HORMONAL THERAPY IN SOWS *(SUS SCROFA DOMESTICA)*

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ABSTRACT

The domesticated sow has a very high reproductive potential, with more than two litters and more than 25 piglets born per year. Inadequate management, feeding, environment and climatic factors and diseases, negatively affect this potential. Hormonal therapies are currently in wide use in modern swine breeding to contain and limit reproductive losses and keep reproductive parameters aligned with economic standards. This review summarizes physiological principles of swine reproduction and provides an overview of most common hormonal therapies for sows in industrial farming.

Key words: Sow, farrowing, estrus, pregnancy, reproduction

INTRODUCTION

swine physiology

The several breeds of domestic swine currently bred in the western world belong to *Sus scrofa domestica*, derived from European wild swine *Sus scrofa ferus*, fam. *Suidi*, ord. *Ungulates*, sub. *Artiodactyles.* In Israel, pigs are bred on 24 farms consisting of a nucleus of 13,000 - 14,000 sows which produce 170,000 slaughtered pigs per year (1,2).

Swine have 4 digits (III-IV; II-V metacarpus/-tarsus) protected by claws and have an extended dental formula of 44 teeth: I.3/3; C.1/1; Pm.4/4; M.3/3. They are monogastric, with a relatively small well-developed small intestine and a large intestine which is poorly developed. Swine are considered unsuitable for kosher diet:

אַךְ אֶת-זֶה, לֹא תֹאכְלוּ .....
וְאֶת-הַחֲזִיר כִּי-מַפְרִיס פַּרְסָה הוּא, וְשֹׁסַע שֶׁסַע פַּרְסָה, וְהוּא גֵּרָה לֹא יִגָּר... (3)

Sows are multi-estral, and multiparous with a potential for over 2.2 litters per year. An average of 10-12 piglets is delivered at each litter. Sows are provided with multiple udders with 12 – 14 teats. The female reproductive tract consists of a single short uterine body (5 cm length), with 2 long uterine horns (up to 120 – 140 cm); the oviducts are 20-22 cm long and the ovaries are about 5 cm long, and irregularly shaped due to the presence of various follicles or *corpora lutea.* (Fig. 1)

The cervix is very characteristic: 15-25 cm long and provided with typical fibrous bearings which "trap" firmly the typical "corkscrew" apex of the boar's penis during insemination (or catheter in the case of artificial insemination). (Fig 2)

Female puberty occurs at 5-6 months of age and generally the first insemination, natural or artificial, is given at the 2nd or 3rd estrus. The placenta belongs to epithelio-chorial and diffused type (which does not allow antibody passage). Pregnancy is 114 days long, with a range of 111 to119 days. After farrowing, lactation of piglets inhibits follicular development and the ovaries remain mostly inactive until the end of lactation. Anecdotally occasional animals may show early estrus, but these are poor in ovulation and pregnancy is rare. The lactation period is 28 days long (range 21 - 35) and weaning of the piglets induces the sows to estrus after about one week (range 4 -10 days). Estrus lasts for 48 - 72 hours with sows showing a typical standing reflex at the estrus peak, both to the boar and to pressure on the back. This is also the most fertile period for insemination. Ovulation lasts 3 - 6 hours (30-36 hours after estrus begins) and 20 -25 ova are released with a vital time of 10 - 15 hours. (Fig.3 and 4)

If sows are not inseminated or do not fall pregnant, a new estrus will take place 21 days later (range 19-24 days). In the swine industry breeders typically farrow 6-7 times.

Herd fertility concept

In the swine industry, evaluating fertility performance of the single sow is of limited value whereas evaluation of fertility and productive parameters of the herd is standard practice. In such a perspective, "standard performances" and/or low performance boundaries or "alarm levels" are identified for each fertility and reproductive parameter and considered at the herd level. Tables 1 and 2 show fertility, reproductive and productive objectives in the swine industry and "alarm levels" for which veterinarian intervention may be required (4, 5). (Table 1 and 2)

The domestic pig appears to reflect some of the seasonality of its ancestral wild pig, which is a short-day-length breeder (6). This results in a lower percentage of pregnant sows in summer-autumn period. Summer-autumn influence on fertility is apparently caused by two different factors: seasonal high melatonin concentrations (6) and high environmental temperatures (7).

