricted fed and the restricted fed group were pairwise littermates. The remaining animals were checked for oestrus daily from day 180 onwards, using a vasectomized boar. Gilts which had not shown oestrus spontaneously by the time they were approximately 390 days old, were intramuscularly injected with 400 I.U. pregnant mare serum gonadotrophin and 200 I.U. human chorionic gonadotrophin (PG600[R], Intervet B.V., Boxmeer, the Netherlands) in order to induce oestrus.

All gilts showing oestrus were artificially inseminated once on the first day of their second or third oestrus. Gilts returning to oestrus were reinseminated once. For all inseminations semen of Dutch Landrace A.I. boars was used. Gilts not responding to oestrus induction and gilts failing to conceive after two inseminations were slaughtered in order to examine their reproductive tracts. Pregnant gilts were slaughtered either on day 34, 35 or 36 after insemination.

3.2.2 Housing

The early weaned piglets were housed individually in battery cages for 16 days after weaning. The ambient temperature was kept at 35°C for the

first few days after weaning and thereafter gradually lowered to approximately 20°C. Between day 16 and day 35 early weaned littermates from the same experimental group were housed together in battery cages. The piglets from the control group stayed in the farrowing house with the sow until weaning on day 35. From day 35 onwards all piglets were kept under the same conditions and housed in pens with a concrete floor. Littermates from the same experimental group were housed together. The gilts were housed individually on partially slatted concrete floors after insemination.

3.2.3 Feeding

The early weaned piglets were fed four times on the first day after weaning, three times a day until day 8 and thereafter two times a day. The unrestricted fed piglets were fed semi-ad libitum from weaning until day 35 and ad libitum thereafter until day 80. During this period the restricted fed piglets were fed at a level which was expected to allow 50-60% of the bodyweight gain of their unrestricted fed littermates.

From weaning until day 8 the early weaned piglets received condensed milk. Between day 9 and 13 milk was gradually replaced by a pre-starter diet which was fed thereafter until day 27. Between day 28 and 34 after weaning the pre-starter diet was gradually replaced by a starter diet. All piglets, including the weaned control piglets, received this starter diet until day 80. All gilts received a sow diet from day 80 onwards. The starter diet was gradually replaced by this ration. Between day 80 and day 180 they were fed ad libitum, thereafter they received approximately 2.0 kg per gilt per day until the experiment was terminated.

The gross energy, dry matter content and crude protein content of the condensed milk, pre-starter diet, starter diet and sow diet are shown in table 3.1.

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Table 3.4 shows the correlation coefficients between the uterine parameters for each of the experimental groups. Within the unrestricted fed and control group all correlation coefficients were significant (p<0.05) and higher than 0.70. In the restricted fed group all correlation coefficients were lower than the comparable coefficients in both other groups. Except for the correlation coefficients between uterine weight and thickness of myometrium and endometrium, they were not significant (p>0.05).

3.3.3 Development and fertility of the remaining gilts

From the group of 66 gilts which were still in the experiment after day 80, ultimately 50 (75.8%) were slaughtered while pregnant. The remaining 16 gilts were culled for various reasons, as shown in table 3.5. In the unrestricted fed, restricted fed and control group 21, 18 and 23 gilts, respectively, had no obvious abnormalities. From these 15 , 12 and 23, respectively, became pregnant with an average of 1.29, 1.08 and 1.09 inseminations, respectively. Although the pregnancy rate in the unrestricted fed and restricted fed group (71.4% and 66.7%, respectively) was lower than in the control group (100%), these values did not differ significantly from the overall average (80.6%; χ^2=1.73, p>0.05).

Table 3.5 Overview of the fate of the gilts which remained in the experiment after day 80.

	Unrestricted fed group	Restricted fed group	Control group
Number of gilts	22	20	24
Culled -cripple	-	-	1
-intersex	-	1	-
Normal pregnant	13	11	21
Induced -no response	5	5	-
-not pregnant	1	1	-
-pregnant	2	1	2
Abnormal genital tract (not pregnant)	1	1	-

All results presented hereafter are based on the data collected for the

50 gilts which were pregnant at slaughter. At an age of 220 days still 9 to 23% of the corrected sum of squares for body measurements could be attributed to differences between experimental groups. The mean bodyweight and body measurements are shown in table 3.6. The mean bodyweight in the restricted fed group was still significantly lower than that in both other groups. The average values for the body measurements of these gilts were also always lower than those in both other groups, but the differences were not always significant. Neither the bodyweight nor the body measurements differed significantly between the unrestricted fed and control group.

Table 3.6 Bodyweight and body measurements at an age of 220 days.

	Unrestricted fed group		Restricted fed group		Control group	
	mean	s.e.m	mean	s.e.m	mean	s.e.m
Body weight (kg)	90.3^a	3.8	75.7^b	4.3	94.4^a	3.1
Body length (cm)	92.5^{ab}	1.5	89.0^b	1.7	93.6^a	1.2
Height at shoulders (cm)	61.0^a	0.8	57.7^b	0.9	61.8^a	0.7
Height at croup (cm)	71.3^{ab}	1.0	68.4^b	1.1	72.0^a	0.8
Width at shoulders (cm)	28.8^{ab}	0.6	27.3^b	0.7	29.3^a	0.5
Width at croup (cm)	29.5^{ab}	0.5	28.3^b	0.6	30.4^a	0.4
Heart girth (cm)	96.3^a	1.5	90.3^b	1.7	98.0^a	1.2
Backfat thickness (mm)	9.7^a	0.6	7.9^b	0.7	10.7^a	0.5

a,b: means with a different superscript differ significantly ($p<0.05$).

The average age at first oestrus (table 3.7) was extraordinary high in each of the three experimental groups. The difference between the unrestricted fed and control group was significant ($p<0.05$). The average age at first oestrus in the restricted fed group was intermediate and not significantly different from that in both other groups. The weight and backfat thickness at first oestrus, also shown in table 3.7, did differ significantly ($p<0.05$) between the restricted fed group and both other

groups. Between the unrestricted fed and control group these differences were not significant. Correction for differences in age at first oestrus did not affect the differences in backfat thickness, but did affect the differences in weight as can be seen from table 3.7. The difference between the unrestricted fed and control group was largely reduced. The differences between the restricted fed group and both other groups remained significant (p<0.05).

Table 3.7   Average age, weight and backfat thickness of the gilts at their first oestrus.

	Unrestricted fed group		Restricted fed group		Control group	
	mean	s.e.m	mean	s.e.m	mean	s.e.m
Age (days)	332.1^a	9.1	318.5^{ab}	10.2	301.7	7.4
Weight (kg)	136.7^a	3.8	116.8^b	4.3	129.0^a	3.1
Backfat thickness (mm)	14.3^a	0.7	11.3^b	0.8	14.7^a	0.6
Age corrected weight	132.2^a	3.5	115.6^b	3.7	132.5^a	2.8
Age corrected backfat thickness	14.3^a	0.7	11.2^b	0.8	14.8^a	0.6

a,b: means with a different superscript differ significantly (p<0.05).

As for the age at first oestrus, average age at slaughter in the unrestricted fed group (401 ± 8 days) differed significantly (p<0.01) from that in the control group (365 ± 8 days). The average age at slaughter in the restricted fed group (383 ± 11 days) was intermediate and did not differ significantly from that in both other groups. The least square mean estimates and their standard errors for the data collected after slaughter are shown in table 3.8. There were no significant two-way interactions between the main effects taken into consideration (see 3.2.7, model 4). As far as the main effects are concerned, oestrus number at which a gilt was

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inseminated did not explain a significant part of the corrected total sum of squares for any of the parameters studied.

Although the number of corpora lutea and the number of embryos were somewhat lower and the embryonic mortality rate somewhat higher in the restricted fed group than in both other groups, the differences were not significant. Within groups the number of embryos, but not the embryonic mortality rate, was significantly related to the number of corpora lutea. The least square mean estimates for the number of embryos at an equal number of corpora lutea was for the unrestricted fed, restricted fed and control group 11.4 ± 0.6, 11.1 ± 0.7 and 11.6 ± 0.5, respectively. The differences between groups remained non-significant ($p>0.05$).

Within groups the embryonic mortality rate increased with $0.127 \pm 0.062\%$ ($p<0.05$) per day increase in age of the gilt at slaughter. If the differences between groups for the age of the gilts at slaughter were not taken into account, the least square mean estimates for embryonic mortality rate in the unrestricted fed, restricted fed and control group were 21.5 ± 4.2, 23.3 ± 4.7 and 18.6 ± 3.4, respectively. The differences between these estimates were also not significant ($p>0.05$).

The average weight as well as the average length of the empty uteri of the gilts from the restricted fed group were less than that in both other groups, but the differences were not significant ($p>0.05$). Within groups the length of the uterus increased with 0.83 ± 0.25 cm ($p<0.01$) per day increase in age at slaughter. Without correction for differences in age at slaughter, the length of the uterus (cm) in the unrestricted fed, restricted fed and control group was 423 ± 18, 397 ± 20 and 405 ± 14, respectively.

Except for the protein content of the allantoic fluid, there were no significant differences between experimental groups for any of the conceptus parameters. The average protein content of the allantoic fluid was significantly lower in the unrestricted fed group than in the restricted fed group. The relatively high protein content in the restricted fed group was mainly due to one gilt with an extreme high protein content of the allantoic fluid. If the data for this gilt were omitted from the analysis, the difference between the unrestricted fed and restricted fed group was no longer significant. The difference in embryonic weight between the restricted fed and control group tended to be significant ($p<0.10$).

CHAPTER 4

EMBRYONIC DEVELOPMENT IN RELATION TO EMBRYONIC MORTALITY IN THE PIG

4.1 Introduction

Embryonic development as well as embryonic mortality are influenced by several genetic and environmental factors (Hafez, 1969; Scofield, 1971; Edey, 1976; Den Hartog and Van Kempen, 1980; Ayalon, 1981). Although little is known about the variation in embryonic development between sows, variation in embryonic mortality is known to be high (Hanly, 1961). Since embryonic death can be the ultimate consequence of a disturbed development, factors which are associated with embryonic mortality might also be associated with embryonic development. Little is known about the relationship between embryonic mortality and the development of the surviving embryos. Lutter et al. (1981) briefly mentioned the fact that in the fourth week of pregnancy embryos in sows with more than 40% embryonic mortality were weighing less than embryos in sows with less than 40% embryonic mortality.

The objective of this study is to determine whether the development of the 35 days old conceptus (embryo and extra-embryonic membranes) is related to embryonic mortality in the pig. For purposes of interpretation of the results, especially concerning the development of the placenta, relevant uterine parameters are also considered.

4.2 Materials and methods

4.2.1 Animals and data collection procedures

A total of 71 sexually mature Dutch Landrace gilts were artificially inseminated with semen of Dutch Landrace boars and slaughtered on day 35 of pregnancy. Of these gilts, 40 were bought in two batches of 23 and 17, respectively. At arrival they had an age of approximately 180 days. The

dissection) were calculated.

For each conceptus or uterine parameter the data were fitted to model 1 and 2 to study their relationships with the embryonic mortality rate.

Model 1 : $Y_{ij} = \mu + GR_i + b_1(EMR_{ij}) + b_2(EMR_{ij})^2 + e_{ij}$
Model 2 : $Y_{ij} = \mu + GR_i + b_1(EMR_{ij}) + e_{ij}$

where Y_{ij} = a conceptus or uterine parameter, measured or calculated per gilt,

μ = fitted mean,

GR_i = the effect of the ith group (i=1,5),

EMR_{ij} = the embryonic mortality rate for the jth gilt in the ith group,

b_1, b_2 = regression coefficients,

and e_{ij} = random error.

The data for each parameter were also fitted to model 3 and 4.

Model 3 : $Y_{ij} = \mu + GR_i + b_1(X_{ij}) + b_2(EMR_{ij}) + b_3(EMR_{ij})^2 + e_{ij}$
Model 4 : $Y_{ij} = \mu + GR_i + b_1(X_{ij}) + b_2(EMR_{ij}) + e_{ij}$

where Y_{ij}, μ, GR_i, b_1-b_3, EMR_{ij} and e_{ij} are as described for model 1 and 2 and

X_{ij} = the value of a covariable for the jth gilt in the ith group.

For embryonic weight and length, X_{ij} was either number of corpora lutea, number of embryos, placental weight, placental length, length of the implantation site per embryo, uterine length per embryo before dissection or uterine length per embryo after dissection. For placental weight and length, X_{ij} was either number of corpora lutea, number of embryos, length of the implantation site per embryo, uterine length per embryo before dissection or uterine length per embryo after dissection. For all other parameters X_{ij} was either number of corpora lutea or number of embryos. In all these analyses either number of corpora lutea or number of embryos was used as a covariable in order to examine the relationship of the embryonic mortality rate with each of the conceptus and uterine parameters at a constant number of corpora lutea or constant number of embryos,

respectively. The other covariables were included separately in some analyses (as indicated) to facilitate interpretation of the results obtained with model 1 and 2.

All analyses were repeated using the absolute embryonic mortality instead of the embryonic mortality rate as a covariable in models 1 to 4. For each model fitted the percentage reduction of variance due to regression within groups (% red.) was calculated as:

$$\% \text{ red.} = \frac{SSE_a - SSE_b}{SSE_a} \times 100$$

where SSE_a = residual sum of squares for a model with only the fixed effect group ($Y_{ij} = u + GR_i + e_{ij}$)

and SSE_b = residual sum of squares for the model of interest, including the fixed effect group and 1, 2 or 3 covariables (models 1 to 4).

All these analyses were performed after preliminary analyses had shown that:

1. the variance of averages per gilt were independent of number of embryos on which the averages were based and

2. the regression coefficients within groups were not significantly different from each other.

4.3 Results

The averages, standard deviations and extreme values for number of corpora lutea, number of embryos, absolute embryonic mortality and embryonic mortality rate are shown in table 4.1. The absolute embryonic mortality increased with 0.36 (p=0.0062) for each additional corpus luteum. Of the total variance in absolute embryonic mortality 10.4% could be attributed to variation in number of corpora lutea. In contrast, the embryonic mortality rate was not related to the number of corpora lutea.

Only 1.7% of the variance in the former could be attributed to the latter (p=0.28). The correlation between the absolute embryonic mortality and the embryonic mortality rate was 0.97 (p<0.0001).

Table 4.1   Averages ($\overline{x}$), standard deviations (s.d.) and extreme   values (min., max.) for number of corpora lutea, number   of embryos, absolute   embryonic   mortality   and   embryonic   mortality   rate (n=71).

