PESQUISA VETERINÁRIA BRASILEIRA
Brazilian Journal of Veterinary Research
ISSN 0100-736X (Print)
ISSN 1678-5150 (Online)

Pesq. Vet. Bras. 46:e07831, 2026
DOI: 10.1590/1678-5150-PVB-7831

Review Article
Livestock Diseases

Inherited diseases of Hereford and Angus cattle in Uruguay: a pathological review[1]

Fernando Dutra-Quintela[2]*, Carolina Briano-Rodríguez[2], Agustín Romero-Benavente[2]

ABSTRACT.- Dutra-Quintela F, Briano-Rodríguez C, Romero-Benavente A. **Inherited diseases of Hereford and Angus cattle in Uruguay: a pathological review.** *Pesquisa Veterinária Brasileira 46:e07831, 2026*. División de Laboratorios Veterinarios "Miguel C. Rubino," Laboratorio Regional Este, Avelino Miranda 2045, CP 33000, Treinta y Tres, Uruguay. E-mail: fdutra@mgap.gub.uy

Uruguay sustains an extensive, pasture-based beef industry with more than 11 million cattle, dominated by Hereford and Aberdeen Angus breeds. Despite their economic importance, inherited disorders are often underreported because most associated losses occur prenatally, thus escaping routine postnatal detection (iceberg effect). This review synthesizes decades (1996–2025, 30 years) of veterinary surveillance and summarizes the clinicopathological features and population impact of hereditary diseases confirmed in Uruguay through integrated pathology and molecular testing. In Hereford cattle, we describe maple syrup urine disease (OMIA 000627-9913), congenital hypotrichosis (OMIA 002114-9913), epidermolysis bullosa simplex (OMIA 002081-9913), cardiomyopathy with woolly haircoat (OMIA 000161-9913), mandibulofacial dysostosis (OMIA 002288-9913), and idiopathic epilepsy (OMIA 000344-9913). In Aberdeen Angus, we detail osteopetrosis (OMIA 000755-9913), neuropathic hydrocephalus (OMIA 000487-9913), dwarfism (OMIA 001485-9913), syndactyly (OMIA 000963-9913), and arthrogryposis multiplex congenita (OMIA 002135-9913). These disorders exert a significant negative impact on reproductive efficiency and may represent a major hidden cause of the country's consistently low weaning rates. This study highlights the need for systematic genomic surveillance to prevent the dissemination of genetic defects and to safeguard productivity, animal welfare, and the international reputation of Uruguay's beef herds.

INDEX TERMS: Hereford cattle, Aberdeen Angus, inherited diseases, congenital defects, veterinary pathology, Uruguay, molecular diagnosis.

RESUMO.- [Doenças hereditárias em gado Hereford e Angus no Uruguai: uma revisão patológica.] O Uruguai mantém uma extensa indústria de carne bovina baseada em pastagens, com mais de 11 milhões de cabeças de gado, predominantemente das raças Hereford e Aberdeen Angus. Apesar de sua importância econômica, as doenças hereditárias são frequentemente subnotificadas, pois a maioria das perdas associadas ocorre no período pré-natal, escapando, portanto, à detecção pós-natal de rotina (efeito "iceberg"). Esta revisão sintetiza 30 anos (1996–2025) de vigilância veterinária e resume as características clinicopatológicas e o impacto populacional de doenças hereditárias confirmadas no Uruguai por meio de patologia integrada e testes moleculares. Em bovinos Hereford, descrevemos a doença da urina com odor de xarope de bordo (OMIA 000627-9913), hipotricose congênita (OMIA 002114-9913), epidermólise bolhosa simples (OMIA 002081-9913), cardiomiopatia com pelagem lanosa (OMIA 000161-9913), disostose mandibulofacial (OMIA 002288-9913) e epilepsia idiopática (OMIA 000344-9913). Em bovinos Aberdeen Angus, detalhamos osteopetrose (OMIA 000755-9913), hidrocefalia neuropática (OMIA 000487-9913), nanismo (OMIA 001485-9913), sindactilia (OMIA 000963-9913) e artrogripose múltipla congênita (OMIA 002135-9913). Essas doenças exercem um impacto negativo significativo na eficiência reprodutiva e podem representar uma importante causa oculta das taxas de desmame consistentemente baixas no país. Este trabalho destaca a necessidade de vigilância genômica sistemática para prevenir a disseminação de defeitos

[1] Received on April 6, 2026.
Accepted for publication on May 7, 2026.
[2] División de Laboratorios Veterinarios (DILAVE) "Miguel C. Rubino," Laboratorio Regional Este, Avelino Miranda 2045, CP 33000, Treinta y Tres, Uruguay. *Corresponding author: fdutra@mgap.gub.uy

genéticos e salvaguardar a produtividade, o bem-estar animal e a reputação internacional dos rebanhos bovinos do Uruguai.

TERMOS DE INDEXAÇÃO: Bovinos Hereford, Aberdeen Angus, doenças hereditárias, defeitos congênitos, patologia veterinária, Uruguai, diagnóstico molecular.

INTRODUCTION

Uruguay's cattle production is primarily based on an extensive, open-range, pasture-based system, with most of the territory covered by native grasslands and abundant natural water resources (Campos grassland biome) (Jaurena et al. 2021). Beef is the country's main export and a primary source of foreign income. With 70% of its production destined for international markets, Uruguay ranks among the top 10 beef exporters globally (INAC 2024). The national herd totals approximately 11.7 million head (i.e., 3.5 cattle per person), with an annual production of 2.8–3.0 million weaned calves (MGAP 2025). About 80% of the cattle stock is composed of the British breeds Hereford (HER) (polled and horned), Aberdeen Angus (AA) (black and red; both varieties are registered within the same Herd Book), and their crosses. These breeds dominate both commercial cow–calf operations and purebred stud herds and have been intensively selected for growth, fertility, rangeland adaptability, and carcass quality (Navajas & Baldi 2016).

A distinctive feature of beef production in Uruguay is the low adoption of systematic crossbreeding compared with other major beef-producing nations (Espasandin et al. 2006, Greenwood 2021). This preference for purebreds has traditionally been associated with the lower maintenance energy requirements of adult cows in extensive grazing systems (Guillenea et al. 2020). Most commercial cow–calf herds in these extensive purebred systems raise their own replacement heifers, making effective bull management critical to prevent inbreeding and the expression of genetic defects (Garrick 2011). Moreover, the international trade of germplasm for productive traits, the widespread adoption of reproductive biotechnologies, and the intensive use of a limited number of elite sires (line breeding) have increased the dissemination of inherited disorders worldwide (Agerholm 2007, Whitlock et al. 2021). Currently, more than 250 Mendelian traits in cattle are registered in the Online Mendelian Inheritance in Animals database (OMIA 2026). Consequently, inherited diseases have reached global significance, with the same anomalies being diagnosed almost simultaneously in most major beef-producing nations, including Uruguay (Kelly et al. 2012, Romero Benavente 2017).

The true impact of hereditary diseases is often underestimated. Early cases are typically sporadic and go unrecognized until lethal allele frequencies rise (Whitlock et al. 2021). Breeders rarely, if ever, submit samples from malformed calves to avoid reputational stigma (Leipold et al. 1983). In addition, the absence of routine genetic testing in most diagnostic laboratories, together with the pathological complexity and multiple analyses required to distinguish genetic from non-genetic congenital malformations, contributes to the underreporting of heritable diseases (Craig et al. 2015, Windsor 2018). Consequently, diagnostic laboratories frequently rely on crude diagnostic morbidity (or crude diagnostic frequency), i.e., the proportion of congenital anomalies present at birth among all diagnostic submissions (Rousseaux & Ribble 1988). Reported values of this metric are consistently low worldwide (0.5–1%) (Leipold et al. 1983, Marcolongo-Pereira et al. 2010, Quigley & Mee 2025), reinforcing the widespread perception that hereditary diseases in cattle are rare or of minor importance. However, because this metric excludes embryo losses and defective fetuses that do not reach term, it consistently underestimates the true biological incidence of genetic defects (Mason et al. 2005).