Swine breeding in temperate areas lays stress on increased environmental temperatures which are considered responsible for extension of the weaning-to-estrus (WTO) length and regular return-to-estrus (RRTO) percentage resulting in a decrease in the farrowing rate (FR) (7). World- wide statistically significant differences in FR are regularly observed in sows between summer-autumn and winter-spring inseminations. Decrease of FR is apparently caused by lower progesterone concentrations (8, 9) observed in summer-autumn period (June to September) at 30 and 60 days of pregnancy. Low progesterone concentrations are possibly the result of reduced luteotropic stimulation (10). Increased environmental temperature may also affect the sexual behavior of gilts (11) resulting in lower percentage of gilts detected on heat in summer and lower percentage of inseminated replacement animals. All the above mentioned changes in reproductive performances are generally summarized as the "summer infertility syndrome".
Table 3 summarizes reproductive and productive parameters affected by summer infertility syndrome. (Table 3)

Management, infectious diseases, feeding and other factors may negatively affect fertility in sows. While infectious diseases and feeding problems strictly require specific interventions , hormonal therapy represents the most suitable and immediately efficacious tool to contain losses caused by worsening of reproductive parameters, minor management mistakes and summer infertility

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principles; objectives; schemes.

Experience in swine industry indicates that best results in terms of improvement of reproductive performances are obtained in healthy animals through estrus induction as early as swine physiology allows. In such a perspective, the objectives of hormonal therapy are: gilts *at puberty* and sows *at weaning*. Hormonal therapies during pregnancy are not, if rarely, applied. Hormonal therapies implicate a low or moderate use of hormonal active principles, while treatment timing and duration are critical. In fact the two key mechanisms of a successful hormonal treatment are represented by:

- Enhancement and optimization of the natural cycle/estrus, already existing but behaviorally unexpressed or silent
- Suppression of an already existing natural cycle in order to induce a more evident estrus at a desired schedule

A list of active compounds commonly used in hormonal therapy in swine is limited:

- Human Chorionic Gonadotropin (HCG) => luteinizing activity
- Pregnant Mare Serum Gonadotropin (PMSG) => follicle stimulating activity
- Altrenogest => progestinic activity

Ancillary hormonal therapies may be successfully applied at farrowing to help piglet expulsion. This will have indirect beneficial effects at weaning few weeks later.

- Oxytocin => myo-contractural activity
- - Prostaglandins => myo-contractural activity / luteolytic

Estrus induction in gilts and sows

Gilts: The purpose of the treatment is to have in estrus and inseminate the right number of gilts requested at a specific time. Taking into account that replacement in swine industry is between 25 to 50%, (average 35%), which means 3-4 gilts per month for every 100 sows on the farm. Assuming 13,000 – 14,000 sows in Israel, replacement gilts must represent no less than 3,900 and up to 5,000 to give an indication of the population under discussion. Timing of the treatments is critical: gilts should be at the age of natural puberty and weigh not too much: at 5.5 to 6 months of age. Later treatments are generally of low and disappointing efficacy.