	$\overline{x}$	s.d.	min.	max.
Number of corpora lutea	14.48	2.42	9	20
Number of embryos	11.53	3.01	4	18
Absolute embryonic mortality	3.00	2.67	0	9
Embryonic mortality rate	0.20	0.18	0	0.67

The number of embryos (NE) increased significantly with an increasing number of corpora lutea (NCL) and decreased significantly with an increasing embryonic mortality (both absolute embryonic mortality (AEM) and embryonic mortality rate (EMR)). The relationships were NE=2.43+0.63 NCL (R^2=0.26; p=0.0001), NE=13.73-0.73 AEM (R^2=0.42; p=0.001) and NE=14.15-12.86 EMR (R^2=0.60; p=0.0001), respectively.

Average values, standard deviations and extreme values for conceptus and uterine parameters are shown in table 4.2. The relationships of these parameters with absolute embryonic mortality were essentially the same as the relationships with embryonic mortality rate. Therefore only the latter will be presented. Unless stated otherwise all relationships were linear.

Table 4.2   Averages ($\bar{x}$), standard deviations (s.d.) and extreme values
(min., max.) for conceptus and uterine parameters.

	$\bar{x}^{1)}$	s.d.	min.	max.
Embryonic weight, g	4.35	0.51	3.11	5.60
Embryonic length, cm	3.84	0.25	3.27	4.30
Placental weight, g	44.2	9.4	24.3	72.8
Placental length, cm	52.4	7.3	35.0	73.0
Amniotic fluid weight, g	5.31	0.68	3.50	7.00
Allantoic fluid weight, g	103.2	46.1	35.0	256.0
Number of areolae	2079	570	878	3181
Uterine length before dissection, cm	379	75	217	620
Uterine length after dissection, cm	424	73	257	703
Uterine length/embryo before dissection, cm	35.2	11.5	18.8	77.3
Uterine length/embryo after dissection, cm	39.8	13.7	21.7	86.0
Length of implantation site/embryo, cm	22.8	5.2	9.4	36.3
Length of uterus occupied by embryos, cm	257	79	99	545
Length of uterus unoccupied, cm	169	45	101	301
Percentage of uterus occupied	59.3	11.1	32.4	77.5

[1] For conceptus parameters: average of the litter averages.

Conceptus parameters

Embryonic weight and length decreased significantly with an increasing
embryonic mortality rate (table 4.3). This decrease was even more obvious
after correction for the effect of either number of corpora lutea,
placental weight, placental length or length of the implantation site per
embryo on embryonic weight and length. In contrast, the decrease was no
longer significant if the effect of either number of embryos or uterine
length per embryo was taken into account.

Table 4.3 Linear regression coefficients and their significances for relationships of embryonic weight (EW) and embryonic length (EL) with embryonic mortality rate (EMR).

| | Regression on EMR | | | |
Held constant	Y	b	p	% red.
-	EW	-0.64	0.053	5.6
	EL	-0.23	0.039	6.4
Number of corpora lutea	EW	-0.69	0.039	7.7
	EL	-0.24	0.033	7.3
Number of embryos	EW	-0.15	0.77	7.7
	EL	-0.11	0.53	7.5
Placental weight	EW	-0.89	0.0079	15.4
	EL	-0.27	0.018	9.1
Placental length	EW	-0.77	0.024	9.3
	EL	-0.26	0.024	8.2
Length of implantation site per embryo	EW	-0.80	0.025	7.8
	EL	-0.27	0.021	8.2
Uterine length/embryo (before dissection)	EW	-0.41	0.40	6.3
	EL	-0.16	0.31	6.8
Uterine length/embryo (after dissection)	EW	-0.65	0.21	6.4
	EL	-0.27	0.12	7.0

Placental weight and length were significantly related to embryonic mortality rate, but the type of relationship for placental length differed from that for placental weight to some extent. In contrast to embryonic weight and length, placental weight significantly increased with an increasing embryonic mortality rate (table 4.4). This remained the case if the effect of number of corpora lutea on placental weight was taken into account. Placental weight was no longer related to embryonic mortality rate after correction for the effect of number of embryos, length of the implantation site per embryo or uterine length per embryo on placental weight. Although the results shown in table 4.4 for placental length highly

Table 4.4 Linear regression coefficients and their significances for the
          relationships of placental weight (PW) and placental length (PL)
          with the embryonic mortality rate (EMR).

		Regression on EMR		
Held constant	Y	b	p	% red.
-	PW	14.2	0.022	7.8
	PL	8.5	0.048	5.9
Number of corpora lutea	PW	15.6	0.012	12.4
	PL	9.8	0.019	14.4
Number of embryos	PW	2.1	0.83	11.5
	PL	-2.2	0.73	11.9
Length of implantation site	PW	3.6	0.51	37.4
per embryo	PL	0.7	0.85	39.5
Uterine length/embryo	PW	-4.3	0.62	18.8
(before dissection)	PL	-8.5	0.13	25.7
Uterine length/embryo	PW	-5.6	0.53	21.2
(after dissection)	PL	-11.1	0.059	28.3

resemble those shown for placental weight, the relationship between
placental length and embryonic mortality rate before and after correction
for either number of embryos and length of the implantation site per embryo
was better described by a function of the type $y=ax^2+bx+c$, as shown in table
4.5. From these equations it can be calculated that placental length first
decreased with an increasing embryonic mortality rate until the latter was
0.21, to increase thereafter. After correction for either number of embryos
or length of the implantation site per embryo, the lowest placental length
was found at an embryonic mortality rate of 0.26.

   The amniotic fluid weight, allantoic fluid weight and number of areolae
per placenta were not significantly related to embryonic mortality rate
(table 4.6). It should nevertheless be noted that the amniotic fluid weight
showed a tendency to decrease while the allantoic fluid weight and number
of areolae per placenta showed a tendency to increase with an increasing
embryonic mortality rate.

Table 4.5 Regression coefficients and the significances of the quadratic regression coefficients for the relationship of placental length with the embryonic mortality rate (EMR), both linear and quadratic.

Held constant	Regression on EMR and EMR^2			
	b_1	b_2	$p(b_2)$	% red.
-	-27.6	65.7	0.0044	17.2
Number of embryos	-29.6	56.5	0.017	19.6
Length of implantation site per embryo	-24.6	47.1	0.014	45.1

Table 4.6 Linear regression coefficients and their significances for the relationships of amniotic fluid weight (AMN), allantoic fluid weight (ALL) and number of areolae (AREO) with the embryonic mortality rate (EMR).

Held constant	Regression on EMR			
	Y	b	p	% red.
-	AMN	-0.6	0.16	3.1
	ALL	40.0	0.20	2.5
	AREO	434.1	0.12	4.2
Number of corpora lutea	AMN	-0.6	0.17	3.2
	ALL	40.9	0.20	2.6
	AREO	441.1	0.11	4.5
Number of embryos	AMN	-0.8	0.28	3.2
	ALL	38.4	0.44	2.5
	AREO	451.5	0.30	4.2

Uterine parameters

Uterine length as well as the absolute and relative part of uterus occupied by embryos decreased significantly with an increasing embryonic mortality rate. In contrast, the length of uterus unoccupied increased significantly with an increasing embryonic mortality rate (table 4.7). After correction for the effect of number of corpora lutea on these uterine parameters the relationships with embryonic mortality rate remained significant and became somewhat more pronounced. After correction for the effect of number of embryos on the uterine parameters the relationships with embryonic mortality rate were no longer significant.

The length of the implantation site and the uterine length per embryo increased significantly with an increasing embryonic mortality rate (table 4.8). This was still the case after correction for the effect of the number of corpora lutea on these parameters. After correction for the effect of number of embryos on the length of the implantation site, the latter was no longer significantly related to embryonic mortality rate. In contrast, the uterine length per embryo was still significantly related to embryonic mortality rate. It could now be best described by a function of the type $y=ax^2+bx+c$. From the equations from table 4.9 it can be calculated that the uterine length per embryo first decreased with an increasing embryonic mortality rate until the latter was approximately 0.15, to increase thereafter.

Table 4.7 Linear regression coefficients and their significances for the relationships of uterine length before dissection (ULb), uterine length after dissection (ULa), uterine length occupied by embryos (ULO), uterine length unoccupied (ULU) and percentage of uterus occupied by embryos (PUO) with the embryonic mortality rate (EMR).

| Held constant | | Regression on EMR | | |
	Y	b	p	% red.
-	ULb	-121.7	0.0060	11.0
	ULa	-91.5	0.051	5.8
	ULO	-230.7	0.0001	30.8
	ULU	130.6	0.0001	30.3
	PUO	-39.7	0.0001	44.9
Number of corpora lutea	ULb	-135.3	0.0017	19.8
	ULa	-104.5	0.023	13.1
	ULO	-251.4	0.0001	46.4
	ULU	138.5	0.0001	37.1
	PUO	-42.8	0.0001	61.9
Number of embryos	ULb	24.6	0.71	20.3
	ULa	58.2	0.41	16.0
	ULO	-105.6	0.86	48.8
	ULU	61.5	0.11	35.8
	PUO	-10.6	0.16	60.7

Table 4.8 Linear regression coefficients and their significances for the relationships of length of the implantation site per embryo (IMP), uterine length per embryo before dissection (UPEb) and uterine length per embryo after dissection (UPEa) with the embryonic mortality rate (EMR).

| Held constant | Regression on EMR | | | |
	Y	b	p	% red.
-	IMP	9.4	0.0029	12.9
	UPEb	44.2	0.0001	54.5
	UPEa	56.0	0.0001	58.0
Number of corpora lutea	IMP	10.2	0.0009	20.1
	UPEb	47.4	0.0001	73.7
	UPEa	60.3	0.0001	78.5
Number of embryos	IMP	2.0	0.68	18.0
	UPEb	14.5	0.029	70.3
	UPEa	20.1	0.010	73.6

Table 4.9 Regression coefficients and the significances of the quadratic regression coefficients for the relationships of uterine length per embryo before dissection (UPEb) and uterine length per embryo after dissection (UPEa) with the embryonic mortality rate, both linear and quadratic.

| Held constant | Y | Regression on EMR and EMR^2 | | | |
		b_1	b_2	$p(b_2)$	% red.
Number of embryos	UPEb	-25.2	82.0	0.0004	75.8
	UPEa	-31.2	105.4	0.0001	79.6

4.4 Discussion

From the presented results it can be concluded that the development of conceptuses at the end of the embryonic stage (day 35 of pregnancy) is related to the incidence of embryonic mortality. The same can be concluded for all the uterine parameters that have been included in the present study. Except for placental length, these relationships were no longer significant if the effect of the number of viable embryos on these parameters was taken into account. Since differences in number of embryos between gilts are mainly due to differences in embryonic mortality (Johnson et al., 1985; Leymaster et al., 1986; Neal and Johnson, 1986; this study) this result is not surprising.

For all parameters studied, except placental length, the values either linearly increased or linearly decreased with an increasing embryonic mortality. In the case of placental length the relationship seems more complex. However, two remarks should be made. At first, if a linear function was fitted to the data for placental length, the increase with an increasing embryonic mortality was significant. Secondly, if the effect of number of corpora lutea on placental length was taken into account, this relationship was comparable to that between placental weight and embryonic mortality.

The results indicate that the growth of embryos in gilts with a high embryonic mortality is retarded in comparison with the growth of embryos in gilts with a low embryonic mortality. These results are in agreement with the results of Lutter et al. (1981). In their work the weight of 4 week old embryos in gilts with more than 40% embryonic mortality was 10.5% lower than that of the embryos in gilts with less than 40% embryonic mortality (0.94 ± 0.014 g and 1.05 ± 0.017 g, respectively). In the present study embryos in gilts with more than 40% embryonic mortality weighed 8.4% less than embryos in gilts with less than 40% embryonic mortality (4.04 ± 0.59 g and 4.41 ± 0.07 g, respectively). The average mortality rate in the material of Lutter et al. (1981) was approximately 40%, which is almost twice as high as the average embryonic mortality rate in the present study.

In contrast to the decrease in embryonic weight and length, the placental weight and length increased with an increasing embryonic mortality. If the decrease in embryonic growth with an increasing embryonic

mortality is a consequence of the concomitant increase in placental growth, than correction for the effect of placental weight or length on embryonic weight or length should abolish the relationship between embryonic weight and length on the one hand and embryonic mortality on the other. In contrast, these latter relationships became more pronounced after this correction. This indicates that the embryos from gilts with high embryonic mortality were already benefitting from their more developed placentae. (In the present study the relationships of embryonic weight or length with placental weight or length were all positive if the embryonic mortality was held constant.) The accelerated development of the placentae with an increasing embryonic mortality might be due to compensatory growth in order to counteract for the relative shortage of a component (or components) which is (are) essential for a normal embryonic development. If this is true, compensatory uptake of nutrients might already be the case by day 35 of pregnancy. Therefore, the relationships of embryonic weight and length with embryonic mortality in an earlier part of gestation might have been more pronounced than the presented relationship in the sense that an increase in embryonic mortality would have been associated with a larger relative decrease in embryonic weight and length. The comparison of the results of Lutter et al. (1981) with the present results, given above, supports this assumption.

The present results do not allow a decisive conclusion as to the mechanism underlying the altered conceptus development in gilts with a high embryonic mortality in comparison to gilts with a low embryonic mortality. The altered embryonic development might be directly associated with the factors which caused (a part of) the embryonic mortality. The altered placental development might be a secondary effect, mediated through the effect that embryos which died had on the uterine length before their death. Despite the decrease in uterine length with an increasing embryonic mortality, the length of uterus unoccupied increased. Due to this, the uterine length per embryo significantly increased with an increasing embryonic mortality, even after correction for the number of embryos. This might benefit the placental growth.

An interesting question is whether the accelerated growth of the placentae in gilts with a high embryonic mortality will be beneficial during the fetal stage of pregnancy, especially after day 70 of pregnancy.

2, 3 and 4 the gilts received 1.50M, 1.80M and 2.70M, respectively, until an age of 5 months and 2.70M, 2.70M and 1.65M, respectively, thereafter. The maintenance requirement was calculated as 0.45 MJ ME/kg$^{0.75}$ * (weight)$^{0.75}$. From week 37 after birth onwards all gilts were fed 2.4 kg of a normal ration for sows.

Of the 195 gilts, 38 were inseminated during first oestrus which had been induced with an intramuscular injection of 400 I.U. pregnant mare serum gonadotrophin and 200 I.U. human chorionic gonadotrophin (PG600^R, Intervet B.V., Boxmeer, the Netherlands).

For each gilt the stage of pregnancy at slaughter was chosen in such a way that confounding of batch, experimental group and time of insemination relative to the first insemination in the concerning group on the one hand and stage of pregnancy on the other hand was avoided. At the slaughter-house the ovaries and complete reproductive tract were removed immediately after stunning and exsanguination. During transport to the laboratory the collected material was kept on ice. Within 3 to 4 hours after slaughter the data collection procedures started. The number of corpora lutea on each ovary was counted. The uterus and cervix were separated from the ovaries, oviducts and mesometrium. The wall of the uterine horns was cut longitudinally along the antimesometrial side, starting at the utero-cervical junction. Each apparently normal and healthy foetus was removed from the uterus and immediately thereafter its weight and crown-rump length were determined. Subsequently each placenta was carefully detached from the endometrium and weighed. The length of the placenta, excluding the necrotic tips of the chorion, was measured under minimal stretch.

