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Intersexuality in Pigs: Clinical, Physiological and Practical Considerations

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Hunter, R.H.F. and T. Greve: Intersexuality in pigs: Clinical, physiological and practical considerations. Acta vet. scand. 1996, 37, 1-12. – Veterinary surgeons and practical pig farmers need to be aware of a condition that can have important deleterious consequences in a breeding herd. The animals in question have sometimes been referred to as hermaphrodites but would more correctly be termed intersexes Whilst there is a complete spectrum of phenotypic sexual development within a population of such animals, the most common form is that of a putative female with a prominent up-turned vulva. Reflection of the vulval lips reveals a much-enlarged clitoris. There may be scrotal development, in conjunction with an enlarged penile and preputial sheath. Coarse hair and incipient tusk development may further indicate differing degrees of masculinization.

Surgical exploration of intersex animals confirms a complete spectrum of gonadal types, ranging from 2 ovaries with a proportion of testicular tissue in one of them (i.e., an ovotestis) to 2, much-enlarged testicular-like structures with no detectable ovarian tissue. The gonads usually remain within the abdomen, but those with testicular tissue may descend to an inguinal or even scrotal location. The genital tract invariably comprises a bicornuate uterus, a partially vestigial Fallopian tube, and some development of one or both Wolffian ducts adjoining an ovotestis or testicular-like structure to form a convoluted epididymis. Spermatozoa are never present, either in abdominal or scrotal testicular tissue, nor are there any germ cells within the seminiferous tubules, only Sertoli-like cells.

Due to the spectrum of gonadal types, sexual behaviour ranges from male-type aggressivity on the one hand to regular oestrous cycles on the other, with periods of standing oestrus during which intromission may be achieved. In animals with functional ovarian tissue in both gonads, foetal development has been observed, at least until days 25-30 of gestation.

Almost all intersex pigs possess XX sex chromosomes and usually 36 autosomes; only a very small proportion are chimaeras or mosaics. Chromosome banding techniques have failed to demonstrate a portion of the Y chromosome translocated onto an X chromosome nor has molecular probing revealed the presence of the sex determining gene Sry or other classical Y-related DNA sequences, except in one instance. Breeding records suggest that the intersex condition results most frequently from the influence of an autosomal recessive gene carried by certain boars. Identification of such boars is therefore essential, as the incidence of intersexuality in their offspring may reach 4-5% or more.

In terms of the pig industry, economic losses may result from:

1. Lack of fertility in intersex animals.
2. Aggressive behaviour in groups of growing/fattening pigs.
3. Boar taint in the carcase of animals possessing ovotestes.
4. Propagation of the deleterious condition, either by mating or more widely by artificial insemination.

hermaphrodites; aetiology; chromosomes; constitution; economics.

Introduction

Careful examination of twentieth century literature in veterinary and animal science reveals a sporadic but increasing number of publications on pigs of ambivalent sexuality, frequently referred to as hermaphrodites. As should become clear in the following pages, such animals are certainly not true hermaphrodites since no such individual produces gametes representative of both sexes. The expression pseudohermaphrodite has also entered the literature, qualified by the adjective male or female to denote the condition of the gonads. Unfortunately, this more detailed terminology is also defective, for an ovotestis is frequently found. Accordingly, the animals are better termed intersexes, and this word will be used throughout the following pages.

Putting aside the question of terminology, comment should be offered on the growing body of literature on these unusual, but by no means rare, animals. First, most of the literature is purely descriptive, listing a variety of anatomical features of intersex pigs (eg. *Hammond,* 1912, *Crew* 1924, *Baker* 1925 & 1928, *Brambell* 1929, *Johnston et al.* 1958, *Scofield et al.* 1969, *Krishnamurthy et al.* 1971). Second, other studies have adopted a more analytical approach, attempting by techniques such as histology and karyotyping to obtain insights into the nature of the anomalies (eg. *Breeuwsma* 1970, *Basrur & Kanagawa* 1971, *Booth & Polge* 1976, *Hunter et al.* 1982, *Hunter et al.* 1985). More recently, such analytical studies have moved to a molecular level in a search for the presence of supposed sex-determing DNA sequences (eg. *Thomsen & Poulsen* 1993, *Pailhoux et al.* 1994). Third, there have been experimental studies that have sought to probe the physiological responses of intersex animals with surgical modifications (eg. *Hunter et al.* 1985) or by means of endocrine challenges *(Hunter et al.* 1982 & 1985, *Cavazos et al.* 1987, *Chalmers et al.*1989, *Cook et al.* 1995).