In contrast, specific relative frequency, defined as the proportion of heritable congenital cases among reproductive-loss submissions, provides a more accurate estimate of the significance of hereditary anomalies (Rousseaux & Ribble 1988, Mason et al. 2005). This metric not only documents the severity of the problem but also indicates whether an inherited anomaly is part of a broader syndrome involving embryo losses, fetal death, and stillbirths (Mason et al. 2005). However, it is rarely calculated because most diagnostic databases lack standardized coding of clinical syndromes (e.g., infertility, abortion, stillbirth, and perinatal loss), which limits the definition of an appropriate denominator for reproductive losses.

Inherited diseases in HER and AA are therefore of particular concern in Uruguay, not only because of their direct effects on fertility, productivity, and animal welfare, but also because of their broader economic, genetic, and reputational consequences for national and international beef markets. This review summarizes the most relevant inherited disorders diagnosed in HER and AA cattle in Uruguay, focusing exclusively on those confirmed through both pathological examination and genetic testing. For each condition, we describe the macroscopic and microscopic pathology, mode of inheritance, and specific morbidity and epidemiological significance within the national herd. The importance of hereditary diseases in Holstein cattle in Uruguay has also been reported previously (Briano-Rodríguez et al. 2021).

MATERIALS AND METHODS

Ethical approval. This study was based exclusively on previously published literature and retrospective diagnostic records; therefore, no animal experimentation was performed and approval by an Ethics Committee on Animal Use (CEUA) was not required.

Retrospective study. Diagnostic information (1996–2025, 30 years) was obtained from the "Unidad de Registro y Análisis de Diagnósticos" (UNIRADD) database of the División de Laboratorios Veterinarios "Miguel C. Rubino" (DILAVE), "Ministerio de Ganadería, Agricultura y Pesca" (MGAP), Uruguay, which compiles historical, standardized, georeferenced records from all official veterinary diagnostic laboratories throughout the country. This unified system maintains species-specific coded information on clinical syndromes and final diagnoses, as well as laboratory analyses and animal data (category, breed, and age). Inherited diseases in database are coded following the Online Mendelian Inheritance in Animals (OMIA) system[3].

Selection criteria. Only hereditary diseases confirmed by pathological examination and molecular testing were included in this review. Tissue sections were stained with hematoxylin and eosin (HE) for histological evaluation. The analysis was restricted to HER and AA cattle. Records from other breeds, such as inherited

[3] Accessed Feb 27, 2026. https://omia.org/home

disorders reported in Holstein cattle (Briano-Rodríguez et al. 2021 and alpha-mannosidosis in crossbred Angus and Braford × Limousin calves (Rivero et al. 2001, Kelly et al. 2012), as well as numerous congenital malformations recorded in the database but lacking molecular characterization, such as brachygnathia superior and degenerative joint disease (AA), anencephaly (HER), lissencephaly-pachygyria (HER), polymelia and conjoined duplication (AA, HER) congenital lipomatosis (HER), and cerebellar abiotrophy (AA), were excluded from this review.

Diagnostic metrics. Crude relative morbidity was calculated as the proportion of congenital diagnoses among all cattle diagnostic submissions in the UNIRADD database. Specific relative morbidity was estimated as the proportion of inherited congenital diagnoses (OMIA-coded) among reproductive-loss submissions registered in the database as infertility/low pregnancy rate, abortion, stillbirth, and perinatal loss. The latter metric was estimated specifically for Hereford and Aberdeen Angus cattle.

RESULTS AND DISCUSSION

Significance of inherited disorders

The crude relative frequency of congenital disorders in cattle in Uruguay was 0.83%, consistent with published worldwide reports. A similar value (0.88%) was reported in Rio Grande do Sul, Brazil (Marcolongo-Pereira et al. 2010). Among reproductive-loss submissions, the specific relative frequency of all congenital anomalies in cattle, including both genetic and non-genetic conditions, was 5% across all breeds. In HER and AA cattle, the corresponding frequency for OMIA-coded inherited disorders was 3.5%, indicating that approximately 75% of congenital anomalies in these breeds in Uruguay have a genetic basis and predominate over those associated with environmental teratogens. This proportion corresponds to an estimated annual economic impact of USD 13.3 million attributable to prenatal losses (Hirigoyen et al. 2023), highlighting the contribution of genetic diseases to the country's persistently low national weaning rate (60%–65%) (MGAP 2025). When reproductive-loss categories were analyzed separately, inherited disorders accounted for 34% of infertility records, 3% of abortion records, and 18% of perinatal mortality records, revealing the hidden significance of this often-overlooked problem. As a group, inherited anomalies are surpassed only by leptospirosis, neosporosis, and brucellosis among abortion syndromes, and by dystocia and leptospirosis in perinatal mortality (Dutra-Quintela 2016). Therefore, heritable anomalies observed at birth represent only the surviving fraction of losses initiated at conception (the "iceberg effect") (Fig. 1).

Inherited pathologies in hereford cattle

Maple syrup urine disease (MSUD) (OMIA 000627-9913). MSUD, previously termed hereditary neuraxial edema and congenital cerebral oedema, is an inherited autosomal recessive aminoacidopathy described in young HER and Shorthorn calves. It has been reported in Australia, the United Kingdom, the United States, Canada, New Zealand, Argentina, and Uruguay (Baird et al. 1987, Harper et al. 1990, González et al. 1997, Healy et al. 2002, Dutra et al. 2015, Robarge et al. 2015). In Uruguay, MSUD has been diagnosed in both Polled HER and Polled Shorthorn calves. MSUD also occurs in human infants worldwide, although its prevalence is much higher in some ethnic groups (Strauss et al. 2020).

MSUD is caused by a deficiency of the branched-chain alpha-keto acid dehydrogenase (BCKADH) enzyme complex (Dennis & Healy 1999). This enzyme is essential for metabolizing the branched-chain amino acids leucine, isoleucine, and valine ingested from colostrum. A mutation in genes regulating this degradation process leads to the accumulation of these branched amino acids and their corresponding alpha-keto acids to toxic levels in the cerebrospinal fluid, blood, and tissues (Windsor et al. 2011). BCKADH consists of four subunits (E1α, E1β, E2, and E3) encoded by separate genes. In Polled HER, the molecular basis is a nonsense mutation (c.148C>T) in the *BCKDHA* gene, whereas in Polled Shorthorn the mutation is a C>T transition (c.1380C>T) in the same gene (Dennis & Healy 1999). Crossbred calves from Polled HER×Polled Shorthorn matings are compound heterozygotes, illustrating the molecular heterogeneity of MSUD in cattle.

MSUD is one of the most important hereditary diseases in HER cattle in Uruguay. Most outbreaks occur in commercial cow–calf farms following the introduction of a newly purchased carrier bull. Based on DILAVE database records (seven outbreaks; 47 affected calves among 899 births at risk), the pooled within-herd cumulative incidence was 5.23%, with a case fatality rate of 100%. Genotyping data from three of these affected farms showed an overall carrier prevalence of 10.9% (21/196 cows and 1/6 bulls). In one of these herds, carrier prevalence reached 16.3%, and the pregnancy rate was drastically reduced to 35%, suggesting MSUD prenatal (embryonic/fetal) losses. Similar carrier prevalence (13%) has been reported in an affected herd in Indiana in the United States (Robarge et al. 2015).