Before as well as after dissection the length of both uterine horns was measured. After removal of all conceptuses, the length of the individual implantation sites was measured.

5.2.2 Statistical analyses

For all statistical analyses the procedure GLM of Statistical Analysis System (SAS, 1985) was used.

The absolute prenatal mortality was calculated as the difference between the number of corpora lutea and the number of foetuses. The prenatal mortality rate was calculated as the ratio between absolute prenatal

mortality and number of corpora lutea. The parameters analysed were the conceptus parameters foetal weight, foetal length, placental weight and placental length and the uterine parameters length of the implantation site per foetus and uterine length per foetus before and after dissection of the uterus. The latter were calculated by dividing the total uterine length before or after dissection through the number of foetuses.

All statistical analyses on parameters for conceptus development were performed with the natural logarithms of the average values per gilt. The logarithmic transformation was necessary to correct for heterogeneity of variance caused by variation in stage of pregnancy. Within the group of non-induced gilts three sub-groups were created on the basis of either their absolute prenatal mortality or prenatal mortality rate (low: ± 20% of the gilts; intermediate: ± 60% of the gilts; high: ± 20% of the gilts). Because the group of induced gilts was small, within this group only 2 subgroups were created (prenatal mortality either lower than or higher than the average).

The data for each conceptus or uterine parameter were fitted to model 1 and 2. Data for non-induced gilts were analysed separately from data for induced gilts.

$$
\begin{aligned}
\text{Model 1: } Y_{ijkl} = \mu &+ EXG_i + BAT_j + SG_k \\
&+ b_1(ST_{ijkl}) + b_2(ST_{ijkl})^2 + b_3(ST_{ijkl})^3 \\
&+ b_{1k}(ST_{ijkl:k}) + b_{2k}(ST_{ijkl:k})^2 \\
&+ b_{3k}(ST_{ijkl:k})^3 + e_{ijkl}
\end{aligned}
$$

$$
\begin{aligned}
\text{Model 2: } Y_{ijkl} = \mu &+ EXG_i + BAT_j + SG_k \\
&+ b_1(ST_{ijkl}) + b_2(ST_{ijkl})^2 + b_3(ST_{ijkl})^3 \\
&+ b_{1k}(ST_{ijkl:k}) + b_{2k}(ST_{ijkl:k})^2 \\
&+ b_{3k}(ST_{ijkl:k})^3 + b_4(NF_{ijkl}) \\
&+ b_5((NF_{ijkl})*(ST_{ijkl})) + b_6((NF_{ijkl})*(ST_{ijkl})^2) \\
&+ b_7((NF_{ijkl})*(ST_{ijkl})^3) + e_{ijkl}
\end{aligned}
$$

where Y_{ijkl} = a conceptus or uterine parameter, measured or calculated per gilt,

μ = fitted mean,

EXG_i = effect of the ith experimental group (i=1,4),

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BAT_j = effect of the jth batch ($j=1,4$),

SG_k = effect of the kth prenatal mortality subgroup ($k=1,3$ for non-induced gilts or $k=1,2$ for induced gilts),

ST_{ijkl} = stage of pregnancy at slaughter (days) for the lth gilt in the ith experimental group, j^{th} batch and k^{th} subgroup,

NF_{ijkl} = number of foetuses for the lth gilt in the ith experimental group, j^{th} batch and k^{th} subgroup,

b_1-b_7 = pooled partial regression coefficients,

b_{1k}-b_{3k} = regression coefficients within prenatal mortality subgroups as deviation from the pooled partial regression coefficients,

and e_{ijkl} = random error.

All these analyses were performed after preliminary analyses had shown that:

1. the variance of average values per gilt (or logarithmic transformed average values per gilt) was independent of number of foetuses on which the averages were based,

2. the interaction between experimental group and batch was not significant and

3. the regression coefficients within the interaction classes of experimental group and batch were not significantly different from each other.

As can be seen from model 1 and 2 the effect of experimental group and batch were taken into account. However, in view of the objectives of the present study these effects were not of interest and will therefore not be discussed further.

5.3 Results

The averages, standard deviations and extreme values for number of corpora lutea, number of foetuses, absolute prenatal mortality and prenatal

mortality rate are shown in table 5.1. The number of corpora lutea was independent of stage of pregnancy. Although the absolute prenatal mortality and the prenatal mortality rate both increased and the number of foetuses decreased with an increasing stage of pregnancy, these changes were for both the non-induced and induced group small and not significant. This is illustrated for the prenatal mortality rate in figure 5.1.

Table 5.1   Averages ($\bar{x}$), standard deviations (s.d.) and extreme   values (min., max.) for number of corpora lutea, number of foetuses, absolute prenatal mortality and prenatal mortality rate.

	$\bar{x}$	s.d.	min.	max.
Non-induced gilts (n=157)				
Number of corpora lutea	13.75	2.21	7	20
Number of foetuses	10.17	2.80	2	17
Absolute prenatal mortality	3.60	2.73	0	12
Prenatal mortality rate	0.26	0.18	0	0.86
Induced gilts (n=38)				
Number of corpora lutea	23.71	9.46	9	53
Number of foetuses	10.50	3.93	2	17
Absolute prenatal mortality	13.21	9.48	0	46
Prenatal mortality rate	0.51	0.22	0	0.88

After correction for experimental group and batch, the correlation coefficients between number of foetuses on the one hand and number of corpora lutea, absolute prenatal mortality and prenatal mortality rate on the other hand were for the non-induced gilts 0.41 ($p<0.001$), 0.71 ($p<0.001$) and 0.84 ($p<0.001$), respectively, and for the induced gilts 0.22 ($p>0.10$), 0.23 ($p>0.10$) and 0.59 ($p<0.001$), respectively. The correlation coefficient between absolute prenatal mortality and prenatal mortality rate was 0.96 ($p<0.0001$) in the non-induced group and 0.79 ($p<0.001$) in the induced group. Since the relationships of the parameters of interest with the absolute prenatal mortality were essentially the same as the
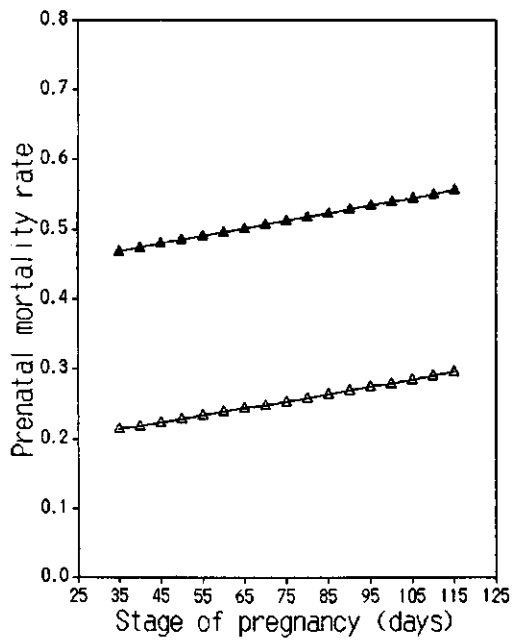
65

Figure 5.1 The change in prenatal mortality rate during the foetal stage
of pregnancy. (non-induced gilts: △——△ ; induced gilts: ▲——▲)

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relationships with the prenatal mortality rate, only the latter will be presented.

Non-induced gilts

The relative frequency distribution for prenatal mortality rate is shown in figure 5.2a. The changes in conceptus and uterine parameters with stage of pregnancy were compared for gilts with a prenatal mortality rate of less than 0.10, between 0.10 and 0.40 (including 0.10) and equal to or greater than 0.40 (n = 31, n = 91 and n = 35, respectively). The relative frequency distribution for each of these three subgroups is shown in figure 5.2b for the period before day 60, between day 60 and 85 and after day 85 of pregnancy. These three distributions did not differ significantly from the overall relative frequency distribution, also shown in figure 5.2b.

The changes in foetal weight, placental weight and placental length between day 35 and 115 of pregnancy differed significantly between the gilts with a low, intermediate and high prenatal mortality rate (figure 5.3a, c, d). This was not the case for foetal length (figure 5.3b). The length of the implantation site per foetus increased in each of the three prenatal mortality subgroups with 0.13 cm per day of pregnancy (p<0.0001). At a given stage of pregnancy it was significantly different between the three prenatal mortality subgroups. Within the groups of gilts with a low, intermediate and high prenatal mortality rate it was 19.7, 20.4 and 21.8 cm, respectively, on day 35 of pregnancy and 29.3, 30.0 and 31.4 cm, respectively, on day 110 of pregnancy.

The uterine length per foetus, before as well as after dissection, was significantly affected by prenatal mortality rate, but it did not significantly change with stage of pregnancy (b = -0.019 cm/day and b = -0.016 cm/day, respectively). Within the groups of gilts with a low, intermediate and high prenatal mortality rate the uterine length per foetus before dissection was 30.9, 34.9 and 51.0 cm, respectively. After dissection it was slightly higher (34.8, 39.3 and 57.6 cm, respectively).

After correction for the effect of number of foetuses on the conceptus and uterine parameters, prenatal mortality rate was not related to any of these parameters, except placental length. For this parameter the relationships as shown in figure 5.3d remained essentially the same and the differences between the gilts with a low, intermediate and high prenatal mortality rate remained significant.

Induced gilts

The relative frequency distribution for prenatal mortality rate is shown in figure 5.4a. The changes in conceptus and uterine parameters with stage of pregnancy were compared between gilts with a prenatal mortality rate less than the average (0.51) and the remaining gilts (n = 17 and n = 21, respectively). The relative frequency distribution for both groups is shown in figure 5.4b for the period before day 60, between day 60 and 85 and after day 85 of pregnancy. These three distributions did not differ significantly from the overall relative frequency distribution, also shown in figure 5.4b.

The changes in conceptus and uterine parameters with stage of pregnancy were for none of the parameters studied significantly different between gilts with a relatively low and relatively high prenatal mortality rate. The overall changes in foetal weight and length and placental weight and length with stage of pregnancy are shown in figure 5.5. For each parameter the change with stage of pregnancy as found within the group of non-induced gilts with a high prenatal mortality rate (equal to or more than 0.40, figure 5.3) is also shown in figure 5.5 to serve as reference.

The length of the implantation site per foetus increased overall with 0.141 cm per day of pregnancy (p<0.01). At day 35 and day 110 of pregnancy it was 15.9 and 26.5 cm, respectively. The uterine length per foetus before as well as after dissection did not significantly change with stage of pregnancy (b = -0.209 cm/day and b = -0.298 cm/day, respectively). Although not significant, the uterine length per foetus before dissection decreased from 45.2 cm on day 35 of pregnancy to 29.5 cm on day 110 of pregnancy. For the uterine length per foetus after dissection this was 54.0 and 31.7 cm, respectively.

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Figure 5.4 The relative frequency distribution for prenatal mortality rate in induced gilts (A) and the relative frequency distribution for induced gilts with a low (L<0.51) and a high (H ≥ 0.51) prenatal mortality rate, shown for the period before day 60, between day 60 and day 85 and after day 85 of pregnancy (B).

Figure 5.5 The change in foetal weight (A), foetal length (B), placental weight (C) and placental length (D) with stage of pregnancy for induced gilts (▲——▲), and non-induced gilts with a high prenatal mortality rate (△——△).

5.4 Discussion

At the end of the embryonic stage of pregnancy (day 35) differences in the extent of development of embryos and their extra-embryonic membranes were observed between gilts with a low and gilts with a high embryonic mortality rate (see chapter 4). This observation was the direct motive to start the present study. For a correct interpretation of the results it is important to consider at first some aspects of the relationship between prenatal mortality and embryonic mortality. In the present study the prenatal mortality rate inc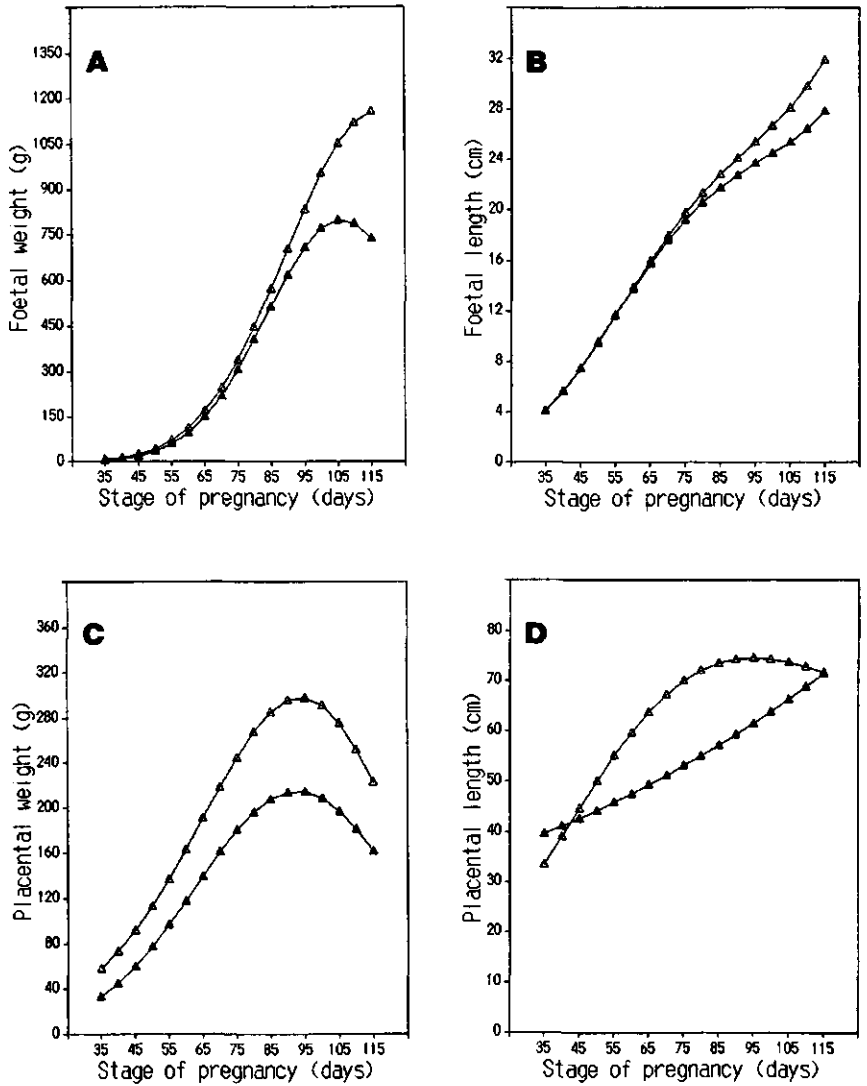reased with stage of pregnancy in both the non-induced and induced group of gilts. Although these increases were not significant, their absolute magnitude (7-8%) is in good agreement with the foetal mortality rate of at most 10% as given by Wrathall (1971), but somewhat lower than the estimate of 10-20% given by Pope and First (1985). As a consequence of these increases, the reliability of the prenatal mortality rate as an estimator for the embryonic mortality rate will decrease as pregnancy progresses. Since the difference in prenatal mortality rate between the non-induced group and induced group remains almost constant throughout the period studied (day 35 - day 112), it is justifiable to conclude that the two groups differ only as far as their embryonic mortality rate is concerned. From the day 35 estimates for the prenatal mortality rate it can be concluded that the embryonic mortality rate in the induced group was somewhat more than twice as high than that in the non-induced group (47% and 22%, respectively).

