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SOME ASPECTS OF INTERSEXUALITY IN PIGS

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Intersexes in both man and domestic animals have always attracted a great deal of attention. Baker (1925) mentioned that the natives of the New Hebrides considered possession of pig intersexes a special status symbol and used them in certain religious rites. Selective breeding for intersexes increased their incidence to 10-20% of the pig population. In other countries such animals have always been considered detrimental to the pig population because of their sterility and the unpleasant taint of their meat. In the Netherlands the "Centraal Bureau voor Slachtveeverzekeringen" has estimated the annual financial loss resulting from intersexes at more than half-a-million gilder (Breeuwsma, 1971). To this figure may be added the greater death rate amongst intersexes and their lower growth rate as a result of pyometria of the abnormal genital tract.

Incidence.

The incidence of intersexes varies in different breeds and populations. However, most authors agree that there is a general increase in this phenomenon. The incidence of intersexuality has been estimated at 0,2% of the total German pig population Freudenberg (1957), 0,5% of the pig population in the Netherlands (Breeuwsma, 1971) while 0,1% of Sweden's Landrace pigs are intersexes (Johanson, Rendel and Grevert, 1966). Johnston, Zeller & Cantwell (1958) found that in the litters in which intersexes appeared, 12,5% were intersexes. Moreover, the senior State Veterinarian in Pietermaritzburg reported 28% intersexes on one farm. It is apparent therefore that inbreeding can raise the incidence.

Morphology.

The gonads of pig intersexes can assume practically all intermediate developmental stages: those with ovaries only are usually referred to as female pseudohermaphrodites, those with both testes and ovaries on one or both sides as true hermaphrodites and those with testes and ovaries only on one side as lateral hermaphrodites. The accessory reproductive organs are always representative of both sexes. Their nature apparently being determined by the type of gonad present. There is a general tendency for the presence of a testis to suppress the oviduct and uterus to some extent but not completely, whereas the presence of an ovary may suppress the male genital ducts either completely or partially. Rare exceptions to this general tendency do, however occur. Both male and female ducts and associated gland systems develop in the presence of an ovotestis. A uterus is therefore invariably present in all pig intersexes. Occasionally however, it may also be severely suppressed and represented only by an enlarged *uterus musculinus*.

Cohrs (1962) prefers to classify intersexes as follows:

1) *Hermaphroditismus ambiglandularis* which can appear in three forms:
   a) *Hermaphroditismus glandularis bilateralis* (on both sides either a testis and an ovary or an ovariotestis).
   b) *Hermaphroditismus glandularis unilateralis* (on the one side an ovariotestis, and a testis or an ovary on the other side).
   c) *Hermaphroditismus glandularis alternans* (on the one side a testis and on the other side an ovary).
2) *Hermaphroditismus testicularis* (male pseudohermaphrodite).
3) *Hermaphroditismus ovarialis* (female pseudohermaphrodite).

Of these forms *H. Testicularis* is by far the most common.

In pig intersexes the sexual instincts are mostly male. A vulva with an enlarged clitoris is an important clinical feature. The clitoris can become erect and protrude. Copulation with females is often attempted but some do show signs of heat. They are apt to show fits of rage caused by seeing females on heat. During these fits of rage their tusks become worn down in a characteristic manner. Such fits of rage could be ascribed to male hormones produced either by the adrenal or the testis.

When present and well developed the uterus may with increasing age become filled with fluid and may even herniate through the inguinal canal and be present within the scrotal sac causing its dilation as a testis would although flabby on palpation. Extreme dilation and endometritis of the uterus may occur in cases where a utero-vaginal opening is present. Extreme dilation of the uterus can also be induced by backflow of urine during urination. The urethral opening in intersexes is situated dorsally on the enlarged clitoris and urination always occurs in dorsally directed spurts. The extra pressure needed for this also forces urine through the utero-vaginal opening where it acts as an irritant causing endometritis.

Cytogenetics.

The gonads present can therefore not be used to define genetic sex. It is well known that the genetic sex is determined at fertilization and depends on the type and number of sex determining genes present on the sex chromosomes denoted as X and Y. The specific sex chromosomes formed determine the specific gonad which, through secreting male or female sex hormones, determines the development of the secondary sexual organs. Females normally possess the sex chromosomes XX while males have one X and a Y chromosome.

In embryos or adults the genetic sex can be determined in one of three ways:

a) by cytological sexing i.e. determination of Barr bodies in cell nuclei. Cytological sexing is already applicable on the blastocyst from approximately 15 days after fertilization. In this instance pigs also follow the Lyon hypothesis (Lyon, 1962) which states that soon after fertilization one X chromosome, either paternal or maternal becomes condensed and is usually visible against the nuclear membrane while the other and perhaps part of the condensed one remains genetically active. Any additional X chromosome thus becomes condensed and the number of Barr bodies plus one gives the number of X chromosomes present.

b) by polymorph sexing i.e. determination of drumsticks in neutrophils of blood smears. This method requires the finding of at least ± 6 drumsticks / 500 neutrophils and was found to be less favourable by Gerneke (1967) and Breeuwsma (1969).

c) By determination of sex chromosomes themselves from spreads prepared from dividing cells eg. bone marrow and blood or tissue cultures.