Affected calves appear normal at birth but develop progressive neurological signs shortly after ingesting colostrum, including ataxia, depression, stiffness, intermittent seizures, and opisthotonus, leading to death within 3–5 days (Fig. 2). A characteristic sweet odor in the urine, attributable to an

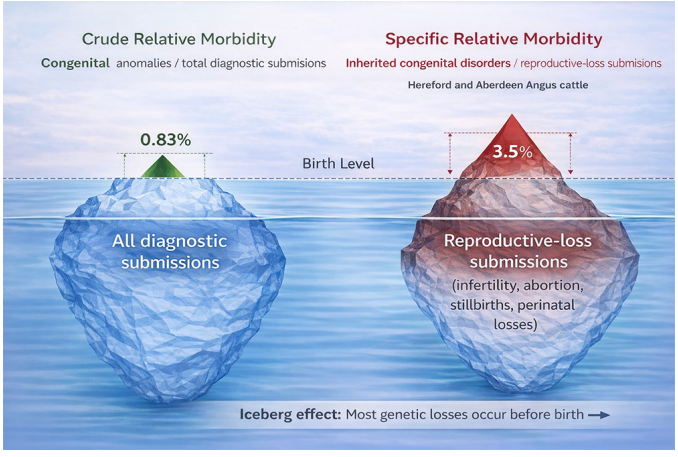

Fig. 1. The "iceberg effect" in bovine inherited disorders. Comparison between crude relative morbidity (0.83%), representing congenital malformations among all diagnostic submissions (predominantly postnatal), and specific relative morbidity in Hereford and Aberdeen Angus cattle (3.5%), representing confirmed inherited cases among reproductive-loss submissions in these breeds. The birth level indicates the threshold at which defects become detectable at parturition, highlighting the hidden impact of prenatal losses. AI-assisted graphic, author-validated.

isoleucine derivative, is a hallmark of the condition (Dutra et al. 2015). Fetal death and premature birth may also occur because the bovine placenta is somewhat inefficient at regulating branched-chain amino acid and keto acid concentrations (Harper et al. 1990).

At necropsy, affected calves present only mild swelling and flattening of the cerebral gyri. Histologically, there is severe intramyelinic vacuolation of the white matter (*status spongiosus*) throughout the central nervous system, primarily in the cerebellum (Fig. 3), with lesser involvement of the cerebrum, basal nuclei, and thalamus, and minimal involvement of the spinal cord. Vacuoles are large (20–100 µm), optically empty, and oriented parallel to axons. Cresyl violet staining confirms periaxonal spongiosis consistent with myelin edema (Fig. 4). Electron microscopy shows that myelin vacuolation is caused by splitting of the myelin lamellae at the intraperiod line, producing vacuoles within the myelin sheath that primarily involve the outer lamellae (Harper et al. 1990). In the cerebellar molecular layer, numerous dendritic spheroids consistent with excitotoxic injury are always present (Fig. 5).

Diagnosis is confirmed by histopathology and polymerase chain reaction (PCR)-based genotyping or high-resolution melt analysis of the c.148C>T mutation in the *BCKDHA* gene. Although biochemical analysis of amino acids is possible, it is not routinely used. Carrier identification by genomic testing is the most effective strategy for the control and eradication of MSUD. Knowledge of high-risk lineages may also help prevent transmission of the defective allele; however, systematic genetic testing has not yet been implemented in Uruguay.

Congenital hypotrichosis (HY) (OMIA 002114-9913). HY, also known as semi-hairlessness or viable HY, is a non-lethal autosomal recessive disorder of HER cattle. It has been reported in New Zealand, the United States, and the United Kingdom (Jolly et al. 2008). In Uruguay, although recognized for decades by farmers and veterinarians, the condition was only recently confirmed by histopathology and molecular testing in commercial herds (Romero-Benavente et al. 2023).

The disease is caused by an 8-bp deletion in exon 1 of keratin 71 (*KRT71*) (g.27331221delTGTGCCCA; c.281delTGTGCCCA) (Jacinto et al. 2021). *KRT71* encodes a structural protein essential for intermediate keratin filaments within the inner

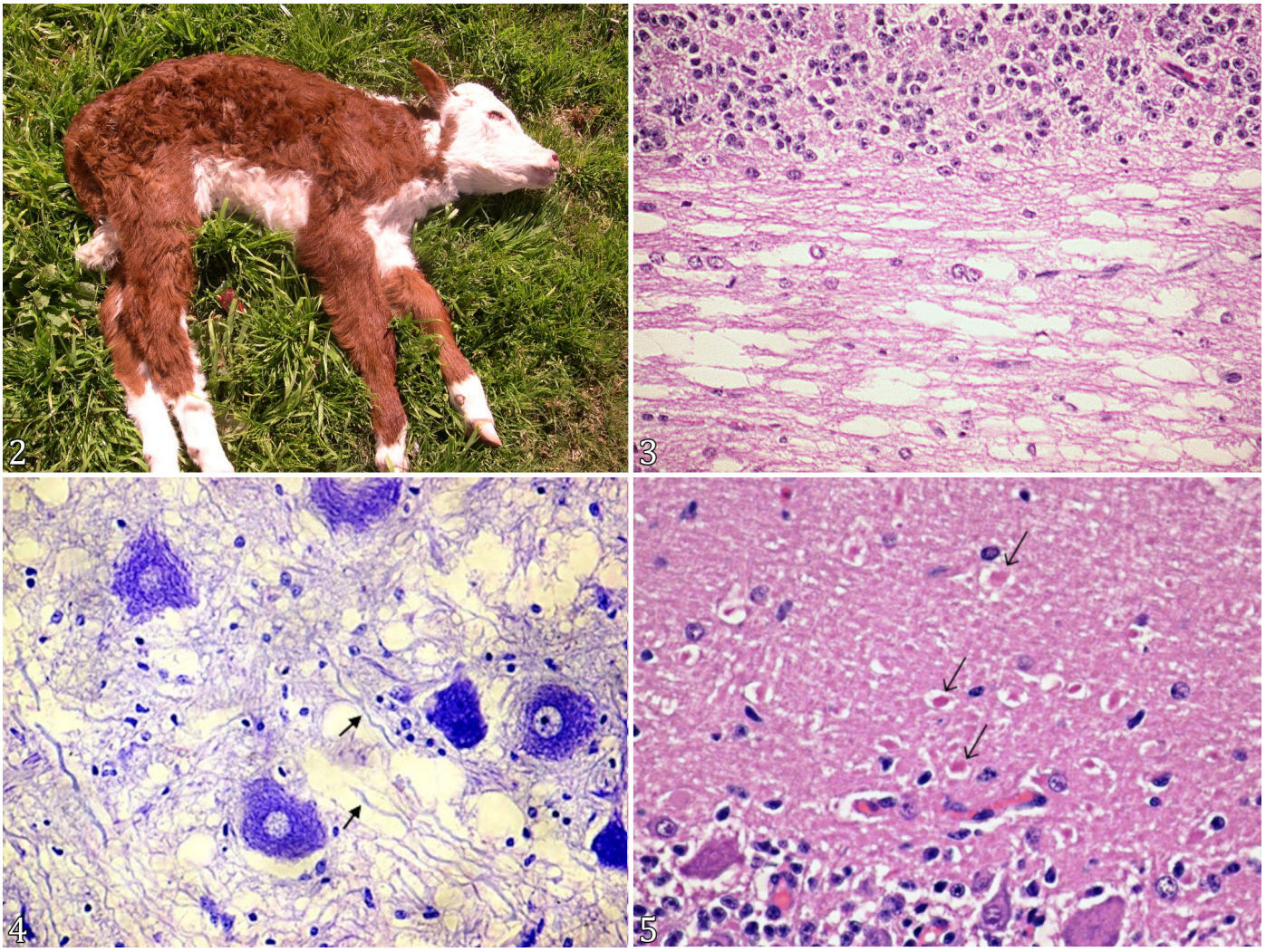

Fig. 2–5. Maple syrup urine disease (MSUD) in Hereford calves. (**2**) Neonatal calf with convulsions and limb rigidity. (**3**) Severe status spongiosus in cerebellar white matter. HE, obj. 400x. (**4**) Periaxonal spongiosis (arrows) in the medulla oblongata. Cresyl violet, obj. 400x. (**5**) Dendritic spheroids in the cerebellar molecular layer. HE, obj. 400x.

root sheath of the hair follicle (Jacinto et al. 2021). Mutations in *KRT71* are also responsible for wavy or curly coat phenotypes in dogs, cats, and humans (Salmela et al. 2019).

Most cases occur sporadically in commercial cow–calf operations or as outbreaks following the introduction of a newly purchased carrier bull. Based on DILAVE records (four outbreaks; nine affected calves among 198 animals at risk), the pooled within-herd incidence was 4.55%, with no recorded fatalities.