Within the group of non-induced gilts the rate of foetal weight gain was significantly different between gilts with a low and gilts with a high prenatal mortality rate. In contrast, no differences were observed for the increase in foetal length. Especially between day 75 and day 100 of pregnancy, the growth rate of foetuses from gilts with a high prenatal mortality rate is clearly higher than that of foetuses from gilts with a low prenatal mortality rate. However, after day 100 of pregnancy this is reversed with the consequence that the differences in foetal weight by day 110 of pregnancy are small. These changes in growth rate are consistent with the changes in placental weight and length. Within the group of gilts with a low and intermediate prenatal mortality rate the change in placental weight is in good agreement with the results of Pomeroy (1960).

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$$L_k(\text{left}) = \frac{\sum\limits_{i=k+1}^{n} (Y_i - \overline{Y}_{(n-k)})^2}{\sum\limits_{i=1}^{n} (Y_i - \overline{Y})^2} \quad \text{with } \overline{Y}_{(n-k)} = \frac{\sum\limits_{i=k+1}^{n} Y_i}{n-k}$$

If $k_{max} > n/2$, for each $k = k_{max}, \ldots, n-1$ the $L_k(\text{right})$ was computed as:

$$L_k(\text{right}) = \frac{\sum\limits_{i=1}^{k} (Y_i - \overline{Y}_k)^2}{\sum\limits_{i=1}^{n} (Y_i - \overline{Y})^2} \quad \text{with } \overline{Y}_k = \frac{\sum\limits_{i=1}^{k} Y_i}{k}$$

Critical values for L_k have been given by Hawkins (1980). Low L_k values indicate the presence of outliers. Once the number of outliers was determined, individual foetuses or piglets were classified as shown in figure 6.1. Foetuses and piglets from normal distributed litters are called normal. One or two outliers to the left are called runts, while one or two outliers to the right are called giants. More than two outliers to the left or to the right are called left-hand individuals or right-hand individuals, respectively. Based on the classification of the individual foetuses or piglets within a litter, the litters were classified as litters with a normal distribution, litters with one or two runts, litters with left-hand individuals, litters with right-hand individuals or litters with one or two giants.

For the statistical analyses of the data, analysis of variance (procedure GLM of SAS, 1985) and Chi-square analysis for 2x2 contingency tables were used. The embryonic mortality rate was calculated as the percentage of corpora lutea not represented by apparantly normal and healthy foetuses. Data for induced gilts and their foetuses or piglets were analysed separately from those for non-induced gilts. A litter with 3 foetuses can only be classified as a litter with a normal distribution, a litter with runts or a litter with giants. The smallest litter which could be classified as one of the five distinguished classification classes is a litter with 7 foetuses. The statistical analysis was therefore conducted within the data for all litters with 3 or more foetuses and within the data

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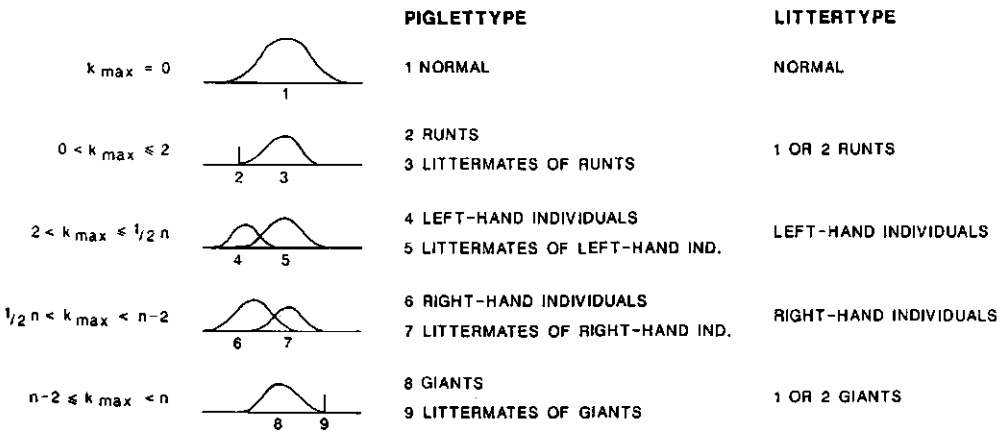|		PIGLETTYPE	LITTERTYPE
$k_{max} = 0$		1 NORMAL	NORMAL
$0 < k_{max} \leq 2$		2 RUNTS 3 LITTERMATES OF RUNTS	1 OR 2 RUNTS
$2 < k_{max} \leq \frac{1}{2} n$		4 LEFT-HAND INDIVIDUALS 5 LITTERMATES OF LEFT-HAND IND.	LEFT-HAND INDIVIDUALS
$\frac{1}{2} n < k_{max} < n-2$		6 RIGHT-HAND INDIVIDUALS 7 LITTERMATES OF RIGHT-HAND IND.	RIGHT-HAND INDIVIDUALS
$n-2 \leq k_{max} < n$		8 GIANTS 9 LITTERMATES OF GIANTS	1 OR 2 GIANTS

Figure 6.1   Classification of individual foetuses or piglets (piglettype)
and foetal litters or litters at term (littertype) on the basis
of the within-litter weight distribution.

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for all litters with 7 or more foetuses. In the first case only data for litters classified as normal, litters with 1 or 2 runts and litters with 1 or 2 giants were included in the dataset.

To establish whether differences between littertypes exist as far as number of foetuses and embryonic mortality rate are concerned, the data were analysed according to model 1.

Model 1: $Y_{ijk} = \mu + DS_i + LT_j + b_1 X_{ijk} + e_{ijk}$

where Y_{ijk} = number of foetuses or embryonic mortality rate,

μ = fitted mean,

DS_i = fixed effect of dataset (i=1,4),

LT_j = fixed effect of littertype (depending on data used either j=1,3 or j=1,5),

X_{ijk} = covariable number of corpora lutea,

b_1 = pooled regression coefficient,

and e_{ijk} = random error.

Data on the number of corpora lutea were analysed according to model 1 without the covariable X_{ijk}. Statistical analyses of the data on foetal weight (model 2) were performed with the natural logarithms of the average values per subpopulation (piglettype) per litter. The logarithmic transformation was necessary to correct for heterogeneity of variance caused by variation in stage of pregnancy. To adjust for heterogeneity of variance due to different numbers of foetuses per subpopulation within a litter, a weighted analysis of variance was performed. Each observation was weighted with the reciprocal value of the within-piglettype variance as obtained from separate analyses per piglettype, using model 2 without LT_j and $PT_{k:j}$.

Model 2: $Y_{ijkl} = \mu + DS_i + LT_j + PT_{k:j} + b_1(X_{ijkl}) + b_2(X_{ijkl})^2 + b_3(X_{ijkl})^3 + e_{ijkl}$

where μ, DS_i and LT_j are as described for model 1 and

Y_{ijkl} = the logarithm of the average foetal weight per subpopulation per litter,

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$PT_{k:j}$ = the fixed effect of piglettype nested within
littertype,

X_{ijkl} — covariable stage of pregnancy,

b_1, b_2, b_3 = pooled partial regression coefficients,

and e_{ijkl} — random error.

6.3 Results

The frequency for each classification class within each of the datasets is shown for non-induced and induced litters in table 6.1 and table 6.2, respectively. Within the group of non-induced gilts the frequencies for the classification classes in dataset 1, 2, 3 and 4 (foetal litters) did not differ significantly from that in dataset 5 (litters at term), neither were any of the differences between the datasets 1 to 4 significant. Within the group of induced gilts the frequencies for litters with a normal distribution and for litters with left-hand individuals in dataset 3 differed significantly from those in dataset 5. The frequencies for the classification classes in dataset 4 did not differ from those in dataset 3 and 5.

Within dataset 3 and 4 the frequencies for the classification classes did not differ significantly between the non-induced and induced litters. Within dataset 5 there were significantly ($p < 0.05$) more litters with a normal distribution in the group of induced litters (78.7%) than in the group of non-induced litters (67.7%), but none of the other frequencies differed significantly between these two groups.

The average number of foetuses or piglets per litter for each of the relevant classification classes as well as the average number of foetuses or piglets per subpopulation within litters are shown in table 6.3 for all litters with more than 2 individuals and in table 6.4 for all litters with more than 6 individuals. The average litter size of the foetal litters was always higher than that of the litters at term, except for the litters with giants. This exception was especially evident for the induced litters.

The least squares mean estimates for the number of corpora lutea, number of foetuses and embryonic mortality rate are shown in table 6.5 for litters with a normal distribution, litters with runts and litters with giants. All

Table 6.1 Classification of litters from non-induced gilts on the basis of the within-litter weight distribution.

	DATASET 1		DATASET 2		DATASET 3		DATASET 4		DATASET 5	
Stage of pregnancy	Day 34, 35 or 36		Day 35		Day 35-115		Day 27-72		At term	
Number of litters (total)	50		40		157		126		826	
	No. of litters	% of total	No. of litters	% of total	No. of litters	% of total	No. of litters	% of total	No. of litters	% of total
Littertype										
Normal	33	66.0	29	72.5	99	63.1	78	61.9	559	67.7
1 or 2 runts	11	22.0	6	15.0	34	21.7	30	23.8	147	17.8
Left-hand individuals	3	6.0	2	5.0	21	13.4	11	8.7	87	10.5
Right-hand individuals	1	2.0	2	5.0	0	0.0	3	2.4	13	1.6
1 or 2 giants	2	4.0	1	2.5	3	1.9	4	3.2	20	2.4

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Table 6.2   Classification of litters from induced gilts on the basis of
            the within-litter weight distribution.

	DATASET 3 Day 35-115 37		DATASET 4 Day 27-72 56		DATASET 5 At term 89	
Stage of pregnancy						
Number of litters (total)						
	No. of litters	% of total	No. of litters	% of total	No. of litters	% of total
Littertype						
Normal	22	59.5	38	67.9	70	78.7
1 or 2 runts	7	18.9	7	12.5	12	13.5
Left-hand individuals	8	21.6	6	10.7	4	4.5
Right-hand individuals	0	0.0	0	0.0	1	1.1
1 or 2 giants	0	0.0	5	8.9	2	2.2

foetal litters with more than two foetuses and belonging to one of the
three mentioned classification classes were included in the statistical
analysis. The number of corpora lutea did not differ significantly between
classification classes for both groups of gilts. The number of corpora
lutea seemed somewhat lower for litters with giants than for litters with
a normal distribution or for litters with runts. Within the group of
non-induced litters the number of foetuses as well as the embryonic
mortality rate for the litters with a normal distribution and the litters
with runts differed significantly from that for the litters with giants,
independent of the stage of pregnancy at slaughter. The differences in
number of foetuses and embryonic mortality rate between litters with a
normal distribution and litters with runts were independent of gestational
age and significant if all data were included in the analysis (gestational
age less than 114 days). An embryonic mortality rate of more than 50%
occurred in less than 16% of the litters with a normal distribution and in
less than 7% of the litters with runts, but for the litters with giants

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Table 6.3 The average number of foetuses or piglets per litter and per subpopulation within litters, shown for litters with more than 2 individuals.

Littertype		Non-induced gilts				Induced gilts			
		Foetal litters		Litters at term		Foetal litters		Litters at term	
		x̄	s.d.	x̄	s.d.	x̄	s.d.	x̄	s.d.
Normal	T[1]	10.12	2.92	8.82	2.61	10.18	3.82	8.86	2.97
1 or 2 runts	T	10.81	2.70	9.65	2.14	8.78	2.52	8.92	1.93
	L	1.41	0.49	1.39	0.49	1.64	0.50	1.50	0.52
	R	9.40	2.73	8.26	2.09	7.14	2.44	7.42	1.62
1 or 2 giants	T	6.80	2.25	8.60	2.60	8.20	3.11	12.50	2.12
	L	5.30	2.31	7.10	2.43	7.00	3.16	10.50	2.12
	R	1.50	0.53	1.50	0.51	1.20	0.45	2.00	0.00

1) T: total litter size; L: size of left distribution; R: size of right distribution

Table 6.4   The average number of foetuses or piglets per litter and per subpopulation within
             litters, shown for litters with more than 6 individuals.

Littertype		Non-induced gilts				Induced gilts			
		Foetal litters		Litters at term		Foetal litters		Litters at term	
		$\bar{x}$	s.d.	$\bar{x}$	s.d.	$\bar{x}$	s.d.	$\bar{x}$	s.d.
Normal	T[1]	10.96	2.25	9.69	1.89	11.32	3.07	10.05	2.04
1 or 2 runts	T	11.21	2.25	10.13	1.72	9.42	2.11	9.19	1.78
	L	1.43	0.50	1.40	0.49	1.67	0.49	1.55	0.52
	R	9.78	2.36	8.73	1.67	7.75	2.05	7.64	1.50
Left-hand	T	11.84	2.21	11.01	1.61	13.29	2.84	9.75	2.22
individuals	L	3.78	1.02	3.73	0.93	4.50	1.29	3.25	0.50
	R	8.06	2.08	7.28	1.64	8.79	2.15	6.50	2.38
Right-hand	T	12.16	2.32	9.84	1.91	-	-	10.00	-
individuals	L	8.33	1.86	6.46	1.90	-	-	6.00	-
	R	3.83	0.75	3.38	0.51	-	-	4.00	-
1 or 2 giants	T	8.80	0.84	9.69	1.35	9.50	1.29	12.50	2.12
	L	7.40	0.89	8.13	1.20	8.25	1.71	10.50	2.12
	R	1.40	0.55	1.56	0.51	1.25	0.50	2.00	0.00

[1] T: total litter size; L: size of left distribution; R: size of right distribution

term, the difference was not significant. The close resemblance of the frequency for each of the classification classes between litters with a gestational age of 27 to 35 days and litters at term provides strong evidence that for the majority of litters the type of distribution at term is already established at the early foetal stage. Definitive proof can only be obtained by accurate longitudinal studies, but as Dawes (1976) stated, we are still limited in our ability to measure the same foetus in utero sequentially.