Table 4 summarizes the most practiced hormonal treatments in gilts. (Table 4)

Altrenogest is a synthetic steroid C_{21}–trienic (C_{21} H_{26} O_2) progesterone-agent` in oil suspension, administered *per os*. Two preparations are marketed: 2.2 mg/ml and 4 mg/ml. Daily dosage should be carefully calculated. Dosage should not be less than 15 mg/day (12). The repeated *per os* treatment may be problematic when gilts are reared in groups and attention must be paid that every gilt receives the correct daily dose. In this case it is helpful to administer the daily dose sprayed on slices of bread. Treatment of gilts reared in cages is easier, as the compound is given as a top dressing on a small quantity of feed in the trough. Eighty to 95% of treated gilts are expected in estrus at day 4 after the last treatment (range 3-5 days). Fourteen days of treatment leads to estrus in a range of 4-9 days (12). Attention must be paid to withdrawal times. Progesterone agonists are known to affect testicular and endocrinal functions in males. Keeping in mind that the average pig slaughter weight (live body weight) in Israel is close to 100 kg at 6 – 7 months of age, it is conceivable that gilts unresponsive to treatment may be sent to slaughter before the withdrawal time.
PMSG and HCG are sterile, purified and titrated dry preparations of glycoprotein fractions obtained from plasma of pregnant mares and urine of pregnant women, respectively. They are administered intramuscularly in combination and at the dosage indicated in Table 4. Alternative schemes exist, with dosages ranging from 400 to 1,200 IU for PMSG and 150 to 500 IU for HCG, given separately at 2-3 days intervals. While sophisticated therapeutic schemes could be justified in high standard premises, with accurate individual data records, the classic (PMSG + HCG) 400 + 200 combination is strongly recommended for standard premises because the good repeatability of results and ease of administration. 70 to 95% of treated gilts are expected to be in estrus starting at the 3rd and within the 10th day of treatment (12, 13).
Sudden management changes close to PMSG + HCG treatment, like regrouping gilts, adding a mature weaned sow to the group, half-a-day fast or a short "trip" around the farm, may enhance and further stimulate estrus, as a consequence of the stress induced by these changes.
Following either Altrenogest or PMSG/HGC treatments, accurate planning should be carried out to decide whether to inseminate gilts at their first estrus after treatment or at their next cycle, according to age and body condition. Recommendation should be

to inseminate at 2nd estrus following the treatments, that means 3 weeks later, and at natural estrus which is expected in 80-90% of treated gilts (13). In this case withdrawal times do not represent a problem.

Sows: The objective is to get the sows regularly back to estrus and inseminate them within one week after weaning. The treatments aim to restore silent sows to visible estrus and reduce unproductive days.

Two different approaches may be applied:

1. *Therapeutic*: individual treatment of:

- sows not in estrus at day 8 from weaning;
- Non-pregnant sows at day 18 from insemination;
- Non-pregnant sows at pregnancy test (generally erformed 24-28 days after insemination).

2. *Preventive*: When a high percentage of sows are not in estrus within 7 days after weaning it would be advisable to check feeding costs, historical data on periodic fertility decreases (summer) and productive commercial needs. All these may give an indication for preventive treatment when percentage of sows not in estrus within 7 days from weaning is greater than 12 – 15%

For both strategies, timing of treatments is critical: the sow's limited response to hormonal treatments gives a narrow margin for intervention. Table 5 summarizes the timing of successful treatments. (Table 5)

Treatment with PMSG + HCG on day 18 post-insemination, or day 21 to 25 from weaning, will induce estrus in non-pregnant sows only; in fact pregnant sows will be totally unresponsive to treatment because 600 IU of PMSG is not adequate to induce follicular growth and estrogen release with *corpora lutea* lysis, in presence of high level of pregnancy progesterone. Retrospectively, starting 18 days post-insemination, PMSG + HCG administration may be used as a pregnancy test where pregnant animals will not respond while non-pregnant sows will be induced back to estrus. In any event, estrus induction in cycling "silent estrus" sows may be difficult due to cyclic *corpora lutea* progesterone release, which may be the main reason for poor results in sows randomly treated beyond day 10 post-weaning.

Altrenogest administered at 20mg/day for at least 7 days before weaning mimics *corpora lutea* activity: following the last treatment day, a dramatic drop of progesterone levels stimulates Follicular Stimulating Hormone (FSH) release and resultant cycle restart.