Using these methods it has been determined that most pig intersexes are genetic females with a normal chromosome number of 2n=38. Very rarely chimeras with XX/XY chromosomes are found. These chimeras represent the porcine equivalent of the bovine freemartin, and, although occurring in about 95% of bovine heterosexual twins, are very rare in pigs. They are caused by early allantochorionic vascular anastomoses occurring between adjacent heterosexual twins. Due to intermingling of early male and female blood cells the female twin usually becomes a chimera containing both XX and XY containing blood cells. To my knowledge only 8 cases of chimerism (in some cases perhaps mosaicism) in pigs have been reported in the literature. McFree, *et al* (1966) described an XX/XY mosaic (chimera?) in a male psendohermaphrodite pig. Breeuwsma (1971) mentions one with 35% XX and 65% XY cells. Hughes (1929) and Benoit (1964) are the only authors who have described one case each of chorio-allantoic anastomoses in pigs, the latter one with the production of a freemartin condition. Bruere, Fielden & Hutchings (1968) and Vogt (1968) have both found XX/XY chimerism in one pig each. Somlev, Boris Hansen-Melander, Melander & Holm (1970) have found XX/XY chimerism in leucocyte cultures of two pigs but not in cultures of their organs. The organs only possessed XX sex chromosomes. This is the best proof so far of freemartinism in pigs.

Although the intersex condition in pigs cannot as yet be ascribed to abnormal chromosome numbers, such abnormalities, not always associated with the intersex condition, have been reported. Breeuwsma in 1968 reported an XXY sex chromosome complex. Harvey (1968) described a male pig with an XXY/XXXY sex chromosome complement. Hansen-Melander and Melander (1970) described mosaicism for translocated heterosygosity in a wellformed pig. Henricson & Bäckström (1964) described a boar with 56%lowered fertility which was heterozygous for an autosomal translocation.

It is significant that in the intersex condition testes can develop in the complete absence of a Y-chromosome. Nevertheless, no spermatogenesis has ever been found in intersexes in the absence of a Y-chromosome. This also applies to man. However, in the development of testes in intersexes one cannot exclude strongly localised mosaicism with Y-chromosomes as an aetiological factor.

Pathogenesis.

Breeuwsma (1971) found that in early histological differentiation of intersexes the cortex and medulla was separated by a *tunica albuginea*. The cortex, containing oogonia could occasionally differentiate and develop Graafian follicles but the medulla, although having numerous interstitial cells and a few rudimentary seminiferous tubules never have any spermatogonia and therefore could never develop spermatozoa. He also thought that. as a result of foetal adrenals producing androgens before sexual differentiation (Price and Ortiz, 1965), and the fact that the testes always developed cranially i.e. nearer to the adrenals in ovariotestes, and on descent underwent rotation to be situated caudally, the adrenals could be implicated in disturbing normal female development. My own observations support this implication because hyperplasia of the adrenal cortex reminiscent of the adrenogenital syndrome of man was seen in two cases (Gerneke 1967). Androgens produced by the adrenal cortex must therefore have a limited musculinising influence.

Macintyre, Hunter & Morgan (1960) found that rat foetal testes could suppress foetal ovaries if the distance between them was not greater than 8 mm. On the other hand Van der Horst and Sybesma (1969) found that testosterone was absent in the majority of cases investigated. 17 - hydroxy pregnenolone, a normal intermediary in testosterone production and normally always present, was not detected in intersex testes. This suggests that formation of testosterone was inhibited. It should be borne in mind that developing intersexual testes contain interstitial cells which normally produce testosterone but here have an XX chromosome complement and supposedly therefore cannot function normally. On the other hand, progesterone was found to be nearly normal in three cases where corpora lutea were present (Van der Horst and Sybesma, 1969). It is therefore clear that any androgens with a suppressing influence do not originate from the testes but possibly from the adrenals or elsewhere.

Gerneke (1967) found that the pineal gland of intersexes reveals a greater degree of hypertrophy and activity than normal and this would indicate a greater inhibitory effect on gonadal development. There exists therefore an interrelationship between the adrenal and pineal in the intersex condition. This interrelationship has not yet been elucidated.

Breeuwsma (1971) found a relationship between the number of foetuses in the uterus and the intersex condition.

He found a greater incidence of intersexuality where foetuses were "crowded". He put this down to a greater diffusion of masculinising substances from male to female foetuses with corresponding intersexuality developing in some cases. He however gave no indication of the manner of diffusion.

Heredity.

The consensus of opinion amongst investigators indicates that the intersex condition is inherited as a sex-limited recessive trait with the possibility of autosomal modifiers. Breeuwsma (1969) found statistically significant differences in the frequency of intersexes in the progeny of certain boars. Both paternal and maternal influences are therefore important.

The concept of freemartinism an an aetiological factor has been shown to be significant in a small number of cases and Breeuwsma (1969) with his concept of "crowding" and diffusion of masculinising substances has given this wider implications which have still to be verified.

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