Affected calves are born partially to completely alopecic. They are smaller than normal cohorts at birth and show poor postnatal growth, being significantly lighter at weaning (Fig. 6). The hair coat is pale yellow-orange rather than the typical rust-brown to deep red of HER cattle. Hair is sparse, short, fine, brittle, and easily epilated. Characteristically, the woolly coat predominates in white-haired areas (Fig. 7), while a wavy or curly pattern predominates in colored areas. Ventral alopecic skin is thin, dry, scaly, and erythematous. The phenotype predisposes affected calves to sunburn, thermal stress, and secondary skin infections (Romero-Benavente et al. 2023).

Trichography reveals thin, soft, curly hairs with irregular clusters of macromelanosomes that distort and fragment hair shafts (Fig. 8). Histologically, the epidermis is thickened, dermal papillae are poorly differentiated, and follicles are confined to the dermis. Follicles may show vacuolation and necrosis of Huxley's and Henle's layers, with abnormally large trichohyaline granules in Huxley's layer (Fig. 9). Diagnosis is confirmed by PCR-based genotyping of *KRT71* exon 1.

Epidermolysis bullosa simplex, EBS-*KRT5* (OMIA 002081-9913). Epidermolysis bullosa (EB) comprises a group of inherited mechano-bullous diseases characterized by extreme fragility of the dermo-epidermal junction. Based on the level of tissue separation, three main types are recognized: junctional, dystrophic, and simplex (Fine et al. 2014).

The simplex form (EBS), also known as "red foot disease," is the subtype identified in Hereford (HER) cattle in Uruguay (Dutra & Baroni 2007, Kelly et al. 2012). It is caused by an

Fig. 6–9. Congenital hypotrichosis (*KRT71*) in Hereford cattle. (**6**) Affected 6-month-old calf at the front, with semi-alopecia, smaller body size, and a pale yellow hair coat compared with normal deep red coat herdmates in the background. (**7**) Close-up of the ventral head showing semi-alopecia, long, twisted hairs, and dry, scaly skin. (**8**) Trichogram showing a fragmented hair shaft with pigment clumping (macromelanosomes); these findings support *ante mortem* diagnosis. (**9**) Dysplastic hair follicle with degeneration of the inner root sheath and prominent trichohyaline granules (arrow). HE, obj. 400x.

autosomal recessive missense mutation (c.483G>A) in the keratin 5 (*KRT5*) gene. This substitution affects the highly conserved L12 linker domain of the KRT5 protein, disrupting keratin heterodimer formation and compromising the structural integrity of intermediate filaments, which results in increased fragility of basal keratinocytes (Ford et al. 2005). In Danish Hereford calves, EBS has been associated with a deletion in the *LAMC2* gene (Murgiano et al. 2015), and more recently a *de novo KRT5* mutation was identified in a crossbred Holstein calf (Jacinto et al. 2020). These findings highlight the genetic heterogeneity of EBS and the importance of genomic characterization of clinical cases.

In Uruguay, EBS typically occurs in commercial herds where the prolonged use of the same lineage leads to high levels of inbreeding. The disease often manifests sporadically and may go unrecognized for years; abortions and stillbirths may also occur (Ford et al. 2005). In a small HER herd (34 cows, one sire) in Uruguay, where the same sire was used for several years and mated with his own daughters (backcrossing), three clinical cases were born during the same calving season. Sporadic cases had been observed in previous years (Dutra & Baroni 2007). The *KRT5* mutation was confirmed by polymerase chain reaction (PCR)-restriction fragment length polymorphism analysis in one of the affected calves (173 bp band), while the sire and dam were identified as carriers by displaying all three diagnostic bands (173, 118, and 55 bp) (Kelly et al. 2012). This case illustrates how endogamy facilitates the emergence of rare inherited diseases.

At birth or within a few days of life, affected calves exhibit skin detachment and extensive reddish ulceration on all four limbs, chiefly over the carpus, tarsus, and coronary band (Fig. 10). Blisters containing serohemorrhagic fluid are common on the nasal planum, tongue, and hard palate, where moderate pressure on the muzzle or gingiva readily produces detachment of extensive epithelial sheets (Nikolsky-like sign) (Fig. 11). Hoof sloughing (exungulation) involves all four feet. Lesions are so severe that calves are unable to stand or suckle, invariably resulting in neonatal death.

Histologically, the hallmark is the formation of extensive subepidermal bullae and vesicles (Fig. 12). The bulla roof consists of intact full-thickness epidermis, while the floor is lined by a residual, periodic acid-Schiff (PAS)-positive basement

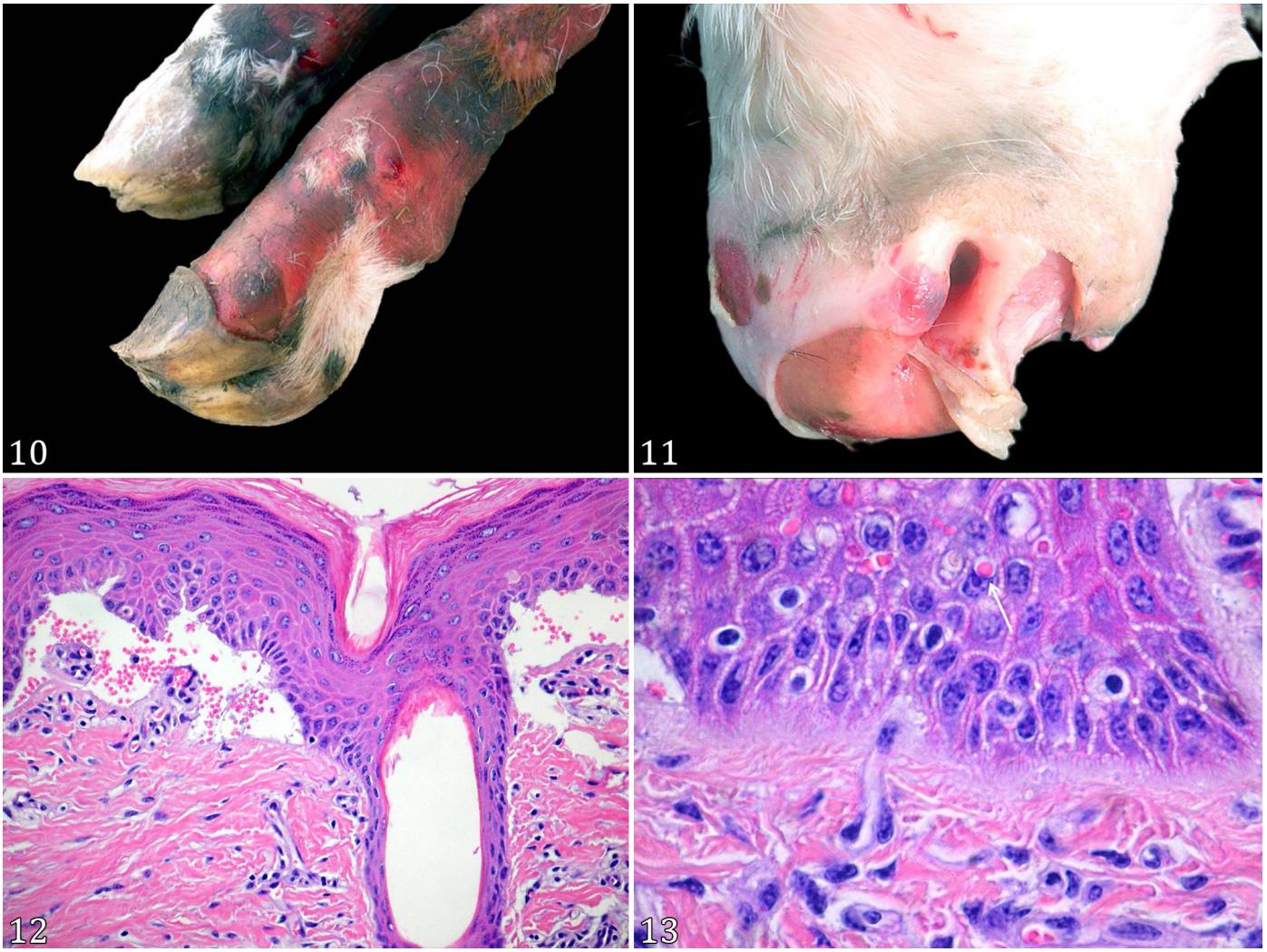

Fig. 10–13. Epidermolysis bullosa simplex in Hereford calves. (**10**) Neonate with extensive "red foot" lesions and skin denudation on distal limbs. (**11**) Severe ulceration and blistering on the nasal planum. (**12**) Subepidermal clefting with an intact epidermal roof. HE, obj. 400x. (**13**) Tonofilament clumps (arrow) and keratinocyte apoptosis. HE, obj. 400x.

membrane. Numerous apoptotic cells and dyskeratotic keratinocytes containing condensed eosinophilic cytoplasmic inclusions (tonofilament clumps) are observed (Fig. 13). Erythrocytes and occasional basal cell remnants are present within the cleft. Similar clefting is observed in the oral mucosa, tongue, and esophagus.