General reviews dealing with intersex animals published in recent years include those of *Breeuwsma* (1970) *Bäckström & Henricson* (1971), *Chalmers* (1988), *Hunter et al.* (1988) and *Hunter* (1989, 1995). The present paper is intended to offer a concise summary of much of the work that should be of interest to veterinary practitioners and to pig producers with some background in animal science.

Results and discussion

Intersex Pigs: Clinical Features

The following remarks are based on a survey of more than 100 intersex pigs of predominantly Large White X Landrace background examined within the same breeding herd, that of the University of Edinburgh at Easter Howgate, Midlothian, Scotland.

Intersex pigs may first come to light in groups of weaned animals either due to features of their morphology or to their patterns of behaviour seemingly not according with their supposed phenotypic sex.

External morphology. The specific morphological feature that first attracts attention concerns the vulva, whose lips may present an unusual upward turn (>80%) and which, during urination, direct the jet of urine in a steep upward curve. Upon closer examination, and with the lips of the vulva reflected, an enlarged clitoris can be demonstrated. This sometimes very swollen structure is the first clear indication of masculinization in animals initially regarded as females. Other features that become more prominent with the approach of puberty may include incipient tusks (approx 55%), a penile sheath and/or swollen preputial sac, and enlargement of scrotal folds (12%). Palpation of such scrotal development may reveal a descended gonad. The hair of such animals is frequently coarser than that of a gilt, the skin much tougher, and an odour characteristic of a boar

may become prominent at the onset of puberty.

Sexual behaviour. Behavioural features are diverse, for some intersex animals show progressive swelling and colouration of the vulval lips for 4 or 5 days followed by a period of standing oestrus (approx 20%). Others, by contrast, undergo no such vulval changes but rather show typical masculine behaviour, not only with aggressive displays but also with much "chomping" of the jaws and extensive production of a frothy saliva. Tusk development in such animals is invariably pronounced. Mounting behaviour is also frequent, accompanied by pelvic thrusting.

Further exploration of such intersex animals is possible during surgery or post mortem. In particular, the internal reproductive organs can be examined with precision, and portions of tissue removed and prepared for histological section or hormone assay. Comments will focus first upon the genital tract and then upon the gonads.

Genital tract. In mature animals, the cervix varied considerably in dimensions and also in patency. In animals with paired ovotestes (21.5%), it was seemingly imperforate, leaving little doubt that intromission would not be possible even if the animal would stand for a boar. The uterus was well developed in all instances in which there was at least one functional ovary (62%), and presented 2 characteristic cornua fusing caudally to give a small uterine body. In the presence of bilateral ovotestes (21.5%), the uterus was usually of immature appearance. Whilst the uterus was freely arranged in the abdominal cavity in most animals, there were a small number of cases (6) in which at least one of the uterine horns had been drawn into an inguinal canal by a descending gonad of masculine type. Scrotal development was always noted in such animals. Although the bicornuate uterus appeared morphologically normal, it was frequently distended with fluid which had a strong, unpleasant odour. The fluid was reminiscent of pyometritis, although sometimes yellowish in colour.

Turning to proximal portions of the genital tract, the utero-tubal junction was morphologically normal as was the isthmus of each Fallopian tube, although the latter was usually smaller than expected. However, the ampullary portion of the Fallopian tubes was always poorly developed when adjacent to an ovotestis, often being completely vestigial and scarcely detectable at the macroscopic level. Extremely prominent, by contrast, in such cases was extensive proliferation of the Wolffian duct into a prominent epididymis-like structure. Wolffian duct development did not extend further than the level of the corresponding utero-tubal junction. The epididymal duct usually showed evidence of fluid distension in its caudal portion. Whether an epididymis was found unilaterally or bilaterally depended on the composition of the adjoining gonad, some testicular tissue being required on a local basis. Similarly, the ampulla and fimbriated extremity of a Fallopian tube only developed in the presence of functional ovarian tissue.