In agreement with the present results the early occurrence of porcine runts has been reported by Perry and Rowell (1969) and Cooper et al. (1978). They studied litters with a gestational age of 31 to 113 days (n=90) and 28 to 112 days (n=17), respectively. Perry and Rowell (1969) defined a runt as a foetus with a weight less than two-thirds of the average for the uterine horn in which the foetus was found. They identified runts in litters of gestational age 31 to 49 days. Cooper et al. (1978) assessed "runting" on the clinical appearance of the foetus and tested whether the foetuses were runts by application of Dixons' test (Dixon, 1951). They concluded that runts are already detectable by day 44 of gestation.

The present results show that there is a relationship between the type of weight distribution within a litter and the embryonic mortality rate. Within the group of non-induced litters the embryonic mortality rate was lower in the litters with two discrete subpopulations than in the litters with a normal distribution, except for the litters with giants. The litters with giants distinguished themselves from the other classification classes in that they had an average embryonic mortality rate which was much higher than that for the other classification classes.

The embryonic mortality rate in the induced gilts was higher than in the non-induced gilts. Within the induced litters only the embryonic mortality rate for the litters with left-hand individuals appears to be lower than that for the other classification classes. It should be kept in mind that there were no litters with right-hand individuals within the group of induced litters.

The within-litter weight distribution might be a consequence of the very early existence of variation in embryonic development and the functioning of an intrauterine mechanism of selective mortality to reduce developmental

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variation before implantation. Within-litter variation in preimplantation development of porcine embryos have been described by Anderson (1978) for 10 and 11 day old embryos, by Richter and Elze (1986) for 1 to 12 day old embryos and by Wright and Grammer (1980) and Wright et al. (1983) for 6 to 9 day old embryos. As far as the protein content of the embryos is concerned, Wright et al. (1983) found in each of the five sows that had been slaughtered on day 9 of pregnancy two or three embryos which contained clearly less protein than the littermate embryos. Although less evident, the same observation was made on day 6, 7 and 8 of pregnancy. If these results are substantiated they imply that in almost every litter some embryos are already retarded in their development before day 10 of pregnancy. Work of Pope et al. (1982a), Pope and First (1985), Wilmut et al. (1985, 1986) and Morgan et al. (1987a, 1987b) strongly suggest that a mechanism exists through which variation in embryonic development within a porcine litter is reduced around day 11 of pregnancy through selective mortality of the less developed embryos. If a certain minimum number of well developed embryos can change the uterine environment to accommodate their own development, they will create an asynchrony between the uterine environment and the less developed embryos. This asynchrony can be detrimental if it exceeds a certain limit. It is also possible that the well developed embryos induce the release of uterine factors which are embryocidic for the less developed embryos or inhibit the release of uterine factors which are still essential for the undisturbed development of the less developed embryos. A study of the changes in the uterine protein secretion around day 11 of pregnancy in comparison with these changes in cyclic sows has shown that the embryos influence the protein secretion through the release of oestrogens (Geisert et al., 1982c). There is reason to believe that the morphologically further developed embryos within a litter start to secrete oestrogens before their littermates (Ford et al., 1982). The effectiveness of this postulated developmental variation reducing mechanism, combined with the existing variation in embryonic development by day 11 of pregnancy, might determine the within-litter weight distribution which will be found by the end of the embryonic stage (day 30-35 of pregnancy) and at term. Further research is needed to substantiate this.

CHAPTER 7

DEATH RISK AND PREWEANING GROWTH RATE OF PIGLETS IN RELATION TO THE WITHIN-LITTER WEIGHT DISTRIBUTION AT BIRTH

7.1 Introduction

From a pig producers point of view a liveborn piglet should have a low death risk and a high growth rate. The death risk of a newborn piglet is dependent on several factors, including the incidence of congenital and genetic abnormalities, susceptibility to diseases, the chance of overlying by the sow and the thermal environment (English and Wilkinson, 1982; English and Morrison, 1984). Two important determinants of the death risk are the birthweight of the piglet and the variation in birthweight within the litter (English and Smith, 1975). According to Hafez (1963) the growth rate before weaning is dependent on birthweight, age at weaning and genotype of the piglet and furthermore the milkproduction, mothering ability and age of the sow. Cöp (1971) added to this the uptake of additional nutrients next to milk, the climate in the farrowing house and the occurrence of diseases.

Although it is generally assumed that the birthweight distribution within a litter is normal (Gaussian), Royston et al. (1982) have shown that in some litters a discrete subpopulation of one or more growth retarded piglets occurs. This was substantiated by Wootton et al. (1983) for 5 polytocous species, including the pig. Of the 64 porcine litters studied by them, 19 had an abnormal (non-Gaussian) birthweight distribution. Until now this aspect has not been considered in studies concerning preweaning death risk and preweaning growth rate of piglets. The purpose of the analyses described in this chapter is to investigate whether the death risk of piglets and the preweaning growth rate of the surviving piglets depends on the within-litter weight distribution.

7.2 Materials and methods

7.2.1 Data

Data for the present study, 819 litters with piglets, were obtained from the Research Institute for Animal Production, Zeist, the Netherlands. The litters were either produced by sows from one of six commercial breeds (n=363) or by Dutch Landrace sows (n=456). The Dutch Landrace sows either belonged to a selection line for short intervals between weaning and first oestrus (n=215) or to a contemporary control line (n=241). Crossfostering was not applied in any of these litters.

The birthweight and sex were known for each liveborn piglet. Furthermore age and weight at weaning were known for each piglet that survived the suckling period, thus allowing computation of the average preweaning growth rate. Commercial breed litters were weaned at an age of 41.4 ± 2.7 days (mean $\pm$ s.d.), Dutch Landrace litters at an age of 34.9 ± 2.2 days.

7.2.2 Statistical procedures

In the present study it was assumed that there are at most two discrete subpopulations within a litter. For each litter the observations on birthweight of the piglets were ordered according to increasing magnitude. The ith largest is denoted as Y_i. The maximum number of possible outliers was first determined, using the method described by Hawkins (1980). For $q = 1, 2, \ldots n-1$, with n being the number of piglets per litter, the value of B_q was computed as:

$$B_q = \frac{\sqrt{\frac{q\ (n-q)}{n}} * \sum_{i=1}^{q} (Y_{(n-i+1)} - \overline{Y})}{\sqrt{\sum_{i=1}^{n} (Y_i - \overline{Y})^2}}$$

The largest value of B_q determined the maximum number of possible outliers (k_{max}). If $k_{max} \leq n/2$, then there could be a maximum of k_{max}

outliers to the left. If $k_{max} > n/2$, then there could be a maximum of $n - k_{max}$ outliers to the right. The L_k test of Tietjen and Moore (1972) was used thereafter to determine the actual number of outliers. If $\leq k_{max}$ $n/2$, for each $k = 1, \ldots, k_{max}$ the L_k(left) was computed as:

$$L_k(\text{left}) = \frac{\sum\limits_{i=k+1}^{n} (Y_i - \overline{Y}_{(n-k)})^2}{\sum\limits_{i=1}^{n} (Y_i - \overline{Y})^2} \quad \text{with } \overline{Y}_{(n-k)} = \frac{\sum\limits_{i=k+1}^{n} Y_i}{n-k}$$

If $k_{max} > n/2$, for each $k = k_{max}, \ldots, n-1$ the L_k(right) was computed as:

$$L_k(\text{right}) = \frac{\sum\limits_{i=1}^{k} (Y_i - \overline{Y}_k)^2}{\sum\limits_{i=1}^{n} (Y_i - \overline{Y})^2} \quad \text{with } \overline{Y}_k = \frac{\sum\limits_{i=1}^{k} Y_i}{k}$$

Critical values for L_k have been given by Hawkins (1980). Low L_k values indicate the presence of outliers. Once the number of outliers was determined, individual piglets were classified as shown in figure 7.1. Piglets from normal distributed litters are called normal. One or two outliers to the left are called runts, while one or two outliers to the right are called giants. More than two outliers to the left or to the right are called left-hand individuals or right-hand individuals, respectively. Based on the classification of the individual piglets within a litter, the litters were classified as litters with a normal distribution, litters with one or two runts, litters with left-hand individuals, litters with right-hand individuals or litters with one or two giants.

For the statistical analysis of the data, analysis of variance (procedure GLM of Statistical Analysis System (SAS), 1985) and Chi-square analysis for 2 x 2 contingency tables were used. Data on litter size at birth, within-litter standard deviation of birthweight, within-litter coefficient of variation of birthweight and the number of piglets weaned per litter were analysed according to model 1.
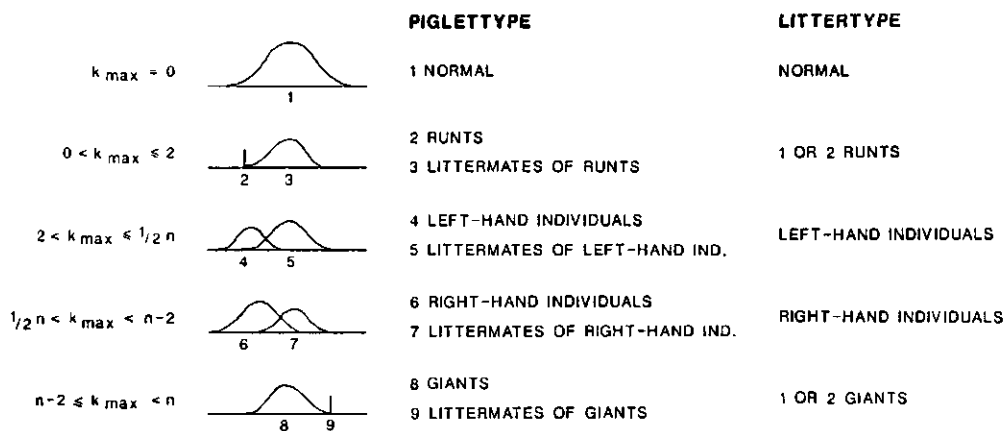
		PIGLETTYPE	LITTERTYPE
$k_{max} = 0$		1 NORMAL	NORMAL
$0 < k_{max} \leq 2$		2 RUNTS 3 LITTERMATES OF RUNTS	1 OR 2 RUNTS
$2 < k_{max} \leq 1/2\,n$		4 LEFT-HAND INDIVIDUALS 5 LITTERMATES OF LEFT-HAND IND.	LEFT-HAND INDIVIDUALS
$1/2\,n < k_{max} < n-2$		6 RIGHT-HAND INDIVIDUALS 7 LITTERMATES OF RIGHT-HAND IND.	RIGHT-HAND INDIVIDUALS
$n-2 \leq k_{max} < n$		8 GIANTS 9 LITTERMATES OF GIANTS	1 OR 2 GIANTS

Figure 7.1 Classification of individual piglets (piglettype) and litters at term (littertype) on the basis of the within-litter weight distribution.

Model 1: $Y_{ijkl} = \mu + LT_i + GG_j + PAR_k + e_{ijkl}$

where Y_{ijkl} = the dependent variable,

μ = fitted mean,

LT_i = the fixed effect of littertype (i=1,5),

GG_j = the fixed effect of genetic group (j=1,8),

PAR_k = the fixed effect of sows parity (k=1,2),

and e_{ijkl} = random error.

Data on average birthweight per litter were analysed according to model 1 and model 2.

Model 2: $Y_{ijkl} = \mu + LT_i + GG_j + PAR_k + b_{1i}(LS_{ijkl}) + b_{2i}(LS_{ijkl})^2 + e_{ijkl}$

where Y_{ijkl}, μ, LT_i, GG_j, PAR_k and e_{ijkl} are as described for model 1 and

b_{1i}, b_{2i} = partial, within-littertype regression coefficients

and LS_{ijkl} = covariable litter size.

The within-litter death risk of piglets was calculated for each litter separately as the ratio between the number of live-born piglets which died before weaning and the total number of liveborn piglets. It was analysed according to model 1 and 3.

Model 3: $Y_{ijkl} = \mu + LT_i + GG_j + PAR_k + b_{1i}(LS_{ijkl}) + b_{2i}(LS_{ijkl})^2$
$$+ b_{3i}(BW_{ijkl}) + b_{4i}(BW_{ijkl})^2 + b_{5i}(X_{ijkl}) + b_{6i}(X_{ijkl})^2 + e_{ijkl}$$

where Y_{ijkl}, u, LT_i, GG_j, PAR_k, b_{1i}, b_{2i}, LS_{ijkl} and e_{ijkl} are as described for model 1 and/or model 2 and

b_{3i}, b_{4i} = partial, within-littertype regression coefficients,

BW_{ijkl} = covariable birthweight,

b_{5i}, b_{6i} = partial, within-littertype regression coefficients,

and X_{ijkl}= either covariable within-litter standard deviation (s.d.) for birthweight or within-litter coefficient of variation (c.v.) for birthweight.

Table 7.7   The preweaning growth rate of piglets after correction for genetic group, parity and litter size at birth (linear and quadratic) (A) or genetic group, parity, litter size at birth (linear and quadratic) and birthweight (linear) (B) for each of the classification classes for individual piglets.

Littertype		A		B	
		Growth rate (g/day)	Sign. L-R	Growth rate (g/day)	Sign. L-R
Normal		223		218	
1 or 2 runts	L	180[c]	0.0001	197[c]	0.0001
	R	225		218	
Left-hand individuals	L	197[c]	0.0001	206[b]	0.0042
	R	233[b]		221	
Right-hand individuals	L	217	0.0344	214	0.3277
	R	249[a]		230	
1 or 2 giants	L	221	0.0142	221	0.4964
	R	247[b]		228	

a, b, c: significantly different from the normal distribution
        (a: p<0.05 ; b: p<0.01 ; c: p<0.001).

Piglets with a birthweight below 1 kg have a high death risk, independent of their status within the litter. This justifies the conclusion that the intrinsic viability of a runt or left-hand individual with a birthweight below 1 kg is not less than that of a comparable piglet from a litter with a normal within-litter weight distribution. The observed tendency towards higher death risks for runts and left-hand individuals with birthweights between 1.0 and 1.8 kg in comparison to piglets with comparable birthweights from litters with a normal within-litter weight

distribution, is due to the fact that the former have by definition the lowest birthweights within their litters, whereas the latter will mainly represent average piglets. Even a runt or left-hand individual with a birthweight of 1.8 kg will still have to compete with its heavier littermates, especially if the litter is large. Based on the results of a study in which the increase in body weight after birth was registered, Dyck and Swierstra (1987) concluded that the failure of a piglet to obtain an adequate milk supply within a few days of birth is the primary factor contributing to piglet death.

The effect of littertype on the average preweaning growth rate within a litter is merely a consequence of the relationship between littertype and litter size. In each of the four littertypes with two discrete subpopulations the average preweaning growth rate differed significantly between the subpopulations if only the effect of litter size on preweaning growth rate was taken into account. Within litters with right-hand individuals and litters with giants this difference was completely due to the difference in average weight of the two subpopulations. Within litters with runts and litters with left-hand individuals this difference (45 g/day and 36 g/day, respectively) decreased due to correction for birthweight, but remained significant (21 g/day and 15 g/day, respectively). This indicates that the growth of runts and left-hand individuals is less than expected on the basis of their birthweight.