The nutritional and health status of sows will definitely influence the response to therapy (as they already negatively influenced return to estrus after weaning): lean (< 17 mm back fat) and fat (>20 mm back fat) sows at weaning; sows with > 4 mm back fat loss between farrowing and weaning; sows with subclinical metritis are unlikely to respond to these treatments. The latter case will be discussed below.

Treatments around farrowing

In sows, farrowing or parturition takes about 20 minutes per piglet, and lasts an average of 2.5 – 3 hours and up to 10 hours. Stillbirths of around 5% are considered physiologic (4). Accurate farrowing supervision is necessary to contain stillbirth and perinatal mortality, for example, due to piglets crushed by sows, inability to reach the udder and colostrum, etc. With this in mind, it may be helpful to avoid sows farrowing during nighttime hours or at week-ends, when personnel is reduced or absent.

Two different strategies may be applied:

Farrowing induction or synchronization:

Farrowing may be induced at 112 to 114 days of gestation, but the real limiting factor is represented by piglet survival, which is directly linked to their weight at birth (Table 6). In fact piglets grow about 140 g/day in the last week of pregnancy, and taking into account a gestation length naturally ranging from 114 to 119 days, farrowing induction too early may definitely affect piglet survival. Thus, farrowing induction or synchronization can be applied and may be recommended only to farms with a very accurate sow data record. Farrowing may be induced with a single injection of prostaglandin from day 112, according to dosages indicated in Table 7. Parturition will begin between 24 and 32 hours later. A further synchronization can be obtained with oxytocin treatment 20 -24 hours after prostaglandin.

Figure 5 illustrates the relationship between different dosages of oxytocin, in International Units (IU) given 20 hours after a single administration of prostaglandin from 112 to 114 days of gestation. (Table 6) (Figure 5)

High dosages of oxytocin cause farrowing within a few hours, but increase the risk of dystocia and piglet stillbirths. Injection of oxytocin in the vulval mucosa may reduce the dosage (5 to 10 IU) and induce farrowing without complications (14).

1. *Assistance at farrowing*

Farms with average management or with high variations in gestation length should invest in personnel assistance at farrowing and utilize oxytocin injection once the first piglet is born and the cervix is completely open. Oxytocin induces myocontractural activity, helping to expel the piglets. A check of the farrowing sow every 30 min. is considered a good practice and to intervene on time in difficult farrowings (14) .

Oxytocin dosage is 5 - 10 IU and it may be repeated after a few hours. If retaining of piglets is suspected, before repeating a second treatment a delicate manual examination is recommended, with removal or repositioning of piglets followed by treatment with a wide-spectrum antibiotic. There are several oxytocins for veterinary use but all of them are titrated in IU per ml, thus simplifying calculations for dosage in the sow.

The immediate post-partum period

Prostaglandins are generally used in the post-partum period for their myocontractural activity rather than their luteolytic activity. Their effects on estrus at weaning are a consequence of expulsion of debris from uterus, enhancement of uterine involution and eventual lysis of *corpora lutea* residues.

Prostaglandins in sows are effective from 12th -14th day of the cycle and until termination of pregnancy (12). C*orpora lutea* progesterone production starts rapidly a few hours after ovulation and begins to decay at 13-15 days in non- pregnant sows (12). This mechanism explains the limits of prostaglandins as estrus inducers through *corpora lutea* lysis in non-pregnant sows. In any event, prostaglandins may play a role in hormonal therapy: post-partum (within 36 hours) treatment with prostaglandins helps in placental residue expulsion, it reduces metritis incidence and eliminates luteal residues (14), thus enhancing responses to further hormonal treatments, especially with PMSG + HCG.

Timing of treatment must be within 36 hours of farrowing, when cervix is still open. Untreated subclinical metritis may be associated with mastitis during lactation and some degree of agalactia (MMA syndrome), but it must be clearly underlined that poor lactation performances or Post Partum Dysgalactia Syndrome (PPDS) (14) may be due to nutritional and physiological reasons, and not infective causes. Treatment with prostaglandins on the farrowing day may be helpful in causing fast lysis of the *corpora lutea* and reduction of progesterone which may inhibit lactogenesis (14).