Diagnosis is supported by characteristic clinicopathologic findings and confirmed by PCR-based genotyping for the *KRT5* variant. Ultrastructural studies (transmission electron microscopy) are required to definitively characterize the specific subtype and differentiate EBS from the junctional form of EB. Differential diagnoses for ulcerative and vesicular lesions include foot-and-mouth disease and mucosal disease caused by bovine viral diarrhea virus (Mauldin & Peters-Kennedy 2015); however, these are typically associated with different epidemiological patterns and lack the extreme skin fragility and congenital onset. Other rare conditions such as bullous pemphigoid and systemic lupus erythematosus are also considered but are highly unlikely to present as neonatal outbreaks. Carrier identification through genomic testing of sires is the only effective measure to prevent the dissemination of EBS on farms. To date, no national-level studies have estimated the allele frequency of the EBS-associated mutation in Uruguayan beef cattle.

Cardiomyopathy with woolly haircoat (CWH) (OMIA 000161-9913). CWH is a lethal autosomal recessive disorder of HER cattle. It is common in Australia, where incidence rates can exceed 2.2% in some herds (Morrow & McOrist 1985). The disease has also been confirmed in Uruguay (Dutra et al. 2011) and recently in Russia (Konovalova et al. 2021).

CWH is caused by a mutation in the *PPP1R13L* gene, resulting in the substitution of three amino acids and a premature stop codon at position 325 of the protein product. This gene interacts with NF-κB, a key regulator of genes involved in inflammation, immune response, and cell proliferation (Simpson et al. 2009).

In Uruguay, CWH is the most frequent hereditary disease in HER cattle, with 122 clinical cases recorded in the DILAVE database. Data from eight outbreaks show a pooled within-herd incidence of 3.69% (47/1273) and a case fatality rate of 97.87% (46/47). These high frequencies likely result from the silent dissemination of the mutation within the HER population through influential sires, such as the Canadian Remitall Deliverance and the American WC Sundance (Dutra et al. 2011), which were used extensively before molecular diagnostic tools became available.

Affected calves are easily recognizable at birth by a distinctive, dense, and tightly curled "woolly" coat that covers the entire body (Fig. 14), except for the distal limbs and inner thighs, where the hair is thick, long, and stiff but not curly. The hair is coarse, dry, and often matted with debris. Histologically, the skin exhibits hypoplastic sebaceous glands, increased hair follicle density, and severe follicular dysplasia characterized by a contorted or spiraled bulb architecture, which explains the woolly haircoat phenotype (Fig. 15). Most affected calves die within the first three months of life and rarely survive beyond six months because of progressive cardiac insufficiency, ventricular arrhythmias, tachypnea, weakness, and heat intolerance. The condition can also cause abortions or stillbirths with the characteristic woolly coat and cardiomyopathy (Dutra-Quintela 2016).

Post mortem examination reveals marked cardiomegaly, with a heart-to-body weight ratio typically ranging from 0.94% to 1.54% (normal: < 0.5%–0.7%) (Dutra et al. 2011). The heart shows severe concentric hypertrophy of the ventricular walls, interventricular septum, and papillary muscles, often leading to obliteration of the ventricular cavities (Fig. 16). Although hypertrophy is global, a disproportionate septal-to-free-wall ratio (> 1.4) is a hallmark finding. Microscopically, the myocardium shows marked fiber disarray: bundles follow a serpentine rather than parallel course, forming deep undulations and interlacing bands that cross at acute or right angles (Fig. 17). Cardiomyocytes are hypertrophic (often > 20 μm in diameter) and tightly packed, with irregular sarcomeric striations and prominent ovoid nuclei.

Diagnosis is supported by characteristic pathologic findings and confirmed by genotyping for the *PPP1R13L* variant. This molecular test is essential for estimating the prevalence of the mutant allele within the national HER population.

Mandibulofacial dysostosis (MD) (OMIA 002288-9913). MD is a lethal, autosomal recessive disorder of HER cattle reported in the United States (Sieck et al. 2020) and Uruguay (Dutra-Quintela 2022). It is caused by a missense mutation in the *CYP26C1* gene (c.1051T>C; p.Phe351Leu), located at Chr26:14404993 (ARS-UCD1.2). This mutation disrupts retinoic acid metabolism, leading to severe first pharyngeal arch defects and the pathognomonic persistence of Meckel's cartilage. This structure is normally present only during embryonic development but is retained in affected calves (Sieck et al. 2021).

MD was diagnosed in Uruguay in three commercial cow–calf operations, with 12 clinical cases among 217 animals at risk (5.53% pooled incidence; 100% lethality). Genotyping of pedigree bulls and cows in one of the source stud farms revealed a 13.04% carrier prevalence (15/115). In HER stud herds in Uruguay, carrier prevalence for MD ranged from 18% to 38% from 2022 to 2025, based on annual genetic testing of breeding animals (n = 444 animals tested across 16 herds) (R. Fossati, Genexa®, personal communication, 2026). The high prevalence of MD in Uruguay is linked to the widespread use of United States carrier sires, particularly NJW 73S W18 Hometown 10Y ET and SHF Wonder M326 W18 ET (Bedwell 2020), whose genetics have been broadly disseminated in the local population (Ravagnolo et al. 2021).

Clinically, the most striking feature is maxillary brachygnathia with lip commissures extending beyond the eyes, creating a sardonic grin reminiscent of the Joker character ("Joker disease," or "enfermedad del Guasón" as it is popularly known in Uruguay) (Fig. 18). Affected calves show lingual prolapse, temporomandibular joint laxity, and often cleft palate with a shortened or crooked upper jaw (maxilla), preventing suckling and resulting in death from starvation within days. A pathognomonic finding is a pedunculated fibroepithelial polyp at the lip commissure, which is consistently associated with underlying persistent Meckel's cartilage (Fig. 19). Several other cutaneous polyps may also be found on the face, neck, and oral cavity, although these are inconsistently located and are never associated with Meckel's cartilage.

Post mortem examination reveals severe craniofacial malformations, best assessed using the Cobbler's cut technique for temporal bone dissection (Singh & Rohilla 2018). There is dysostosis of the temporomandibular joint, maxillary

brachygnathia, and, in some cases, campylognathia and cleft palate. The temporal and zygomatic processes of the temporal bone are synostosed, forming a thickened zygomatic arch that encloses persistent Meckel's cartilage (Fig. 20), a rod-shaped hyaline structure extending from the commissural papilloma to the middle ear. There is marked shortening of the coronoid process and flattening of the mandibular fossa, resulting in abnormal laxity and increased mandibular mobility (Fig. 21). The middle ear is malformed, characterized by a sclerotic tympanic bulla and hypoplastic or absent ossicles, which explains the deafness observed in affected animals. No abnormalities are observed in other bones or joints.