It has been shown that newborn porcine runts have low protein/DNA ratios in quadriceps muscles, kidneys and heart (Widdowson, 1971), anatomically and chemically less mature bones (Adams, 1971) and a lower respiratory enzyme activity in the longissimus dorsi but not in diaphragm and heart muscle (Hayashi et al., 1987). According to Hegarty and Allen (1978), runts have a reduced muscle growth potential. As a consequence of this they needed 23 days more to reach a weight of approximately 105 kg in comparison with littermates. Unfortunately, in all mentioned studies the runts were compared with littermates with a birthweight which was approximately equal to or clearly higher than the within-litter average. Only a comparison between runts and piglets with corresponding weights from litters with a normal within-litter weight distribution will give decisive information concerning possible physiological differences which are not merely weight dependent.

CHAPTER 8

GENERAL DISCUSSION AND CONCLUSIONS

In the present study aspects of the impact of early pregnancy on the within-litter average prenatal development and the within-litter weight distribution at birth have been investigated. Before discussing the results some general remarks must be made concerning the calculation of the prenatal mortality rate, the observed variation in prenatal mortality and the relationship between embryonic mortality and foetal mortality.

General remarks

In this study the difference between the number of corpora lutea and the number of apparently normal and healthy embryos or foetuses with no signs of degeneration was assumed to be a consequence of prenatal mortality and not due to fertilization failure. This assumption is supported by the work of Haines et al. (1959) and Perry and Rowlands (1962). Both research groups found that more than 95% of all ovulated oocytes are fertilized after a single insemination. According to Perry and Rowlands (1962) the fact that this is not 100% is mainly due to a small proportion of animals in which fertilization does not occur at all. However, Van der Hoeven et al. (1985) found on average 6.8% unfertilized oocytes in 10 gilts which were all pregnant at slaughter on day 5 or 6 after insemination on the first day of standing heat, indicating that fertilization is not necessarily an all or nothing phenomenon. Although in a small proportion of gilts some oocytes might not be fertilized, it seems justifiable to conclude that variation in the calculated prenatal mortality rate gives reliable information about the actual variation in prenatal mortality. Whether this is also true for induced gilts is not clear. According to Polge (1982) fertilization in superovulated gilts is generally normal except when the ovulation rate is excessively high and a number of follicles with immature oocytes may ovulate. However, the superovulated gilts mentioned by Polge were cycling gilts which were given gonadotrophic hormones at an appropriate time of the

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cycle (day 15 or 16 of the oestrous cycle). In contrast, the induced gilts in the present study were treated with gonadotrophic hormones because they did not start to cycle spontaneously. The number of corpora lutea in the induced gilts varied between 5 and 53 (coefficient of variation 45%) whereas in the non-induced gilts it varied between 6 and 20 (coefficient of variation 17%). Especially in gilts which responded with superovulation, the fertilization rate might not be as high as in non-induced gilts, thus influencing the reliability of the calculated embryonic or prenatal mortality rate.

Despite numerous studies concerning embryonic mortality in the pig, hardly any attention has been given to the fact that considerable variation in embryonic mortality exists between gilts, even if they are kept under the same conditions. In the present study the embryonic mortality rate for non-induced gilts which were slaughtered on day 35 of pregnancy varied between 0% and 67%. The prenatal mortality rate for non-induced gilts which were slaughtered during the foetal stage of pregnancy varied between 0% and 86%. The latter is in good agreement with the results reported by Perry (1960). Based on corpora lutea counts during pregnancy and the actual litter size at birth he found a total mortality rate that varied between 0% and 85%. Unpublished own results revealed that the distribution of embryonic mortality rates in a group of gilts which had been kept under the same conditions, is not binomial. There were more gilts with a very low or a high embryonic mortality rate than expected on the basis of a binomial distribution. These results indicate that embryonic mortality is not a random phenomenon. Because of this and because of its large variation between gilts, the embryonic mortality rate was considered to be an interesting parameter to characterize the course of early pregnancy.

In the pig the majority of prenatal mortality is embryonic mortality (Wrathall, 1971; Pope and First, 1985; this study). In the present study it was assumed that the variation in total prenatal mortality as determined after day 35 of pregnancy is largely due to variation in embryonic mortality. However, the ranking of gilts on the basis of their prenatal mortality rate does not necessarily resemble the ranking on the basis of their embryonic mortality rate. Especially in gilts with a high ovulation rate and a low embryonic mortality rate, foetal mortality might be more important than in other gilts, mainly due to intrauterine crowding.

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Experiments in which intrauterine crowding was induced have shown that it increases the extent of foetal death, mainly due to placental insufficiency (Dziuk, 1968; Fenton et al., 1970; Webel and Dziuk, 1974; Knight et al., 1977; Leymaster et al., 1986).

The point of time of foetal mortality is not well established. Knight et al. (1977) found in unilaterally hysterectomized-ovariectomized gilts, in comparison to intact gilts, increased prenatal mortality rates from day 40 onwards. The mortality occurred mainly between day 40 and day 70 of pregnancy. Leymaster et al. (1986) also compared unilaterally hysterectomized-ovariectomized gilts with intact control gilts and found, in contrast to Knight et al. (1977), the occurrence of significant foetal loss due to overcrowding after day 86 of pregnancy. On the basis of these results no general conclusion about the point of time of foetal mortality can be drawn. In the present study the prenatal mortality increased linearly with stage of pregnancy (see chapter 5, figure 5.1). The average number of dead foetuses found per gilt was also independent of stage of pregnancy (results not shown). From these results it seems that the foetal mortality occurred evenly distributed between day 35 and day 114 of pregnancy. Whether this is also true for foetal mortality due to overcrowding is not clear, but as has been discussed in chapter 5, the results of the present study concerning the relationship between prenatal mortality and prenatal development indicate that this might have occurred mainly during late pregnancy.

Prenatal development and embryonic mortality

Given the fact that the fertilization rate in the pig is almost 100%, variation in litter size is due to variation in ovulation rate and variation in prenatal mortality rate. According to Leymaster et al. (1986) prenatal mortality is 1.7 times as important as ovulation rate in determining litter size at birth in normal intact gilts. In the present study the correlations of ovulation rate and embryonic mortality rate with number of embryos on day 35 of pregnancy were 0.51 and -0.77, respectively (chapter 4; square roots of R^2 values given in section 4.3). The corresponding correlations during the foetal stage of pregnancy were 0.41 and -0.84, respectively (chapter 5). These results are in good agreement

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with those of Johnson et al. (1985) who found phenotypic correlations of ovulation rate and prenatal mortality rate with litter size of 0.31 and -0.73, respectively. If this high correlation between number of conceptuses and embryonic or prenatal mortality rate is taken into consideration, it is not surprising that almost all relationships between conceptus parameters and embryonic or prenatal mortality seem to be due to the effect of embryonic or prenatal mortality on the number of embryos or foetuses present.

At birth piglets from small litters are on average heavier than piglets from large litters. The correlation between birthweight and litter size varies between -0.20 and -0.48 (reviewed by Cöp, 1971). At the end of the embryonic stage of pregnancy the embryos from litters with a low embryonic mortality rate, i.e. the larger litters, were heavier than embryos from litters with a high embryonic mortality rate, i.e. the smaller litters (Lutter et al., 1981; this study, chapter 4). The faster growth of foetuses from litters with a higher embryonic mortality rate (the smaller litters) finds its roots in the relationship which was found between embryonic mortality and placental development of the day 35 embryos. In comparison with the embryos from gilts with a low embryonic mortality rate the embryos from gilts with a high embryonic mortality rate had better developed placentae by day 35 of pregnancy and will benefit from this during the foetal stage. The fact that the present study (chapter 5) indicates a low birthweight in litters with a high prenatal mortality rate might be due to the inadequacy of the fitted model to describe the extreme values of the growth curves accurately. It is also possible that in some litters with a low embryonic mortality rate (probably the largest litters) foetal mortality occurred late during pregnancy. These litters are then classified as litters with a high prenatal mortality rate while the development of the surviving foetuses resembles that of foetuses from large litters. In this respect it is of interest that Leymaster et al. (1986) have established the occurrence of significant foetal loss between day 86 of pregnancy and farrowing.

The negative relationship of embryonic weight and length with embryonic mortality rate as established in the present study (chapter 4) strongly suggests that favourable conditions for embryonic survival are also favourable for embryonic development. There are two possible explanations

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which are of interest in this respect. At first, variation between gilts in average oocyte quality might exist. Qualitative good oocytes might give qualitative good embryos, i.e. embryos which have a good growth potential and therefore (or also) a good viability. Secondly, the variation between gilts in the quantitative, qualitative and temporal characteristics of the uterine environment might be of importance. The functions of uterine secretion products have recently been reviewed by Roberts and Bazer (1988). This review emphasizes the complexity of the changes in the uterine environment during early pregnancy and simultaneously confirms that our knowledge about the role of specific components of uterine secretion products as far as embryonic development is concerned, is still limited. The experiment which has been described in chapter 3 was implemented to enable studies aimed at a better understanding of the role of the uterus and its secretion products as determinants of embryonic development and embryonic mortality, but also to enable studies concerning the impact of aspects of early pregnancy on subsequent prenatal development and even postnatal performance. The results shown in chapter 3 clearly indicate that it is impossible to affect the functional integrity of the uterus of gilts adversely by means of a severe, long lasting growth retardation during the first 80 days of life. This period was chosen because the endometrial glands which produce relatively large amounts of uterine secretion products during early pregnancy, differentiate during early life (Bal and Getty, 1970).

In comparison to day 35 embryos in gilts with a low embryonic mortality rate, the embryos in gilts with a high embryonic mortality rate not only had longer placentae but also more uterine space available per embryo, even at a same number of embryos present. Although the most plausible inference seems to be that more uterine space available allows an increase in placental length, the results concerning the length of the implantation site per embryo, i.e. the length of endometrium in contact with the placenta, are not in agreement with this conclusion. After correction for the number of embryos, the length of the implantation site per embryo hardly changed with an increasing embryonic mortality. This indicates that the placental length can increase while the length of the implantation site remains constant. This is only possible if the degree of folding of the uterine wall adjacent to the placenta increases. The present results do not

litter weight distribution, but right-hand individuals and giants were somewhat heavier.

It has been postulated that within-litter variation in developmental stage of preimplantation embryos is reduced shortly after day 11 of pregnancy by a mechanism of selective mortality of the less developed embryos (Pope et al., 1982a; Pope et al., 1986a, 1986b; Morgan et al., 1987a, 1987b; see also chapter 2, section 2.2.2.). The relationship between littertype and embryonic mortality rate therefore indicates that a relationship between the within-litter weight distribution at day 35 of pregnancy and at day 11 of pregnancy might exist. In order to be compatible with the results as summarized in figure 8.1 the alternatives which can be expected by day 11 of pregnancy must be as shown in figure 8.2. Although the within-litter distribution of developmental stage of embryos might be normal (Gaussian) by day 11 of pregnancy, in figure 8.2 only alternatives for litters with two discrete subpopulations are shown. There is some evidence to support the hypothesis that a group of retarded embryos exists in the majority of preimplantation litters. As far as protein content of blastocysts is concerned, Wright et al. (1983) found in each of five sows which had been slaughtered on day 9 of pregnancy, two or three embryos which contained clearly less protein than their littermate embryos. Although less evident, the same observation was made on day 6, 7 and 8 of pregnancy (n – 5 on each day).

According to the hypothesis visualized in figure 8.2, the majority of gilts with a normal within-litter weight distribution by day 35 of pregnancy had by day 11 of pregnancy a relatively large group of fully developed embryos and a relatively small group of highly growth retarded embryos. Because of the extent of their retardation all retarded embryos will die shortly after day 11. From figure 8.1 it is clear that the average retardation of runts is larger than that of left-hand individuals. Thus it was assumed that the average degree of retardation by day 11 of pregnancy depends on the size of the group of retarded embryos: the larger the group, the smaller the average degree of retardation. If this is the case, the average chance of retarded embryos to die will decrease with an increasing size of the retarded group. For litters with 1 or 2 runts and litters with left-hand individuals this seems to be the case. The results for the litters with right-hand individuals and litters with giants, however, are

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WITHIN–LITTER WEIGHT DISTRIBUTION ON DAY 11 OF PREGNANCY

CHANCE TO
SURVIVE LOW

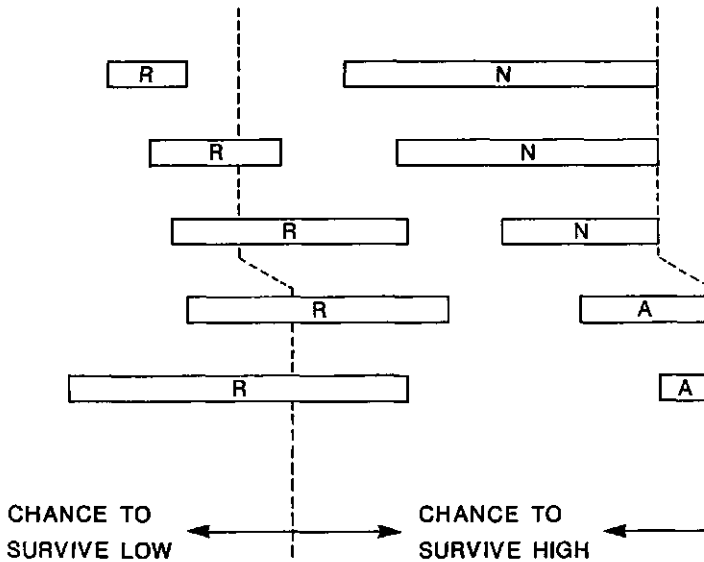CHANCE TO
SURVIVE HIGH

Figure 8.2 Hypothetical alternatives for the within-litter weight
distribution by day 11 of pregnancy based on the results
summarized in figure 8.1 and the postulated mechanism for the
reduction of within-litter variation in preimplantation
development through selective mortality of retarded embryos.
Going from the top to the bottom, these alternatives represent
the day 11 version of litters with a normal within-litter
weight distribution, litters with 1 or 2 runts, litters with
left-hand individuals, litters with right-hand individuals and
litters with 1 or 2 giants. (R — retarded development; N —
normal day 11 development; A — accelerated development)

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not compatible with this concept. Especially the high average embryonic mortality rate in litters with giants and, to a lesser extent, the fact that the right-hand individuals and giants seem to be slightly enhanced in development (see figure 8.1), lead to the assumption that an increasing difference in embryonic developmental stage between the two subpopulations exists if the group of retarded embryos becomes relatively large or if the well developed group shows an enhanced development. The difference in weight between the giants or right-hand individuals and their respective littermates as found by day 35 of pregnancy (see figure 8.1) is not in agreement with the last assumption, but it should be kept in mind that the average weights for giants, right-hand individuals and their respective littermates were based on very low numbers of observations.