In the case of vulvar discharges from uterine origin, two different approaches may be applied:

1. *Therapeutic:* treatment of single sows showing vulvar discharges in early post-partum.
2. *Preventive:* when percentage of sows with vulvar discharges in early post-partum reaches or overrides 10-12%; when vulvar discharges appear at estrus after weaning.

There are several veterinary prostaglandins in the market, mainly for indications for use in cows, while dosages in sows may differ considerably.

Table 7 below summarizes most common prostaglandins and the recommended dosage for use in the sow. (Table7)

Withdrawal times are not a concern for use in sows, and are 1 to 2 days.

DISCUSSION

Hormonal therapy in the sow has the purpose to contain and reduce the so called "non- productive days", which are mainly:

- Days since introduction of gilts in production, starting from 180-190 days (hypothetical age/weight suitable for slaughtering, e.g. in Israel and other countries) to first successful mating,
- Days from weaning piglets to next successful mating.

To these non-productive days a value must be attributed, and should include costs of daily feeding, manpower, structure and space occupancy. Western countries' average cost per sow per is 2.2 to 3 € per day (10 to 15 NIS (New Israel Shekel). A 1% decrease in farrowing rate (FR) will mean a single unproductive sow (out of 100) per year, with unproductive costs of 3,650 to 5,475 NIS per sow. Hormonal therapy should be therefore addressed to reduce the unproductive days. Table 8 summarizes, as example, results obtained from sows treated with an association of PMSG + HGC compared with control, untreated sows. (Table8)

A group of sows is treated with a combination of 400 IU PMSG + 200 IU HGC the day of weaning, while a group of sows remain as untreated.

81.8% of treated sows were in estrus in 5.1 days; 6.1% returned to estrus at 8–25 day; versus 45.9% of untreated sows were back to estrus in 10.4 days, and another 44.4% at 25 days. For simplicity, the results at 25 days for both groups have been considered. It is not considered advisable to use single data of single animals.

Cumulative results were as follows:

Treated: 81.8% + 6.1% = 87.9% total sows in estrus

Untreated: 45.9% + 44.4% = 90.3% total sows in estrus

Apparently, there is no advantage in treating sows relative to the percentage of cycling animals.

We calculate the total non-pregnant days for each group; (for simplification on 100 sows basis):

Treated: (81.8% x 5.1 days)+ (6.10% x 25 days)= 570 days

Untreated: (45.9% x 10.4 days)+(44.4% x 25 days)=1587 days

The results according to the previous assumption must be attributed to animals which became pregnant. To simplify the calculation we assume a pregnancy/farrowing rate equal to sows in estrus for each group: treated = 87.9%, and non-treated = 90.3%.

Total non-pregnant days per pregnant or productive sow, will be:

Treated: 570 days x 100 sows/87.9%=648 days = 6 ½ unproductive days / sow

Untreated: 1587 days x 100 sows / 90.3%=1757 days=17½ unproductive days/sow

Cost of the hormonal treatment should be calculated in relation to the benefits that are related to the reduction in unproductive days.

Assume a therapy cost of 40 NIS:

Treated sow: 40 NIS + 6 ½ days x 15 NIS = 137.5 NIS

Untreated: 0 NIS + 17 ½ days x 15 NIS = 262.5 NIS

Assuming the daily cost of 10 NIS, results will be 105 NIS / treated vs. 175 NIS/ untreated. Or the decision not to treat will cost the farmers 66% to 91% more than not treating, therapy cost included.