Composition of gonads. Three features of the gonads in intersex animals were particularly striking. First, the range of gonadal types (Table 1), with the left frequently being of different composition than the right hand one (Figs. 1-3). Second, the large size achieved by gonads of testicular type within an abdominal location. Third, the location of at least one of a pair of gonads (almost invariably the right) in the inguinal canal or situated beyond within a scrotal sac.

As to gonadal type, there was a complete spectrum ranging from – most frequently – an ovary on the left side and an ovotestis on the right (45.7%) to both gonads being composed of testicular-like structures (Fig. 4) of reddish-brown appearance (2.8%). When present unilaterally, an ovary usually showed evidence of some cy-

Table 1. The distribution of gonadal types in a total of 107 animals described as intersexes on the basis of the presence of some testicular tissue in pigs karyotyping with XX chromosomes. The results are presented as percentages

1 ovary and 1 ovotestis	1 ovary and 1 testis*	1 ovotestis and 1 testis*	2 ovotestes	2 testes	1 abdominal and 1 scrotal gonad
45 7	15.9	7.5	21 5	2.8	6.5

* Testis indicates testicular-like structure although never containing germ cells. Histological examination revealed interstitial cells of Leydig and Sertoli-like cells

clic activity, with Graafian follicles of varying diameter or even fully developed corpora lutea. In the absence of active or regressed luteal tissue, Graafian follicles did not exceed 4-5 mm in diameter. The ovotestis in such animals ranged in proportions from an equal distribution of ovarian and testicular tissue to greater than 90% of testicular tissue. In some instances, there was no macroscopic evidence for ovarian tissue in the right gonad, and such spherical gonads could measure as much as 8 cm in diameter (Fig. 5). However, Graafian follicles within an ovotestis seldom exceeded 2-3 mm in diameter and were sometimes haemorrhagic rather than clear-walled in appearance.

Testis-like gonads varied in their presence or absence of a tunica albuginea, and this was seemingly not related to the location of the gonad. In the presence of a tunica albuginea, the gonadal surface was usually undulating or lumpy in appearance. In the absence of a tunica, the gonad tended to have a relatively smooth, curved outline. Testis-like gonads had an extremely prominent and extensive vasculature, reminiscent of a pampiniform plexus (Fig. 6). The blood vessels supplying and draining such gonads were highly coiled and pronounced. The mesenteries overlying the adjoining epididymis also had a prominent vasculature, especially in comparison with those supporting a contralateral Fallopian tube.

Histology of gonads. Histological sections revealed ovarian tissue of seemingly grossly normal composition, whether from an intact ovary or from ovotestis tissue. This was true of both Graafian follicles and, when present, of luteal tissue. There was no evidence for luteinization of intact follicles. But close inspection indicated degenerative processes in the wall of Graafian follicles. Whereas granulosa cells resembled those of normal control females, the theca interna was frequently poorly developed or even absent. In marked contrast to the ovarian morphology, the testicular component of an ovotestis or of a full testis-like structure was more strikingly abnormal. Although there were always prominent interstitial cells of Leydig and seminiferous tubules in seemingly conventional proportions (Fig. 7), the content of the seminiferous tubules was bizarre. There was no central canal or lumen and the occupying cells were large, poorly-staining Sertoli-like cells. There was no evidence of a germ cell line. This was a consistent finding in all testicular tissue examined from intersex animals, irrespective of its proportions with respect to neighbouring ovarian tissues and whether the testis-like structure was abdominal or scrotal.

It is now appreciated that spermatozoa cannot be produced in animals of XX sex chromosome complement (Fig. 8). It is also evident that whereas the Leydig cells function normally to

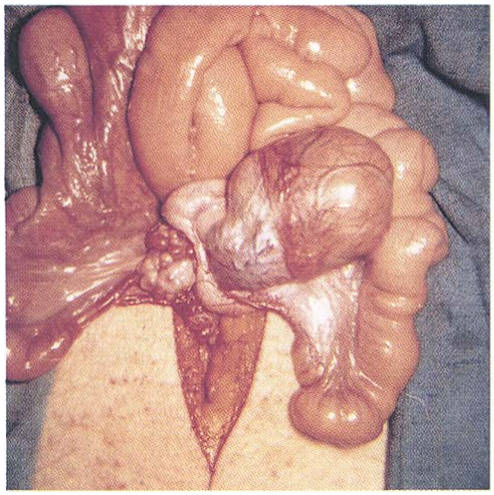

Figure 1. The reproductive system of an XX female intersex pig as revealed at mid-ventral laparotomy. The left gonad is represented by a normal ovary whereas the right is a much enlarged testis-like structure with an adjoining epididymis. Note the normal bicornuate uterus. However, development of the right Fallopian tube has been suppressed, especially in its ampullary portion.