Histologically, Meckel's cartilage is composed of well-differentiated hyaline cartilage with chondrocytes in lacunae and an abundant basophilic extracellular matrix. In normal development, both the proximal and caudal extremities of Meckel's cartilage undergo endochondral ossification, contributing to the anterior portion of the mandible as well as to the malleus and incus of the middle ear, while the intermediate portion typically undergoes dedifferentiation into fibrous connective tissue. In MD, this normal regression fails, and remnants of Meckel's cartilage persist, becoming entrapped within the zygomatic arch and middle ear and incorporated into the commissural polyps.

Diagnosis is primarily clinical. The characteristic facial deformity, combined with bilateral cutaneous polyps at the lip commissures, is distinctive and virtually pathognomonic of this condition. *Post mortem* identification of retained Meckel's cartilage is unique to this disease but requires careful temporal bone dissection. Molecular diagnostic tests are available to confirm the disease and could be used to assess the true prevalence of the mutant allele within the national HER herd.

Idiopathic epilepsy (IE) (OMIA 000344-9913). IE is an autosomal recessive disorder predominantly observed in HER calves with horned ancestry. The disease appears to be frequent on commercial farms in Uruguay but is seldom diagnosed because cases are sporadic, semi-lethal, and rarely submitted for necropsy.

A DNA test for IE has been developed, but information about the causal gene or variant has not been published in peer-reviewed journals (OMIA 2026). Technical sources

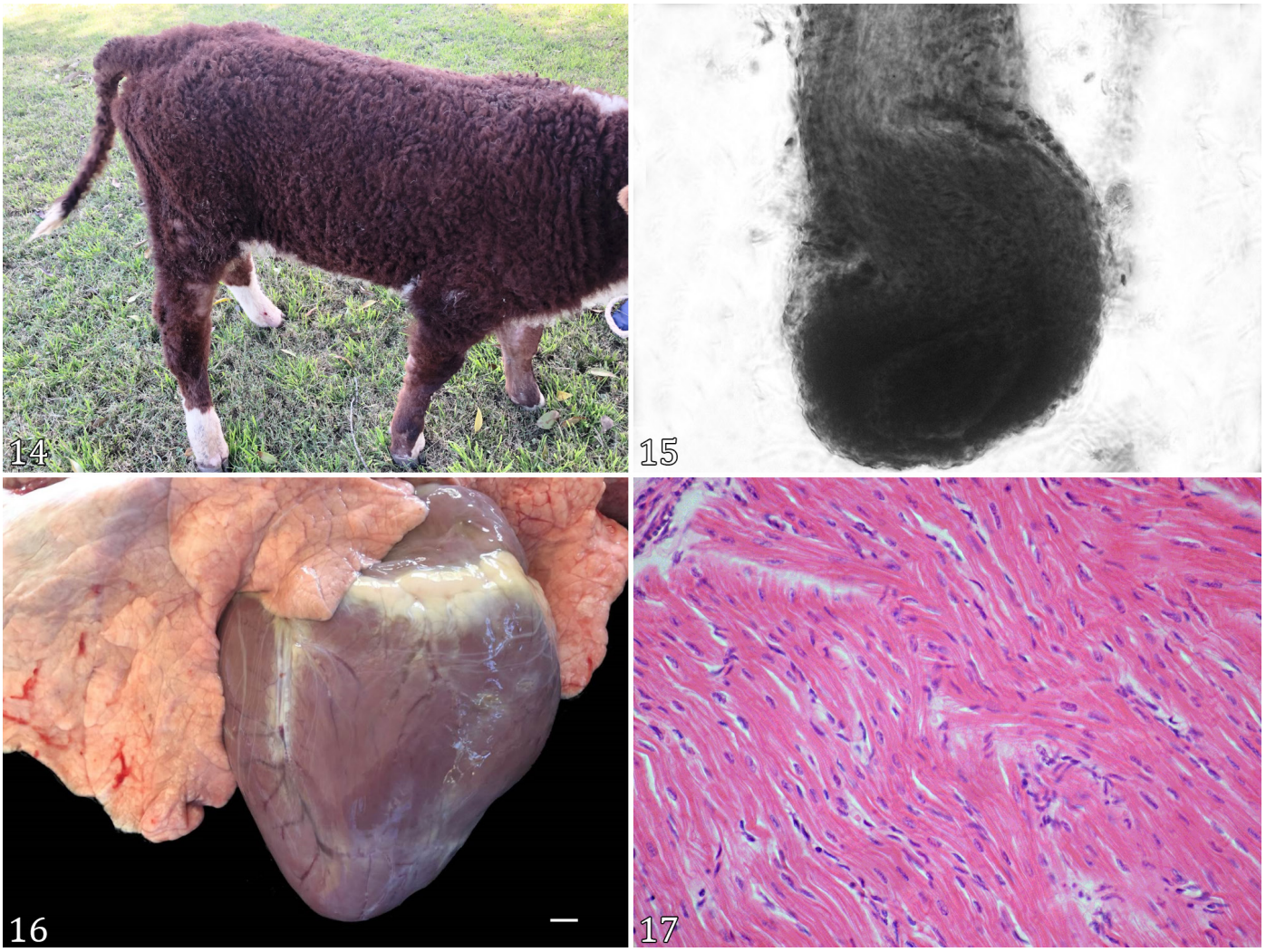

Fig. 14–17. Cardiomyopathy with woolly haircoat in Hereford cattle. (**14**) Seven-day-old calf with the characteristic dense, woolly haircoat. (**15**) Thick section/phase-contrast image showing contorted hair bulb architecture. 1000x magnification. (**16**) Marked cardiomegaly with a globoid shape, rounded apex, and disproportionate heart-to-lung relationship. Bar = 1 cm. (**17**) Myocardial fiber disarray with hypertrophic cardiomyocytes in interlacing bands. HE, obj. 400x.

describe the DNA change as a complex duplication/deletion event resulting in a net 5-bp insertion (Kaiser 2009, Whitlock 2010). The mutation is highly prevalent in Line 1 (L1) Hereford (MacNeil 2009) and has been traced back to a single foundation sire born in 1982 (HH Advance P242), whose grandson, HH Advance 9012Y (born in 1989) (Beever 2007), has been widely used in Uruguay (Ravagnolo et al. 2021).

In Uruguay, IE was confirmed on a small-scale farm (3/15 calves), where cases appeared sporadically following the introduction of a HER bull. Affected calves appear normal at birth but may sporadically develop myoclonic spasms and seizures from the neonatal period up to several months of age. Episodes may occur spontaneously or be triggered by handling in corrals (Fig. 22) or during mustering (Fig. 23). Seizures can range from several minutes to over an hour. Although calves are neurologically normal during the interictal period, they ultimately die due to accidental trauma, exhaustion during prolonged convulsions, or drowning in streams or water reservoirs.

Diagnosis of IE relies on clinical observation of episodic seizures and molecular confirmation, as no pathognomonic lesions have been established. MSUD is readily excluded through DNA testing or histopathology (characteristic *status spongiosus*). Another major differential diagnosis is *GLRA1*-related hyperekplexia (formerly termed inherited congenital myoclonus; OMIA 000689-9913), characterized by neonatal hypertonia and an exaggerated startle reflex (Harvey et al. 2008). However, hyperekplexia lacks microscopic lesions and has not yet been molecularly confirmed in Uruguay (Kelly et al. 2012). "Shaker calf syndrome" (Rousseaux et al. 1985) may represent the same clinical entity as IE; although it was originally associated with intraneuronal neurofilament accumulation, these findings have not been definitively correlated with the modern IE molecular variant.