This calculation may be also applied to cost/benefit evaluation for:

- Treatment in replacement gilts (calculating the non-pregnant days from days 180 – 190 to the first successful mating)
- Treatments at post partum (calculating percentage of sows returning to estrus after weaning and average days from weaning to estrus)
- Treatment at farrowing (calculating the value of perinatal mortality and costs of treatments)
- Cost-benefit of a new technique of insemination or for a switch from natural to artificial insemination

CONCLUSIONS

As in other livestock farming, maintenance of breeders has precise costs,which can be kept at a basic level if breeders carry out treatments consistent with physiologic potentials. Several factors may affect this potential and reduce it, thus affecting the economic output of the enterprise. Without considering reproductive or infectious diseases, some of these factors are mainly linked with sub-optimal reproductive performances and can be treated in cost effective ways.

Efficacy of treatments should be evaluated both in terms of successful/unsuccessful pregnancies, and considering the time between the treatment and the expected result and in comparison with untreated animal or in comparison with historical comparative results.

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FIGURE CAPTION:

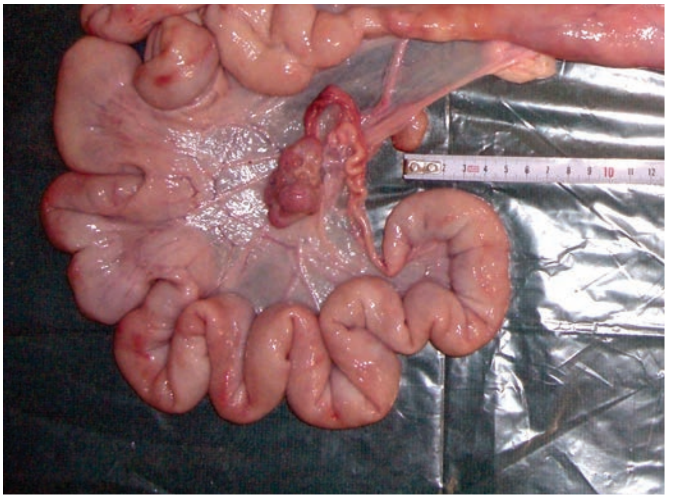

Fig. 1: Female reproductive tract

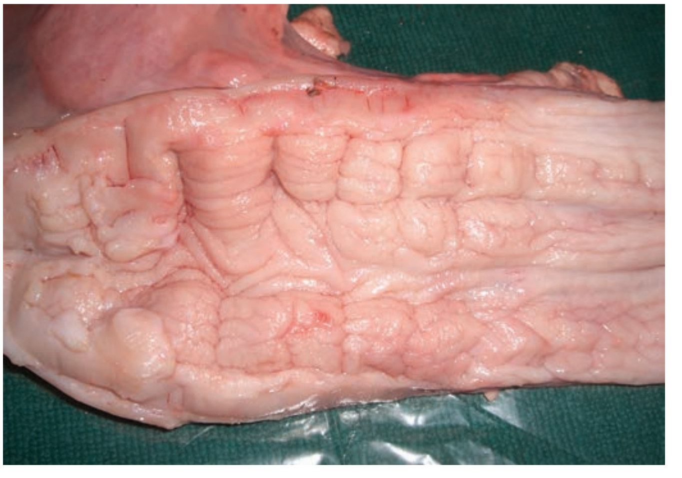

Fig. 2: Sectioned cervix with fibrous bearings

Fig. 3: Ovary with corpora lutea

Fig. 4: Ovary with pre-ovulatory follicles

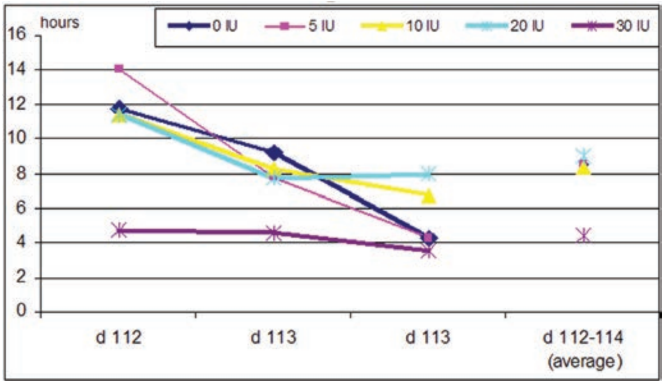

Fig 5: Beginning of parturition (in hours) after dosages of oxytocin given 20 hours after prostaglandin once at 112 or 113 or 114 days of gestation (14 and modified)