Figure 2. Close – up view in another XX intersex pig of a left gonad featuring as a normal ovary and a right gonad as a testis-like structure. A prominent epididymis adjoins the rete region of the testis, with its lumpy morphology at one pole

Figure 3. A functional left ovary revealed in contrast to a lumpy testis-like gonad on the right, encased in a tunica albuginea

Figure 4. The bicornuate uterus of an XX intersex pig with both gonads appearing as testis-like structures. A tunica albuginea was not detected.

secrete testosterone, the Sertoli-like cells are deficient either in their synthesis and secretion of anti-Mullerian hormone (AMH) or in the timing of these processes (reviewed in *Hunter* 1995).

Chromosome constitution. On the basis of examination of blood leucocytes, all the animals karyotyped from the Edinburgh herd were genetically female with an unambiguous XX compliment of sex chromosomes. There was no evidence for sex chromosome chimaeras or mosaics, nor did banding techniques produce any evidence for a portion of a Y-chromosome translocated onto an X. The standard diploid number of 38 chromosomes was not revealed in all spreads, but the presence of only 35 and 36 chromosomes in 2 preparations reflected breakage of cells on the microscope slide and a consequent loss of chromosomes from the metaphase plate.

In other reports of intersex pigs, an XX sex chromosome constitution has been the predominant finding, but there has also been an extremely low incidence (<5%) of mosaics or chimaeras (eg. see *McFeely* 1967, *Breeuwsma* 1970, *Basrur & Kanagawa* 1971, *Thomsen & Poulsen* 1993).

Experimental observations in intersex pigs

Three kinds of challenge experiment have been performed to examine the responsiveness of XX gonads to endogenous or exogenous endocrine stimulation.

Response to gonadotrophins. The sensitivity of ovarian tissue combined with testicular tissue within an ovotestis has been examined in response to a systemic injection of placental gonadotrophin. A single subcutaneous injection of 1,000 i.u. PMSG (Folligon; Intervet) to each of 2 animals with bilateral ovotestes containing Graafian follicles of 1-2 mm diameter failed to stimulate any visible development of ovarian tissue or characteristic oestrogenic responses in the genital tract *(Hunter et al.* 1982). In a further intersex animal with a small ovary on the left and a large ovotestis on the right, ovarian tissue in the right gonad failed to respond detectably to a similar dose of PMSG within one week of treatment. Nor did unilateral ovariectomy prompt compensatory hypertrophy by endogenous gonadotrophins in the ovarian portion of an ovotestis *(Hunter et al.* 1985).

In both of these experimental models, failure of the ovarian tissue to respond to gonadotrophic stimulation was ascribed to an influence of the neighbouring testicular tissue within the ovotestis. However, there remains the intriguing paradox that Graafian follicles in the ovotestis had achieved a diameter of 1-2 mm before commencement of experimental manipulation, inferring a sensitivity to gonadotrophic hormones at some earlier stage of development. Protein secretion from the ovotestis, such as anti-Mullerian hormone (AMH), may have inhibited or destroyed receptors for gonadotrophins in the follicular tissue.

Response to positive feedback. A second experiment has been to examine the sensitivity of the hypothalamus and anterior pituitary gland in terms of the luteinizing hormone (LH) response to an oestradiol challenge in intersex pigs possessing ovotestes or testis-like gonads. A mature female would be expected to respond to the positive feedback influence of an oestradiol challenge with a surge of LH release, so this experiment should offer some description of "brain sex" in intersex animals (see *Short* 1982).

