

Review Article

Anomalies of Sexual Differentiation in Cattle

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Abstract: Hermaphroditism is a sexual anomaly that causes the animal to have sexual functions of both sexes (male and female). The present work aims to review hermaphroditism in cattle, showing the concept, causes, diagnosis, and possible treatments. Animals with this anomaly may show reproductive failure, sexual behavior for both sexes, and absence of estrus. It is divided into three forms: Freemartinism, True Hermaphroditism, and Pseudo-Hermaphroditism, with the most common form in cattle being true freemartinism. Finally, anomalies of sexual differentiation are diagnosed through palpation, vaginoscopy, ultrasound and genetic tests, sometimes being visually verifiable. In cases of hermaphroditism, the animal that is born with this anomaly can be surgically corrected.

Keywords: Hermaphroditism, bovines, freemartinism, pseudohermaphroditism.

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INTRODUCTION

The process of sexual differentiation can result in anomalies. These can occur both at the stage of fetal and embryonic development. There are three aspects to be evaluated, chromosomal sex, gonadal sex, and phenotypic sex. These alterations have already been described in several animal species, such as cattle, horses, sheep, pigs, dogs, and humans (Almeida M *et al.*, 2021).

In production animals, intersexuality generates economic problems, which can lead to a great loss for industries. Females with this condition are usually sterile, which prevents reproduction. In males, the loss occurs due to carcass degeneration (Corcini CD *et al.*, 2009, Ticianelli JS *et al.*, 2011).

Anomalies of sexual differentiation can present in three different ways: true hermaphroditism, pseudohermaphroditism and freemartinism (Almeida M *et al.*, 2021).

Hermaphrodite is the individual who presents the two sexes anatomically and functionally (Ticianelli JS *et al.*, 2011). They are developmental anomalies, in which there is a genetic, phenotypic and gonadal gender mismatch. It can occur simultaneously, in the same individual, testicle and ovary, being a very rare

situation. These individuals may have testes on one side and an ovary on the other, or have a testicle fused to an ovary, called ovotestis, on one or both sides (Druziani JT *et al.*, 2011).

The term pseudohermaphrodite is used to refer to animals with sexual traits of two genders (Corcini CD *et al.* 2009). These changes occur during sexual differentiation of the reproductive system and may be related to genetic factors, and this anomaly is caused by the translocation of the SRY gene to the X chromosome, thus promoting testicular development in XX individuals (Ticianelli JS *et al.*, 2011 e Mendes DB *et al.*, 2020). Pseudohermaphroditism presents only one type of gonadal tissue, presenting the same chromosomal sex and gonadal sex, but accessory sex organs usually have heterosexual characteristics, that is, of the opposite sex (Corcini CD *et al.*, 2009).

Pseudohermaphroditism can be suspected through clinical exams, such as the visualization of anomalies of the animal's external genital organs by evaluating the vaginal canal and penis, but its definitive diagnosis can be performed through histopathological analysis of its gonads to confirm ovarian or testicular tissue. Other complementary exams can also be used as a diagnostic aid, such as abdominal ultrasound, pelvic radiography to assess the presence or absence of penile bone or a contracted exam such as vaginography, and

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karyotyping to determine the individual's chromosomal pattern (Bolzan AC *et al.*, 2022).

Male pseudohermaphroditism corresponds to incompletely masculinized individuals who have genetic sex and testicular nature of the gonads. The external genitalia, however, are not normally formed and, like the internal genitalia, can be ambiguous or female. Changes to the external genitalia are generally of the female type. Often the clitoris appears hypertrophied and the vulva, infantile, with a morphology like a "parrot's beak" or a rudimentary penis, displaced between the hind limbs (Mendes DB *et al.*, 2020).

Freemartinism is the most frequent form of intersexuality found in cattle, this anomaly occurs in twin pregnancies with a male and a female fetus, therefore, freemartinism is characterized as the female that is born sterile and with male characteristics, for having been generated with a male fetus, resulting from the anastomosis of the placental blood vessels around the fortieth day of gestation, which lead to a common circulation between the embryos, allowing the sexual differentiation of the male, before that of the female, to interfere with the normal development of the reproductive tract of the latter. Thus, twin fetuses are chimeras, having cells from the twin fetus. Cell exchange in this case occurs when female gonadal differentiation is not yet complete, resulting in alteration in female genital organogenesis (Almeida M *et al.*, 2021).

Clinical signs in the adult phase of the animal begin with a history of reproductive failure, absence of estrous behavior or failure to conceive in the presence of the male (Almeida M *et al.*, 2021). Freemartinism also presents clinical signs such as masculinization of the female's reproductive tract, in addition to sterility, hypertrophied clitoris, presence of long hair on the vulva, shorter vagina, blind bottom, absence of cervix, testis and hypoplasia of Müller's ducts (Ticianelli JS *et al.*, 2011).

In cattle, the diagnosis of freemartinism is made by clinical examination of rectal palpation, complementary ultrasound examination and vaginoscopy. In addition to these methods, diagnosis requires histological verification of ovarian and testicular tissue (Costa PPC *et al.*, 2017).

Cytogenetic diagnosis for freemartinism is usually performed by karyotyping peripheral lymphocytes and other tissues or by PCR (polymerase chain reaction) studies. Cytogenetic evaluation by lymphocyte karyotyping allows the detection of two types of "XX/XY" DNA, with 93% confidence in the diagnosis of bovine freemartinism (Almeida J *et al.*, 2012), which makes it possible to identify and eliminate the reproduction of affected animals, avoiding further

damage to the breeder (Almeida M *et al.*, 2021). Genetic testing is necessary to accurately verify the reason why this intersexuality occurs. Cytogenetic investigation through the culture of peripheral lymphocytes and the molecular analysis of blood through PCR are widely used and valuable methods for a more accurate diagnosis of the genetic anomalies responsible for this intersexuality (Bueno VLC *et al.*, 2017).

Clinical treatment should be done with hormone replacement with gonadotropins. Surgical correction can also be performed with correction of the internal and external genitalia, it will depend on the choice of breeding sex to be defined by the medical team together with the owner of the animal (Almeida J *et al.*, 2012 e Costa PPC *et al.*, 2017). Surgical intervention is usually the treatment of choice for these cases, justified by the preventive nature and being performed before puberty. In addition, surgical treatment aims to remove remaining structures of the opposite sex so that they do not interfere anatomically, functionally, or psychologically with the adopted sex (Mendes DB *et al.*, 2020).

Additional file 1. Freemartin bovine showing testis and vulva
[<https://youtube.com/shorts/OwTioY05RVk?feature=share>]

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