The cause (or causes) of within-litter variation in preimplantation development is (are) not clear. A possible cause is the length of the ovulation interval, i.e. the length of the period between the first and the last ovulation. According to Wilde et al., (1987) the majority ($73 \pm 2\%$) of follicles ovulates almost simultaneously while the remaining follicles ovulate during the next 4 hours. They also demonstrated experimentally that the variation in developmental stage among littermate embryos by day 11 of pregnancy is at least for a part due to this ovulation pattern. Apart from extrinsic factors like this, intrinsic factors, like oocyte quality and genotype of the embryos, might also be important. In this respect it is of interest that a gene has been described in mice which influences the time of onset of the first cleavage division and the subsequent rate of embryonic cleavage (Goldbard et al., 1982; Warner et al., 1988). This gene, called preimplantation-embryo-development (Ped) gene, is linked to the mouse major histocompatibility complex (MHC), the H-2 complex (Warner et al., 1987a). Two functional Ped gene phenotypes, fast and slow, have been defined (Goldbard et al., 1982). Recently it has been shown that only embryos expressing the fast Ped allele show the presence of Qa-2 antigen (Warner et al., 1987b). The latter is a Class I antigen encoded in the Q region of the mouse MHC. These results suggest that the Ped gene is located in the Q region of the H-2 complex. The Qa-2 antigen might be the Ped gene product (Warner et al., 1987b). Although there is still no evidence for a Ped gene in pigs, there is increasing evidence that reproduction in the pig, including litter size, is associated with the swine MHC complex, the

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SLA complex (Renard and Bolet, 1983; Rothschild et al., 1984; Grob, 1987; Mallard et al., 1987; Conley et al., 1988).

The results of the present study have indicated that the preweaning death risk and average preweaning growth rate within a litter are independent of the type of within-litter weight distribution if this comparison is made at a constant litter size. It has also been shown that the litters with an abnormal within-litter weight distribution (mainly litters with 1 or 2 runts and litters with left-hand individuals) were on average approximately 0.7 piglet larger than the litters with a normal within-litter weight distribution. From an economic point of view the occurrence of litters with two discrete subpopulations of piglets is therefore positive rather than negative. Since approximately 33% of all litters have an abnormal within-litter weight distribution, the average litter would have been 0.23 piglet smaller if all litters resembled normal litters. It can be concluded from these results that a reduction of embryonic mortality will be profitable, even if it increases the occurrence of litters with an abnormal within-litter weight distribution.

Impact of early pregnancy on prenatal development

From a pig producers point of view, the number of piglets weaned per litter should be high. To achieve this, the number of liveborn piglets per litter and the survival rate of these piglets during lactation should be high. Since the preweaning survival rate of liveborn piglets depends at least to some extent on the average birthweight per litter and the within-litter variation in birthweight, it is important to know the determinants of prenatal development. Based on the available information about pregnancy in the pig, there are several reasons to assume that the important determinants of differences in prenatal development, between and within litters, are associated with the course of early pregnancy. The results of the present study provide some evidence for this assumption. There are, however, more results to support it. These results refer to spacing, transuterine migration, embryo-induced growth of the uterus and placental development. Spacing and trans-uterine migration occur between day 7 and day 12 of pregnancy (Dziuk et al., 1964; Dhindsa et al., 1967) and optimize the chance of each individual foetus to survive and develop normally until

term (Dziuk, 1985). Since each foetus requires at least 30 cm of uterine space to survive and requires 35 cm to develop fully (Wu et al., 1988a), it is of interest to know that the increase in length of the uterine horns of pregnant sows between day 15 and day 27 of pregnancy is dependent on the presence of embryos (Wu et al., 1988b). The latter was concluded from the fact that the non-gravid uterine horns of unilaterally pregnant sows did not show the increase in length that was observed for the gravid uterine horns. A better understanding of the mechanism of this growth, the nature of the embryonic signal involved and the factors which limit this growth, is important. If this growth can be enhanced through exogenous stimuli, the capacity of the uterus to maintain more foetuses might be increased. Uterine space available per embryo is of importance, at least as far as placental development is concerned. This has been demonstrated by Knight et al. (1977). They concluded from their studies with unilaterally hysterectomized-ovariectomized sows that the extent of placental development between day 20 and day 30 of pregnancy influences the subsequent foetal growth.

If the whole period of pregnancy is considered, the developmental processes during the embryonic stage of pregnancy seem to be more complex than those during the foetal stage of pregnancy. The impact of early pregnancy on litter size, i.e. the importance of variation in embryonic mortality as a cause of variation in litter size, has been recognized and efforts have been, and still are, undertaken to reduce embryonic loss. The impact of early pregnancy on prenatal development has been recognized to some extent, but has not been investigated in depth. A better understanding of the regulation and mechanism of early pregnancy might contribute to a better understanding of the sources of variation in embryonic and fetal development within and between litters. Whether it will be possible to manipulate early pregnancy in order to optimize birthweight and minimize variation in birthweight is not clear, but should not be precluded. Taking into consideration the results of the present study together with the large volume of information about variation in early embryonic development and embryonic mortality, priority should be given to research aimed at a better understanding of the causes of variation in early embryonic development. A reduction of this variation might not only reduce the extent of embryonic mortality, but also the variation in prenatal development and thus

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birthweight, between as well as within litters. This will be to the benefit of the pig producer, because the increase in litter size at birth and the decrease of the death risk of piglets during lactation will have additive positive effects on the number of piglets weaned per litter. If the reduction of embryonic mortality increases the occurrence of litters with two subpopulations, which is not likely to be the case, it will still be beneficial for the pig producer because litter size will increase without an unexpected increase in piglet mortality or decrease in average preweaning growth rate.

Conclusions

From the results of the present study the following conclusions can be drawn:

1. The functional integrity of the uterus of gilts as measured by its ability to support the survival and normal development of embryos, can not be adversely affected by a regular, severe growth retardation during the first 80 days of life, i.e. during the period of differentiation of the uterine glands.

2. Day 35 embryos in gilts with a low embryonic mortality rate (the larger litters) are better developed than day 35 embryos in gilts with a high embryonic mortality rate (the smaller litters), indicating that factors that are favourable for embryonic survival are also favourable for embryonic development or are associated with factors that are favourable for embryonic development.

3. The placentae of day 35 embryos in gilts with a high embryonic mortality rate (the smaller litters) are better developed than the placentae of day 35 embryos in gilts with a low embryonic mortality rate (the larger litters). As a consequence the foetuses in gilts with a high embryonic mortality rate will grow faster than foetuses in gilts with a low embryonic mortality rate.

4. The within-litter weight distribution is normal (Gaussian) in

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approximately 67% of all litters; within the remaining litters two discrete subpopulations of variable size can be identified.

5. The within-litter weight distribution at birth is established at the end of the embryonic stage of pregnancy (day 35) and is related to the embryonic mortality rate.

6. The within-litter weight distribution at birth is neither an important determinant of the within-litter variation in birthweight, nor an important determinant of the preweaning death risk of liveborn piglets.

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SUMMARY

In the present study aspects of the impact of early pregnancy on the average prenatal development per litter and on the within-litter weight distribution at birth have been investigated. The aims of the present study are given in the introduction (chapter 1). A brief review of the literature concerning the chronology of early pregnancy and embryonic mortality in the pig is given in chapter 2.

In chapter 3 an experiment is described in which it was attempted to affect the development and functioning of the uterus structurally in order to obtain a model in which the role of the uterus and its secretion products as determinants of embryonic mortality and/or embryonic development could be studied. The possibility to affect the functional integrity of the uterus by means of a severe growth retardation during the first 80 days of life, i.e. during the period in which the uterine glands differentiate, was investigated. A group of female piglets were weaned within 24 hours after birth and either fed unrestricted (n=35) or restricted (n=34). The restricted fed piglets were allowed to grow at a rate of approximately 50% of that of their unrestricted littermates. This contrast was maintained until day 80 after birth. Another group of piglets (control group, n=38) were normally weaned at an age of 35 days and subsequently fed unrestricted until day 80. From day 35 onwards all piglets were kept under the same conditions and from day 80 onwards they were also treated the same. A representative sample from each of the three groups (unrestricted fed (n=8), restricted fed (n=8) and control (n=10)) were slaughtered at an age of 80 days to study the histomorphology of their uterus. The remaining gilts which reached puberty and became pregnant (n=50) were slaughtered on either day 34, 35 or 36 of first pregnancy. The uterine and conceptus development were subsequently studied.

At day 80 the average weight of restricted fed piglets was 45% of that of unrestricted fed piglets and 48% of that of control piglets. Although the averages for uterine length and weight, thickness of the myometrium and endometrium and the relative glandular surface area were all lower in the restricted fed than in both other groups, only the difference in thickness of the myometrium between the restricted fed group and control group was significant. All differences were merely due to differences in bodyweight.

No negative effects were seen on ovulation rate, number of embryos, embryonic mortality rate, uterine length and weight or any of the parameters for conceptus development. This indicates that the functional integrity of the uterus is not affected by a severe growth retardation during the first 80 days of life.

With the data collected for the gilts which were slaughtered on day 35 of pregnancy in this experiment (n=31) and data collected for another group of Dutch Landrace gilts which were also slaughtered on day 35 of pregnancy (n=40), the relationship between conceptus development and embryonic mortality was studied. The results of this study are described in chapter 4. For purposes of interpretation of the results, especially concerning the development of the placentae, relevant uterine parameters were also considered. The results indicate that the embryonic weight and length significantly decrease with an increasing embryonic mortality rate, whereas the placental weight and length significantly increase with an increasing embryonic mortality rate. Statistical analyses have shown that this decrease in embryonic development with an increasing embryonic mortality rate was not due to the concomitant increase in placental development. After correction for differences in number of embryos, these relationships (except for placental length) were no longer significant, indicating that embryonic mortality is related to conceptus development through its relationship with number of embryos. It was concluded that factors that caused a high embryonic mortality - and thus small litters - also caused a low embryonic weight and length. From the fact that the uterine length available per embryo significantly increased with an increasing embryonic mortality, even after correction for the number of embryos, it was concluded that the relationship of embryonic mortality with placental development might be due to the effect that embryos which died had on the uterine length before their death.

To study whether the accelerated growth of the placentae in gilts with a high embryonic mortality rate will be beneficial for the foetal development until birth, the relationship between foetal development and the prenatal mortality rate was studied. The results of this study for which 195 pregnant Dutch Landrace gilts were slaughtered between day 35 and day 112 of pregnancy, are described in chapter 5. From these results it was clear that the weight gain of foetuses between day 35 and day 100 of

pregnancy was higher within gilts with a high prenatal mortality rate than within gilts with a low prenatal mortality rate. There were also marked differences between these two groups for placental development during this period. Within the group of gilts with a high prenatal mortality rate the placental weight and length increased until day 95 of pregnancy, to decrease thereafter. Within the group of gilts with a low prenatal mortality rate it increased until day 65, remained fairly constant until day 95, to increase rapidly thereafter. Although the prenatal mortality rate during the early foetal stage is most probably still a good estimator of the embryonic mortality rate, towards the end of pregnancy this is almost certainly no longer the case. The present study therefore does not allow decisive conclusions as to the relationship between embryonic mortality rate and the average birthweight.

In chapter 4 and 5 the emphasis has been on the variation in prenatal development between litters. In chapter 6 and 7 one aspect of differences in prenatal development within litters (the within-litter weight distribution) has been studied. Although it is generally assumed that the within-litter weight distribution is normal (Gaussian), evidence has been provided for the fact that in approximately one-third of litters the distribution is abnormal in a sense that two subpopulations can be identified within these litters. On the other hand there is an accumulation of indications that within-litter variation in embryonic developmental stage can occur very early in pregnancy and that this variation is reduced before or shortly after the time of maternal recognition of pregnancy (day 11) through selective mortality of the less developed embryos. The results described in chapter 6 confirms the fact that the within-litter weight distribution is abnormal in 33% of all litters studied (466 foetal litters and 915 litters at term). On the basis of the within-litter weight distribution 5 littertypes were defined: normal litters (one normal distribution), litters with one or two runts (two discrete subpopulations: one main distribution and one or two growth retarded outliers), litters with left-hand individuals (two discrete subpopulations, the left-hand distribution numerically smaller than or equal to the right-hand distribution and both larger than 2), litters with right-hand individuals (two discrete subpopulations, the right hand distribution numerically smaller than the left-hand distribution and both larger than 2) and litters

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with one or two giants (two discrete subpopulations: one main distribution and 1 or 2 growth accelerated outliers). The results strongly suggest that the within-litter weight distribution as found at term has been established by the end of the embryonic stage (day 35) of pregnancy, at least in the majority of litters. The average embryonic mortality rate differed between littertypes. The lowest mortality rate was found for the litters with left-hand individuals, the highest for litters with giants.

The preweaning death risk and preweaning growth rate of piglets in relation to the within-litter weight distribution of the litter in which they were born and suckled were subsequently studied. The results, based on data for 819 litters, are described in chapter 7. The preweaning death risk of piglets from litters with two discrete subpopulations was not higher than that for piglets from litters with a normal within-litter weight distribution. In all 5 littertypes the death risk was similarly dependent on birthweight, litter size and within-litter variation in birthweight. The average preweaning growth rate per litter differed between littertypes but was entirely due to differences in average litter size at birth. Within each of the 4 littertypes with two discrete subpopulations the average growth rate of the piglettype with the lower average birthweight was always less than that for the piglettype with the higher average birthweight. Within litters with runts and left-hand individuals this remained the case even after correction for birthweight, indicating that the growth rate of runts and left-hand individuals is less than would be expected on the basis of their birthweights.

A general discussion of the results and the conclusions are given in chapter 8. The results of the present study allows the following conclusions:

1. The functional integrity of the uterus of gilts as measured by its ability to support the survival and normal development of embryos, can not be adversely affected by a regular, severe growth retardation during the first 80 days of life, i.e. during the period of differentiation of the uterine glands.

2. Day 35 embryos in gilts with a low embryonic mortality rate (the larger litters) are better developed than day 35 embryos in gilts with a high

embryonic mortality rate (the smaller litters), indicating that factors that are favourable for embryonic survival are also favourable for embryonic development or are associated with factors that are favourable for embryonic development.

3. The placentae of day 35 embryos in gilts with a high embryonic mortality rate (the smaller litters) are better developed than the placentae of day 35 embryos in gilts with a low embryonic mortality rate (the larger litters). As a consequence the foetuses in gilts with a high embryonic mortality will grow faster than foetuses in gilts with a low embryonic mortality rate.