After challenge with an injection of oestradiol benzoate (Intervet, Cambridge, UK) given intramuscularly in oil at 60 μg/kg bodyweight, the maximum LH concentration in systemic blood in 5 intersex pigs possessing both ovarian and testicular tissue or only testicular tissue was one quarter of that in mature females (2.1 ng/ml

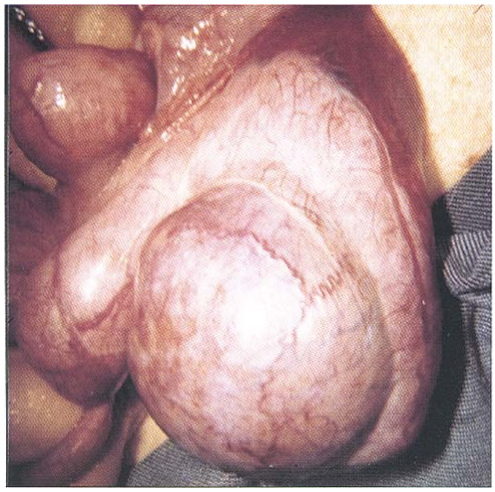

Figure 5 Abdominal gonad and adjoining duct structure in a female (XX) intersex pig showing an oval testis-like structure with adjoining fully-developed epididymis.

Figure 6 Another XX intersex animal with the gonadal rete region exposed at surgery to reveal the extensive pampiniform plexus form of vasculature characteristic of a mature male

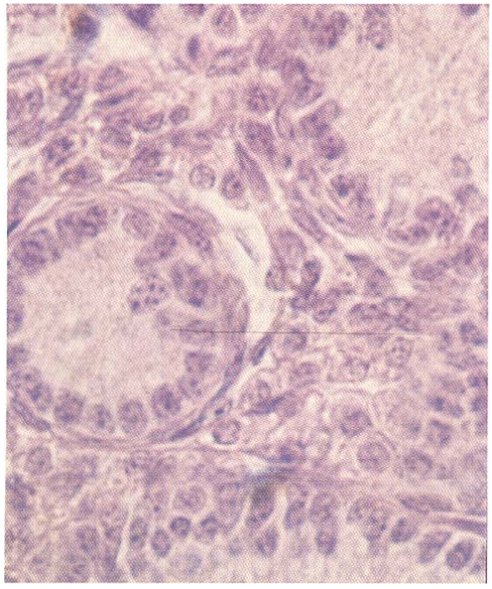

Figure 7. Histological preparation of testis-like tissue from an XX female pig showing the arrangement of seminiferous tubules and interstitial cells of Leydig Although the latter are well-developed, the tubules contain only Sertoli-like cells There is no evidence of a germ cell line.

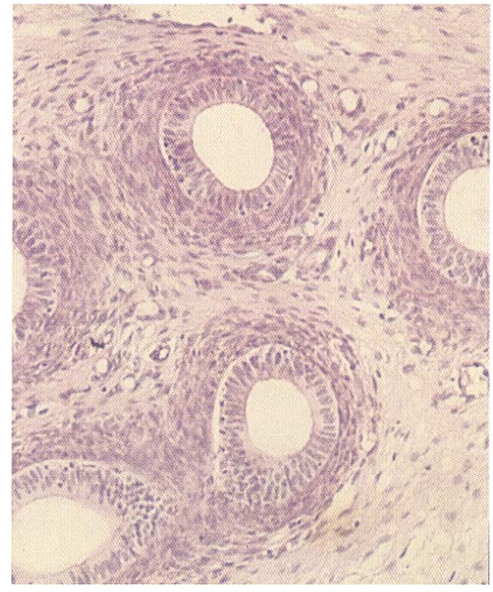

Figure 8 Representative section through the adjoining epididymal duct of specimens such as seen in Figs 5, 6 and 7 to emphasize the complete absence of a sperm suspension in these mature XX intersex animals

versus 8.9 ng/ml plasma). This indicates a modification of brain gender (masculinization) in such intersex animals and hence of the gonadotrophin response due to the presence of testicular tissue *(Chalmers et al.* 1989). Even so, because some animals with ovotestes can exhibit normal oestrous cycles, it must be concluded that the LH response modification in the presence of testicular tissue is primarily quantitative rather than qualitative.

Gonadal response to ACTH challenge. A third experiment bears on the proximity during embryonic development of the gonads to the adrenal glands and the possibility that adreno-cortical cells may have colonised the developing gonad, in due course leading to partial masculinization as an ovotestis. The presence of adrenal tissue in an ovotestis might be established by histology, although this would be a formidable undertaking in a structure as large as a pig gonad. An alternative, more elegant approach would be to challenge the gonad with an injection of ACTH and then monitor cortisol in the gonadal effluent. A standard clinical challenge of synthetic ACTH (Synacthen; Ciba), used to monitor human adrenal function, would be appropriate in pigs because of comparable bodyweights. Such a challenge experiment has been performed in a series of 6 animals. In every instance, there was a response in terms of elevated cortisol secretion from the intersex gonad, suggesting that adrenal cells must have been present to enable a response to ACTH *(Cavazos et al.* 1987, *Cook et al.* 1995). Whilst such an interpretation accords with dogma, the studies of *Juniewicz & Johnson* (1984) need to be taken into consideration, for they found that testicular tissue in normal boars appears to have ACTH receptors.