Inherited pathologies in AA cattle

Osteopetrosis (OS) (OMIA 000755-9913). OS, also known as "marble bone disease," is a lethal autosomal recessive disorder of AA cattle, particularly within Red Angus

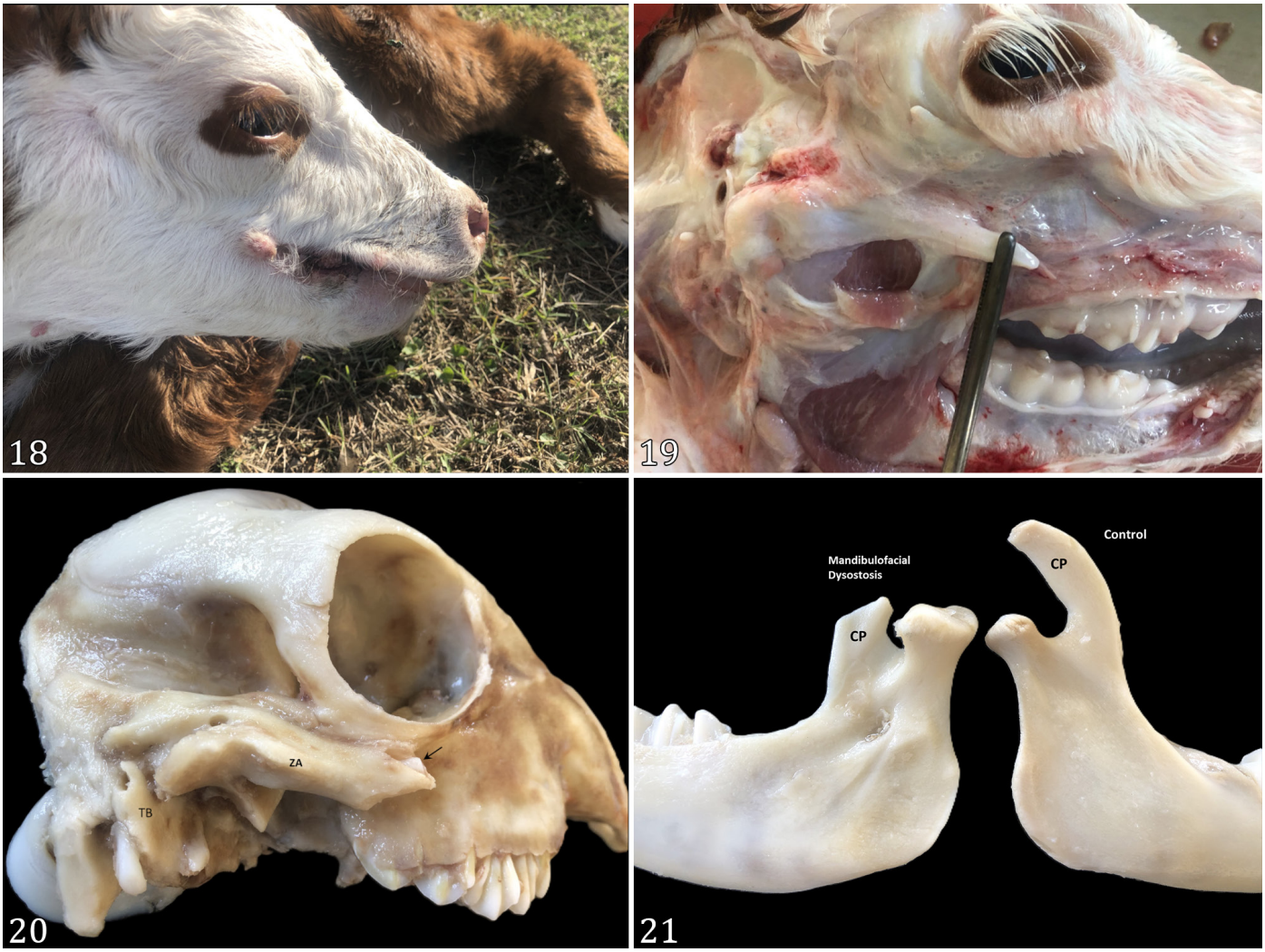

Fig. 18–21. Mandibulofacial dysostosis ("Joker disease") in Hereford calves. (**18**) Affected calf showing the characteristic "smiling" appearance, maxillary brachygnathia, and the commissural polyp; note an accessory submandibular polyp. (**19**) Free end of persistent polyp-associated Meckel's cartilage. (**20**) Skull showing a thickened zygomatic arch (ZA), persistent Meckel's cartilage (arrow), and malformed tympanic bulla (TB). (**21**) Mandible showing a shortened coronoid process (CP) in an affected calf compared with a normal age-control (bleached specimens).

lineages. It emerged with high incidence in the United States and Canada during the 1960s and 1970s, declined following implementation of progeny testing, and re-emerged in 2005 in Red Angus (Wight-Carter 2006, Meyers et al. 2010). A carrier prevalence of 2% has been reported among pedigree Red Angus bulls, reaching up to 20% in populations heavily dependent on carrier bulls, mainly of the BUF CRK ROMEO lineage (Meyers et al. 2010).

OS is caused by an approximately 2.7-kb deletion in *SLC4A2*, which encodes a bicarbonate-chloride transporter essential for osteoclast-mediated bone resorption. The mutation causes intracellular alkalinization, preventing the necessary acidification of resorption lacunae. This results in retention of primary trabecular bone within medullary cavities and the formation of dense but fragile bones (Meyers et al. 2010).

In Uruguay, eight OS-affected calves were diagnosed on two small-scale commercial farms in AA, Red Angus, and their crosses (Dutra et al. 2012). All cases occurred following the introduction of a newly purchased Red Angus bull. Affected calves were stillborn or died within hours of birth. Although well developed, they presented a compact body, marked brachygnathia, and tongue prolapse; farmers referred to them as "terneros de mandíbula corta" ("short jaw calves") (Fig. 24).

A complete skeletal examination is necessary to identify the classical lesions. Mandibles are shortened with crowded molars; frontal bones are solid with absence of paranasal sinuses; nasal passages are obstructed by compact osteocartilaginous turbinates; and the cranial vault is narrowed, with intracranial projection of the presphenoid wings (Fig. 25). Compressed cerebral hemispheres appear flattened, and the cerebellum may herniate through the foramen magnum (Arnold–Chiari type II malformation).

Long bones are shortened, dense, and prone to fracture. On section, medullary cavities are absent, with narrow diaphyses and flared metaphyses. The medullary cavity is replaced by dense primary spongiosa forming a characteristic "double-cone" structure (Fig. 26). Histologically, there is severe osteosclerosis with persistent chondro-osseous primary trabeculae, absent Howship's lacunae, and few inactive osteoclasts with pyknotic nuclei (Fig. 27) (Dutra et al. 2012, O'Toole et al. 2012). Diagnosis is based on the pathognomonic skeletal phenotype; molecular tests are essential for carrier control.

Neuropathic hydrocephalus (NH) (OMIA 000487-9913). NH, also known as "water head," is a lethal autosomal recessive genetic disorder of the AA breed (American Angus Association 2019). It is caused by a mutation that disrupts the function of a protein essential for central nervous system development. The gene involved is highly conserved across species, and analogous mutations in murine models lead to nearly 100% embryonic mortality (Beever 2009). A diagnostic DNA test has been available since 2008, but the specific molecular details remain unpublished (Beever 2009).

The founder NH mutation is believed to have arisen *de novo* in the bull GAR Precision 1680. This sire and his popular son, CA Future Direction 5321, are both carriers of NH and arthrogryposis multiplex congenita (AM); however, the two mutations segregate independently within the same bloodline (Whitlock 2010, Windsor et al. 2011). Consequently, although carrier frequencies for AM and NH are similar in registered United States bulls (approximately 10%), NH-affected calves are less frequent at birth. This reflects a significantly higher rate of embryonic and fetal loss associated with NH, which is estimated to reach 50%–70% (Beever 2009, Windsor et al. 2011, Whitlock et al. 2021).

Fig. 22–23. Idiopathic epilepsy in Hereford calves. (**22**) Seizure in a corral characterized by opisthotonus leading to a backward fall into dorsal recumbency. (**23**) Epilepsy episode triggered by exercise or excitement during herd movement in grassland.

In Uruguay, four NH cases were confirmed on two small commercial farms. Affected calves are born at or near term but are small and deformed, with marked dome-shaped enlargement of the head (Fig. 28). Abortions were also recorded in the affected herds, and the number of heifers that calved was significantly lower than expected, indicating prenatal losses. Dystocia may occur in severe cases of NH, requiring cranial incision, cerebrospinal fluid drainage, and removal of cranial bones to permit traction-assisted delivery (Windsor 2018, Agerholm et al. 2025).