4. The within-litter weight distribution is normal (Gaussian) in approximately 67% of all litters; within the remaining litters two discrete subpopulations of variable size can be identified.

5. The within-litter weight distribution at birth is established at the end of the embryonic stage of pregnancy (day 35) and is related to the embryonic mortality rate.

6. The within-litter weight distribution at birth is neither an important determinant of the within-litter variation in birthweight, nor an important determinant of the preweaning death risk of liveborn piglets.

SAMENVATTING

In dit onderzoek zijn aspecten van de invloed van de vroege dracht op de gemiddelde prenatale ontwikkeling per toom en de aard van de verdeling van geboortegewichten binnen een toom bestudeerd. De doelstellingen van het onderzoek worden in de inleiding (hoofdstuk 1) aangegeven. In hoofdstuk 2 wordt een kort overzicht gegeven van de literatuur met betrekking tot de chronologie van de vroege dracht en embryonale sterfte bij het varken.

In hoofdstuk 3 wordt een experiment beschreven waarin is getracht de ontwikkeling en het functioneren van de uterus van gelten structureel te beïnvloeden, teneinde een model te verkrijgen waarmee de invloed van de uterus en haar secretieproducten op de incidentie van embryonale sterfte en de embryonale ontwikkeling kan worden bestudeerd. Getracht is de differentiatie van de uteriene klieren negatief te beïnvloeden door middel van een sterke voerbeperking gedurende de periode waarin deze differentiatie optreedt. Een groep Nederlands Landras gelten werd binnen 24 uur na geboorte gespeend en vervolgens onbeperkt of beperkt gevoerd (n=35 en n=34, respectievelijk). De beperkt gevoerde gelten werden zodanig gevoerd dat hun groei ongeveer 50% bedroeg van dat van hun onbeperkt gevoerde toomgenoten. Dit verschil in voeropname werd gehandhaafd tot een leeftijd van 80 dagen. Een derde groep Nederlands Landras gelten (de controle groep, n=38) werd gespeend op een leeftijd van 35 dagen en vervolgens onbeperkt gevoerd tot een leeftijd van 80 dagen. Vanaf dag 35 werden alle gelten onder dezelfde omstandigheden gehuisvest en vanaf dag 80 werden alle gelten gelijk behandeld. Een representatieve steekproef uit elk van de drie proefgroepen (onbeperkt gevoerd, n=8; beperkt gevoerd, n=8; controle groep, n=10) werd geslacht op een leeftijd van 80 dagen teneinde de histomorfologie van de uterus te bestuderen. Van de resterende gelten zijn er uiteindelijk 50 geslacht op dag 34, 35 of 36 van de eerste dracht. Bij deze gelten werd de ontwikkeling van de uterus, embryo's en vruchtvliezen bestudeerd.

Op een leeftijd van 80 dagen was het gemiddelde gewicht van de beperkt gevoerde gelten 45% van dat van de onbeperkt gevoerde gelten en 48% van dat van de controle gelten. De waarden voor de lengte en het gewicht van de uterus, de dikte van het myometrium en endometrium en het percentage van de oppervlakte van een doorsnede van het endometrium dat bestond uit klierdoorsneden waren allen lager in de beperkt gevoerde groep dan in beide

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andere groepen. Alleen het verschil in dikte van het myometrium tussen de beperkt gevoerde en de controle groep was significant. De gevonden verschillen bleken echter slechts een gevolg te zijn van het reeds genoemde verschil in lichaamsgewicht.

Bij de gelten die gedurende de dracht zijn geslacht, werden geen verschillen gevonden ten aanzien van het aantal ovulaties, aantal embryo's, embryonaal sterftepercentage, lengte en gewicht van de uterus en de ontwikkeling van de embryo's en hun vruchtvliezen. Uit dit onderzoek is duidelijk geworden dat het functioneren van de uterus niet te beïnvloeden is door een sterke groeivertraging gedurende de eerste 80 levensdagen.

Met de gegevens die in het hiervoor beschreven experiment zijn verzameld bij de gelten die op dag 35 van de dracht zijn geslacht (n=31) en overeenkomstige gegevens verzameld bij een groep van Nederlands Landras gelten die eveneens op dag 35 van de dracht zijn geslacht (n=40), is onderzocht of er een relatie bestaat tussen de ontwikkeling van embryo's en hun vruchtvliezen op dag 35 van de dracht en de incidentie van embryonale sterfte. Teneinde de resultaten beter te kunnen interpreteren, in het bijzonder voor wat betreft de ontwikkeling van de placentae, zijn relevante uteriene parameters in het onderzoek meegenomen. De resultaten van dit onderzoek geven aan dat het gewicht en de lengte van embryo's significant afnemen met een toename van het embryonale sterftepercentage'. Het gewicht en de lengte van de placentae nemen daarentegen juist toe met een toename van het embryonale sterftepercentage. Uit de statistische analyses kwam duidelijk naar voren dat de negatieve relatie tussen embryonale ontwikkeling en embryonale sterfte niet een gevolg is van de positieve relatie tussen placenta-ontwikkeling en embryonale sterfte. Indien werd gecorrigeerd voor het aantal aanwezige embryo's waren de hiervoor genoemde relaties niet meer significant, met uitzondering van de relatie tussen placenta lengte en embryonale sterfte. Dit geeft aan dat de relatie tussen embryonale sterfte en de ontwikkeling van de embryo's en vruchtvliezen hoofdzakelijk samenhangt met de relatie tussen embryonale sterfte en het aantal aanwezige embryo's. Uit dit onderzoek wordt geconcludeerd dat de factoren die ten grondslag liggen aan een hoge embryonale sterfte - en dus aan kleine tomen -ook ten grondslag liggen aan een verminderde ontwikkeling van de embryo's. Gezien het feit dat de per embryo beschikbare lengte van de uterus significant toeneemt met een toename van

de embryonale sterfte, zelfs indien er gecorrigeerd wordt voor het aantal aanwezige embryo's, kan worden geconcludeerd dat de relatie tussen embryonale sterfte en de ontwikkeling van de placentae waarschijnlijk samenhangt met de invloed die ook de embryo's die reeds zijn afgestorven, nog voor hun dood hebben gehad op de lengte toename van de uterus.

Teneinde na te gaan of de versnelde groei van de placentae in gelten met een hoge embryonale sterfte een gunstig effect heeft op de foetale groei, is de relatie tussen foetale ontwikkeling en prenatale sterfte bestudeerd. Voor dit onderdeel zijn in totaal 195 Nederlands Landras gelten geslacht tussen dag 35 en dag 112 van de dracht. De resultaten, beschreven in hoofdstuk 5, geven aan dat de gewichtstoename van foeten tussen dag 35 en dag 100 van de dracht hoger is in gelten met een hoge prenatale sterfte. Er waren tussen de gelten met een hoge embryonale sterfte en de gelten met een lage embryonale sterfte gedurende genoemde periode eveneens duidelijke verschillen in de ontwikkeling van de placentae. In de groep van gelten met een hoge prenatale sterfte namen het gewicht en de lengte van de placentae toe tot dag 95 van de dracht, om daarna af te nemen. In de groep van gelten met een lage prenatale sterfte namen het gewicht en de lengte van de placentae toe tot dag 65, bleven vervolgens vrijwel constant tot dag 95 om daarna snel toe te nemen. Hoewel het prenatale sterftepercentage gedurende het eerste deel van de foetale fase hoogstwaarschijnlijk betrouwbare informatie geeft over het embryonale sterftepercentage, zal dit tegen het einde van de dracht veel minder het geval zijn doordat dan de foetale sterfte een rol gaat spelen. Uit dit onderzoek kan daarom geen eenduidige conclusie worden getrokken voor wat betreft de relatie tussen embryonale sterfte en gemiddelde geboortegewicht.

In het in hoofdstuk 4 en 5 beschreven onderzoek heeft de nadruk gelegen op de variatie in prenatale ontwikkeling tussen tomen. In het onderzoek dat beschreven is in hoofdstuk 6 en 7 heeft één aspect van de variatie in prenatale ontwikkeling binnen tomen centraal gestaan. Het betrof hier de gewichtsverdeling binnen tomen. Alhoewel algemeen wordt aangenomen dat de gewichtsverdeling binnen tomen normaal (een Gausse verdeling) is, is aangetoond dat in ongeveer een-derde van alle voldragen tomen twee van elkaar te onderscheiden subpopulaties kunnen worden aangetroffen. Dit is met name van belang omdat er steeds meer aanwijzingen zijn dat variatie in ontwikkelingsstadium van embryo's binnen tomen al in een heel vroeg stadium

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van de dracht (reeds voor dag 10) kan worden waargenomen en dat deze variatie wordt gereduceerd vóór of kort na het tijdstip van maternale herkenning van de dracht (dag 11), en wel door selectieve sterfte van de minder goed ontwikkelde embryo's.

De resultaten die zijn beschreven in hoofdstuk 6 bevestigen dat de gewichtsverdeling in 33% van de onderzochte tomen (466 foetale tomen en 915 voldragen tomen) niet normaal is. Op grond van de gewichtsverdeling binnen tomen zijn 5 typen tomen gedefinieerd: normale tomen (één normale (Gausse) verdeling), tomen met 1 of 2 achterblijvers (twee discrete subpopulaties: een hoofdgroep en één of twee minder goed ontwikkelde uitbijters), tomen met meerdere achterblijvers (twee discrete subpopulaties, de minst ontwikkelde subpopulatie is numeriek kleiner dan, of gelijk aan, de beter ontwikkelde subpopulatie maar bestaat uit meer dan twee individuen), tomen met meerdere voorlopers (twee discrete subpopulaties, de minst ontwikkelde subpopulatie is numeriek groter dan de beter ontwikkelde subpopulatie en de laatstgenoemde bestaat uit meer dan twee individuen) en tomen met 1 of 2 voorlopers (twee discrete subpopulaties: een hoofdgroep en 1 of 2 duide- lijk beter ontwikkelde uitbijters). Uit dit onderzoek kwamen sterke aan- wijzingen dat de gewichtsverdeling binnen voldragen tomen reeds aan het einde van de embryonale fase van de dracht (dag 35) is vastgelegd. Er lijkt verder een verband te bestaan tussen het embryonale sterftepercentage en de aard van de gewichtsverdeling binnen een toom. Het laagste gemiddelde sterftepercentage werd gevonden bij gelten met tomen met meerdere achter- blijvers, het hoogste bij gelten met tomen met 1 of 2 voorlopers.

Tot slot is onderzocht of er een verband bestaat tussen de aard van de gewichtsverdeling binnen een toom enerzijds en de gemiddelde groei van de biggen en de kans op biggesterfte tijdens de zoogperiode anderzijds. De resultaten van dit onderzoek, gebaseerd op gegevens van 819 tomen, zijn beschreven in hoofdstuk 7. De kans op biggesterfte tijdens de zoogperiode was onafhankelijk van de aard van de gewichtsverdeling binnen de tomen. In elk van de 5 typen tomen was de kans op biggesterfte op dezelfde wijze afhankelijk van het geboortegewicht. De gemiddelde groeisnelheid vóór het spenen was verschillend tussen typen tomen, maar deze verschillen waren geheel het gevolg van verschillen in toomgrootte bij de geboorte. In elk van de 4 typen tomen met twee discrete subpopulaties was de groeisnelheid van de subpopulatie met het lagere gemiddelde geboortegewicht lager dan van

de subpopulatie met het hogere gemiddelde geboortegewicht. Binnen de tomen met 1 of 2 achterblijvers en de tomen met meerdere achterblijvers, bleef dit verschil na correctie voor geboortegewicht significant, hetgeen erop duidt dat deze achterblijvers minder hard groeien dan op grond van hun geboortegewicht is te verwachten.

Een algemene discussie over de resultaten staat in hoofdstuk 8, evenals de conclusies. Uit dit onderzoek kunnen de volgende conclusies worden getrokken:

1. Het functioneren van de uterus van gelten, gemeten aan het embryonale sterftepercentage en de ontwikkeling van de embryo's, kan niet negatief worden beïnvloed door een regelmatige, sterke groeivertraging gedurende de eerste 80 levensdagen, d.w.z. gedurende de periode waarin de uteriene klieren zich differentiëren.

2. Op dag 35 van de dracht zijn de embryo's van gelten met een laag embryonaal sterftepercentage (de grotere tomen) beter ontwikkeld dan de embryo's van gelten met een hoog embryonaal sterftepercentage (de kleinere tomen), hetgeen aangeeft dat de factoren die gunstig zijn voor embryonale overleving ook gunstig zijn voor embryonale ontwikkeling of samenhangen met factoren die gunstig zijn voor embryonale ontwikkeling.

3. Op dag 35 van de dracht zijn de placentae van de embryo's van gelten met een hoog embryonaal sterftepercentage (de kleinere tomen) beter ontwikkeld dan de placentae van embryo's van gelten met een laag embryonaal sterftepercentage (de grotere tomen). Dit heeft tot gevolg dat de foeten van gelten met een hoog embryonaal sterftepercentage sneller zullen groeien dan de foeten van gelten met een laag embryonaal sterftepercentage.

4. De verdeling van geboortegewichten binnen een toom is normaal (Gausse verdeling) in ongeveer 67% van alle tomen; in de overige tomen kunnen twee discrete subpopulaties van variabele omvang worden aangetoond.

5. De aard van de verdeling van geboortegewichten ligt reeds vast aan het einde van de embryonale fase van de dracht (dag 35) en hangt samen met

het embryonale sterftepercentage.

6. De aard van de verdeling van geboortegewichten is niet een belangrijke determinant van de variatie in geboortegewicht binnen een toom, noch van de sterftekans van levend geboren biggen tijdens de zoogperiode.

CURRICULUM VITAE

Tette van der Lende werd op 24 september 1954 geboren te Pretoria, Zuid-Afrika. Sinds 1971 woont hij in Nederland. Hij behaalde in 1973 het HAVO-diploma aan het Christelijk Lyceum te Arnhem en in 1974 het Atheneum B-diploma, eveneens aan het Christelijk Lyceum te Arnhem. In september 1974 begon hij met zijn studie Zoötechniek aan de Landbouwhogeschool te Wageningen. Deze studie werd vanaf mei 1975 tot en met augustus 1976 onderbroken door militaire dienst bij de Koninklijke Landmacht. Na in januari 1981 cum laude te zijn afgestudeerd, kwam hij per 1 februari 1981 als wetenschappelijk medewerker in tijdelijke dienst bij de vakgroep Veehouderij van de Landbouwhogeschool te Wageningen. Na aanvankelijk betrokken te zijn geweest bij immunologisch onderzoek, werd hij vanaf 1 november 1982 verantwoordelijk voor het onderwijs en onderzoek op het gebied van de voortplanting en vruchtbaarheid der landbouwhuisdieren. Per 1 april 1983 is de tijdelijke aanstelling omgezet in een aanstelling in vaste dienst.