Aetiology of intersexuality. Whilst each of the above experiments in turn sheds a valuable light upon potential physiological responses in intersex pigs, none of these approaches has provided a specific explanation for the formation of the condition. Even so, the results of the PMSG and ACTH challenges do offer tentative clues. It has already been suggested that the failure of Graafian follicles to respond to PMSG may have been a consequence of protein secretion from the testicular portions of an ovotestis. More specifically, it can now be proposed that death of oocytes and gradual breakdown and dissolution of vesicular follicles in an ovotestis is due to the influence of AMH from Sertoli-like cells. Testicular tissue may have arisen in the first place as a result of a limited colonisation of the embryonic gonad by adreno-cortical cells and a subsequent influence from these cells that has masculinized adjoining tissues *(Breeuwsma* 1970).

Because intersex animals can be shown to have a genetic predisposition, and can be generated at an elevated incidence by certain boars *(Bäckström & Henricson* 1971), it is important to consider possible underlying genetic explanations. The involvement of one or more autosomal recessive genes has been invoked *(Sittmann et al.* 1980). One model that may still have validity in this context was proposed in 1988 (Fig. 1). In essence, it focuses on the presence of a deleterious gene (ie. male determining sequence) carried on a paternal X chromosome or generated spontaneously as a mutation, and a variable timing of X inactivation involving such a DNA sequence to account for the spectrum of gonadal types so imposed (Fig. 9). A necessary presumption also is that development of the 2 gonads is asynchronous. Despite the relative simplicity and attractiveness of such an explanation, the male determining DNA sequence – that is the offending gene – has yet to be identified. Molecular techniques are essential here.

In fact, molecular probes have now been applied to the tissues of XX intersex animals containing testicular tissue in the hope of revealing the putative testis-determining gene, Sry, or the