TABLES

Table 1: Parameters in swine reproduction and intervention levels

Fertility parameters	***Standard***	***Alarm level***
age of gilts at insemination (days)	210 - 230	250
Weaning-Oestrus interval (days)	< 7	> 9 - 10
Farrowing rate	85%	80%
Back in oestrus (after insemination)	9%	12%
of which: # regular (18-22days)	6%	10%
# irregular (> 23 days)	3%	5%
Abortions	0,8 - 1%	> 2,5%
Empty sows at farrowing date	2%	
Infertile sows	3%	5%
Sows mortality	2,5 - 3%	4%

Table 2: Standard production in swine breeding and intervention levels

Productive parameters	***Standard***	***Alarm level***
Piglets live per farrowing; 1st parity	9,5 - 10	9
Piglets live per farrowing; multiparous	10,5 - 11	10
Stillborn	5%	8%
Mummified	0,5%	1%
Farrowing per sow per year	2,2 - 2,25	≤ 2
Piglets weaned per sow per year	21	19

Table 3: Fertility parameters affected in summer-autumn and output changes

Parameters	*Result*
% of gilts inseminated	reduced, due to low
at 210-220 days of age	oestrus expression
Weaning-Oestrus interval	increased
Farrowing rate	decreased
Back in oestrus (after insemination)	increased
of which: # regular (18-22days)	increased
# irregular (> 23 days)	increased
Abortions	may increase
Empty sows at farrowing date	increased
Infertile sows	increased
Sows mortality	may increase
Piglets live per farrowing; 1st parity	no changes
Piglets live per farrowing; multiparous	no changes
Stillborn	no changes
Mummified	no changes
Farrowing per sow per year	decreased
Piglets weaned per sow per year	decreased

Table 4: Hormonal treatments in gilts and withdrawal times

Active Principle	*Dosage head / day*	*Days of treatment*	*withdrawal time*
Altrenogest	20 mg	18 days	> 20 days
PMSG + HCG	400 IU + 200 IU	once	none
IU = international unit;			

Table 5: Timing of therapeutic and preventive treatments

Approach	*Active Principles*	*Time of treatment*
therapeutic	PMSG + HCG	7th or 8th or 9th or 10th day (from weaning)
	PMSG + HCG	$\geq$ 18th day (from insemination)
preventive	PMSG + HCG	1st or 2nd day (from weaning)
	Altrenogest	last 7days of lactation

Table 6: mortality rate of piglets at birth, related to birth weight.

Birth weight and mortality rate	
Weight, Kg	*Mortality, %*
< 0,5	100
0,5 - 0,7	90
0,7 - 1	40
1 - 1,2	30
1,2 - 1,4	20
1,4 - 1,6	15
1,6 - 1,8	10
1,8 - 2	6
>2	5

Table 7: Dosage of several prostaglandins for use in the sow.

Active principle	***Dosage***
Cloprostenol	190-200 mcg
D-Cloprostenol	150 mcg
Alfaprostiol	2 mg
Luprostiol	7,5 mg
Dinoprost	10 mg

Table 8: Percentage of sows in estrus (within 7 days from weaning) and weaning- estrus interval in sows treated or not with a combination of PMSG + HCG at weaning.

	Parameters considered		
Treatment	*% in estrus*	*weaning-estrus, days*	*% estrus; 8 -10 to 25 days*
400 pmsg + 200 hcg	81.8 (<7days)	5.1	6.10%
control-untreated	45.9	10.4	44.40%