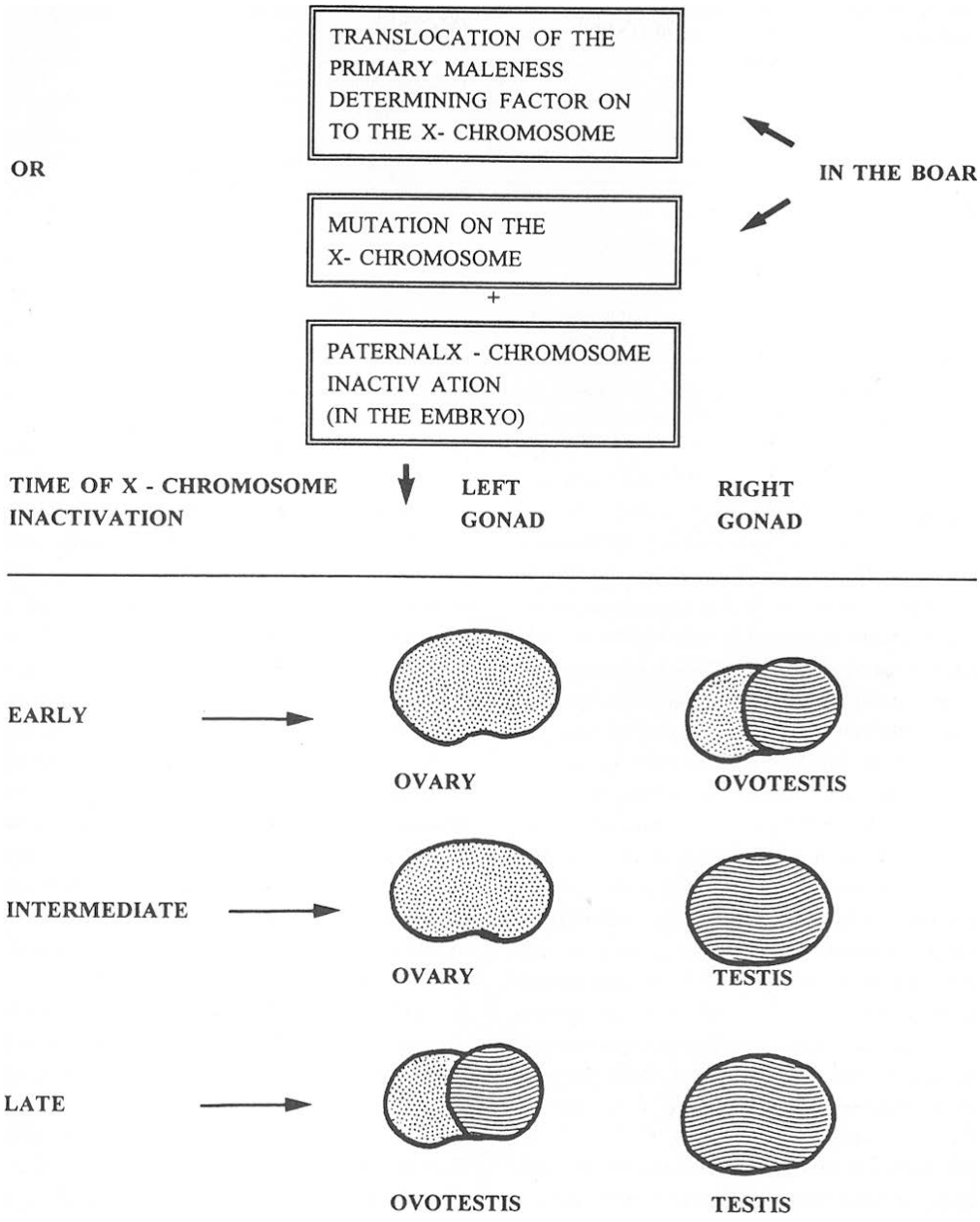

Figure 9. The model suggests the manner whereby varying gonadal constitutions could arise from translocation of male-determining sequences onto an X-chromosome, or by an appropriate mutation on an X-chromosome, in the boar followed by inactivation of the paternal X-chromosome at different times in the embryo. A presumption in this model is that the right hand gonad develops at a different rate than the left

Table 2. Summarised molecular observations on intersex pigs possessing some testicular tissue Adapted from *Thomsen & Poulsen* (1993) and *Pailhoux et al* (1994).

	Original description of intersex animals		
	38, XX Male with ambiguities	38, XX "true hermaphrodite"	38, XX intersexes
Origin of study	French	French	Danish
No. of animals	5	6	5
Sry gene present	1	0	Not tested
Sry gene absent	4	6	Not tested
Zfy gene absent	Not tested	Not tested	4*
DYZ1 gene absent	Not tested	Not tested	4

* A fifth animal exhibited a weak male-specific band during Southern blot analysis with a human ZFY probe and a male-specific PCR product with DYZ1 primers, suggestive of an XX/XY gonadal chimaera.

associated male determining genes, Zfy and DYZ1. In 2 separate studies, there was minimal evidence for such genes (Table 2). In one study at INRA, France, on 38 XX intersex animals, the Sry gene was present in only 1 of 11 animals *(Pailhoux et al.* 1994). In Danish intersex pigs examined at the Royal Veterinary and Agricultural University, Copenhagen, no detectable male-specific DNA sequences were revealed in 4 of five 38 XX animals, monitoring both Zfy with a human probe and the porcine male-specific DYZ1 gene *(Thomsen & Poulsen* 1993). The fifth animal revealed a weak male-specific polymerase chain reaction product with DYZ1 primers, a situation that was interpreted as tentative evidence for an XX/XY chimaeric gonad. In the light of this molecular evidence, ovotestis formation in XX animals requires a primary explanation not involving these particular sex-determining genes. There must be a role for other genes or mutations.

One such explanation has recently been proposed. It concerns the well-known masculinizing influence of AMH upon the gonad, this protein acting first to cause death of the oocytes with, in turn, failure of follicular development and then virilization of the resultant gonadal tissue *(Vigier et al.* 1987). AMH is now appreciated to be closely related to the hormone inhibin, both AMH and inhibin being members of a bioactive glycoprotein family and sharing a common subunit *(Matzuk et al.* 1992). Inhibin is synthesized by Graafian follicles. In the light of this background information, a current hypothesis – yet to be confirmed by molecular techniques – is that a mutation of the inhibin gene in XX animals prompts AMH activity, and thereby underlies formation of testicular tissue in the embryonic ovaries *(Hunter* 1995). Varying amounts of AMH secretion or differing timescales for the transition from inhibin to AMH could explain differing degrees of testis formation.

Practical considerations. It might be argued that since a majority of pigs produced in breeding herds will be destined for the meat fattening trade, the nature and function of their gonads are not important. This is by no means true, and it also overlooks the fact that a proportion of young females will be required as replacements for the breeding herd.

Losses associated with intersexuality arise from 4 practical considerations. First, the lack of fertility in intersex animals due to the com-

position of their gonads. Second, the displays of aggressive behaviour in groups of growing or fattening pigs which may inflict physical damage and also retard the rate of fattening. Third, the presence of boar taint in the carcase of animal possessing ovotestes, due to the influence of circulating androgens. And fourth, the propagation of the deleterious condition by widespread use of semen from carrier boars. Together, these negative components make it a priority to specify the precise causes of intersexuality in pigs and essential to adopt breeding policies to keep its incidence to a minimum. In an industry that may increasingly extend the practice of artificial insemination, this last point is especially significant. Artificial insemination is a powerful means of disseminating beneficial genes. Unfortunately, its influence is equally powerful with deleterious genes.

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Sammendrag

Interseksualitet hos svin Kliniske, fysiologiske og praktiske aspekter

I denne artikel beskrives den medfødte lidelse normalt kaldet hermafroditisme, men som rettere burde betegnes som interseksualitet, og som kan medføre betydelige tab som følge af reproduktionsproblemer i vore svinebesætninger. Den mest almindelige fænotypiske form er en formodet hun-gris med en prominent opaddrejet vulva og en forstørret clitoris. Der kan endvidere ses udvikling af skrotum og præputium Groft hårlag og begyndende tegn på udvikling af kraftige hjørnetænder indicerer yderligere maskulinisering

Nærmere undersøgelse af de indre kønsorganer viser et meget varieret spektrum af misdannelser lige fra 2 ovarier med en del testikelvæv i én af dem (ovotestis) til 2 store testikellignende strukturer uden ovarievæv Gonaderne findes normalt i abdomen, men den type, som indeholder testikelvæv kan descendere og befinde sig i lyskekanalen og endog i skrotum Genitalkanalen afslører altid en bicornuat uterus, dele af ovidukten og nogen udvikling af den ene eller begge Wolffske gange, som ligger tæt op ad ovotestis eller den testikellignende struktur og som danner en snoet epididymis Der er aldrig spermatozoer tilstede, hverken når testiklerne er i bughulen eller i skrotum. Og der findes aldrig kønsceller i tubuli seminiferi, kun Sertoli-lignende celler

Seksualadfærden vil tilsvarende variere meget lige fra handyrs-aggressivitet til brunst, hvor der kan ske bedækning. Hos dyr, hvor der er funktionelt ovarievæv i begge sider, er der set fosterudvikling.

Stort set alle grise besidder XX kønskromosomer og sædvanligvis 36 autosomer; kun en meget ringe del er kimærer eller mosaik Moderne cytogenetiske undersøgelser (banding) har ikke været i stand til at afsløre dele af Y-kromosomet translokeret til X-kromosomet. Molekylærbiologiske metoder har heller ikke været i stand til at afsløre tilstedeværelsen af det kønsdeterminerende Sry-gen eller andre klassisk relaterede DNA sekvenser undtaget i et tilfælde Nærmere genealogiske analyser antyder, at intersex tilstanden skyldes indflydelse af et autosomalt recessivt gen, som stammer fra visse orner Identifikation af sådanne orner er meget vigtigt eftersom hyppigheden af interseksualitet hos deres afkom kan nå op på 4-5%

Økonomiske tab som følge af intersex grise er betydelige af bl.a følgende grunde.

- de er infertile
- de er aggressive.
- de har ornelugt ved tilstedeværelsen af ovo-testis
- tilstanden spredes let i intensive avlssystemer og særlig ved brug af kunstig sædoverføring

I artiklen beskrives endvidere en række eksperimenter, hvor intersex dyr er blevet belastet med forskellige hormoner i et forsøg på at forstå tilstandens patogenese

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