Pathologically, the bones of the skull are poorly ossified, translucent (Fig. 29), and disintegrate easily upon cranial opening. Cleft palate may also be present. The brain appears as a fluid-filled sac (hydranencephaly) that collapses upon opening the cranial cavity (Fig. 30). The collapsed cerebral hemispheres appear as membranous sacs with only vestigial thin remnants of the cerebral cortex and meninges (Fig. 31). The thalamus, hippocampus, and corpus striatum are absent, whereas the brainstem, cerebellum, and spinal cord are compressed and atrophic. No aqueductal stenosis is observed. Histologically, no inflammatory lesions are observed in the white and gray matter of the cortical remnants.

Diagnosis is based on the presence of severe hydranencephaly and is confirmed by identification of the causative mutation. Although no inflammatory leukocyte infiltrate is observed, this finding alone cannot be used to rule out an *in utero* viral infection, such as BVD, bluetongue, or Akabane viruses, because inflammatory reactions associated with viral infections may resolve before birth, leaving no cellular evidence at the time of parturition (Agerholm et al. 2015).

Dwarfism, *PRKG2*-related (OMIA 001485-9913). Chondrodysplastic dwarfism is one of the most frequent congenital malformations in cattle. Several phenotypes are recognized, such as short-headed (brachycephalic) or long-headed (dolichocephalic), all of which are inherited as autosomal recessive traits. To date, dwarfism has been molecularly characterized in only a few breeds, including

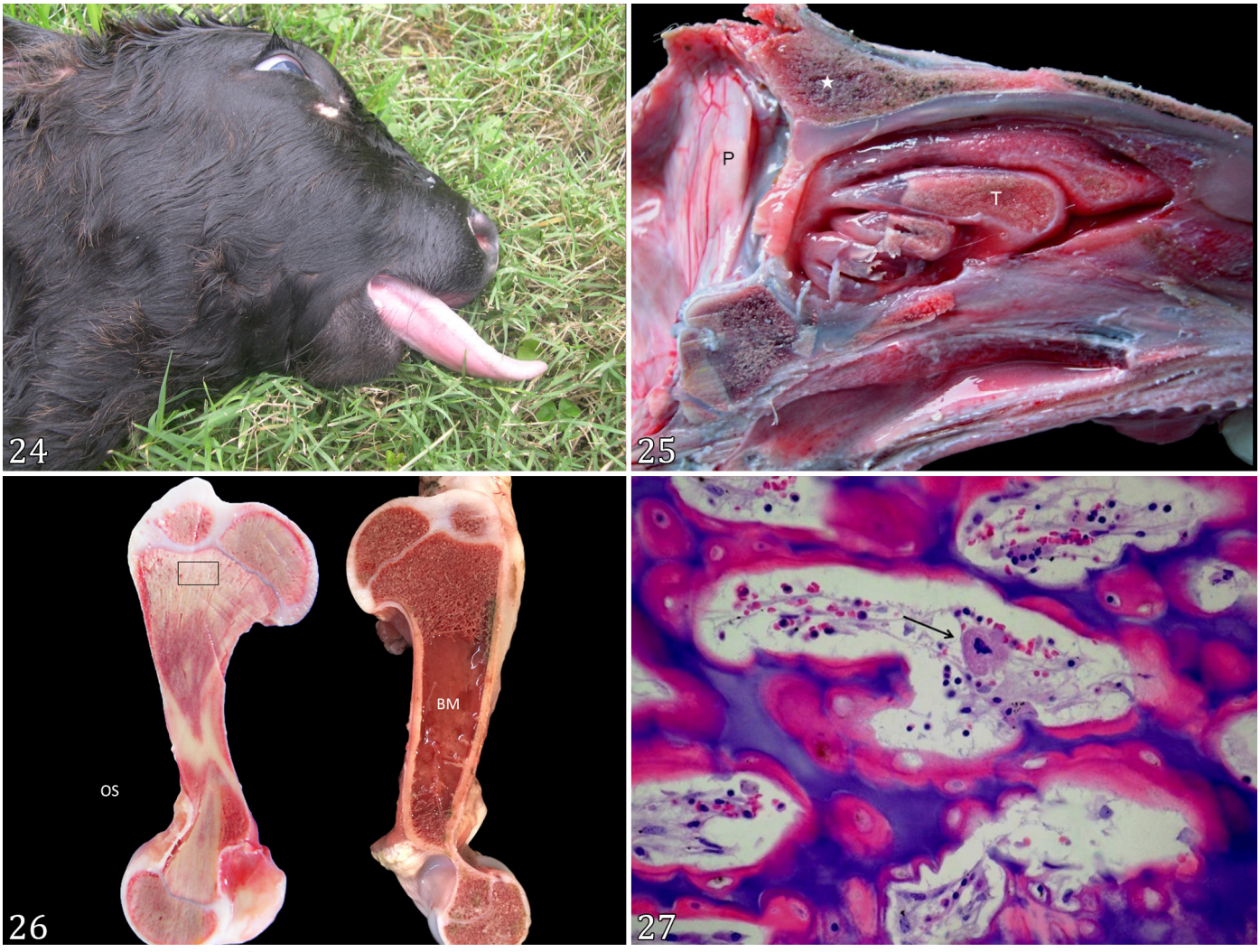

Fig. 24–27. Osteopetrosis ("marble bone disease") in Angus calves. (**24**) Stillborn calf with mandibular brachygnathia and tongue prolapse; coat shows black and red hairs (AA × Red Angus). (**25**) Sagittal skull section showing enlarged nasal turbinates (T), absence of frontal sinuses (asterisk), and intracranial projection of presphenoid wings (P). (**26**) Sagittal section of the humerus. Left: affected calf showing persistence of proximal and distal primary spongiosa ("double-cone" appearance), absence of the medullary cavity, and normal proximal and distal growth plates. Right: age-matched Angus control showing a normal metaphyseal trabecular bone pattern and bone marrow (BM). (**27**) Histology of retained primary chondro-osseous spongiosa (rectangle in c) with pyknotic osteoclasts (arrow) and absent Howship's lacunae. HE, obj. 400x.

Dexter (*ACAN*), Japanese Brown (*EVC2*, formerly *LIMBIN*), Japanese Brown Kumamoto line (*EVC2*), Holstein (*EVC*, *EVC2*, or *COL2A1*), and AA (*PRKG2*).

PRKG2-related dwarfism in AA cattle is molecularly characterized by a C-to-T transition in exon 15 of the cGMP-dependent type II protein kinase (*PRKG2*) gene on chromosome 6 (Koltes et al. 2009). *PRKG2* is essential for growth plate development because it regulates SOX9, a critical transcription factor that controls the expression of type II and X collagens; consequently, mutations in this gene result in impaired endochondral ossification. The gene is located near quantitative trait loci for production traits such as growth rate, muscling, and milk yield, suggesting that strong selection pressure in this genomic region increases homozygosity and the expression of the recessive dwarfism allele (Koltes et al. 2009). This is a clear example of how selection for productivity can inadvertently increase the prevalence of deleterious mutations within a population.

Affected calves exhibit a compact conformation, small stature, enlarged major joints, and rotation of both forelimbs, with variable degrees of carpal varus, metacarpophalangeal varus, and supination of the phalanges (Fig. 32). They present a slightly domed forehead but, contrary to most bovine chondrodysplasias characterized by a brachycephalic face (such as "snorter," "Telemark," or "bulldog" phenotypes), the muzzle profile is normal to narrow and slightly elongated (dolichocephalic) (Craig et al. 2015).

Long bones, particularly the humerus, exhibit markedly shortened diaphyses with flared, enlarged metaphyses and epiphyses, creating a characteristic "mushroom-like" appearance (Fig. 33). This occurs because the mutation affects endochondral growth, whereas periosteal ossification continues normally; consequently, the bones become disproportionately thick despite their reduced length. This same mechanism explains why the skull vault appears domed, as its intramembranous development is unaffected. Within the axial skeleton, vertebrae are shortened; sagittal sections reveal highly irregular growth plates and multiple ectopic ossification centers (Fig. 34).

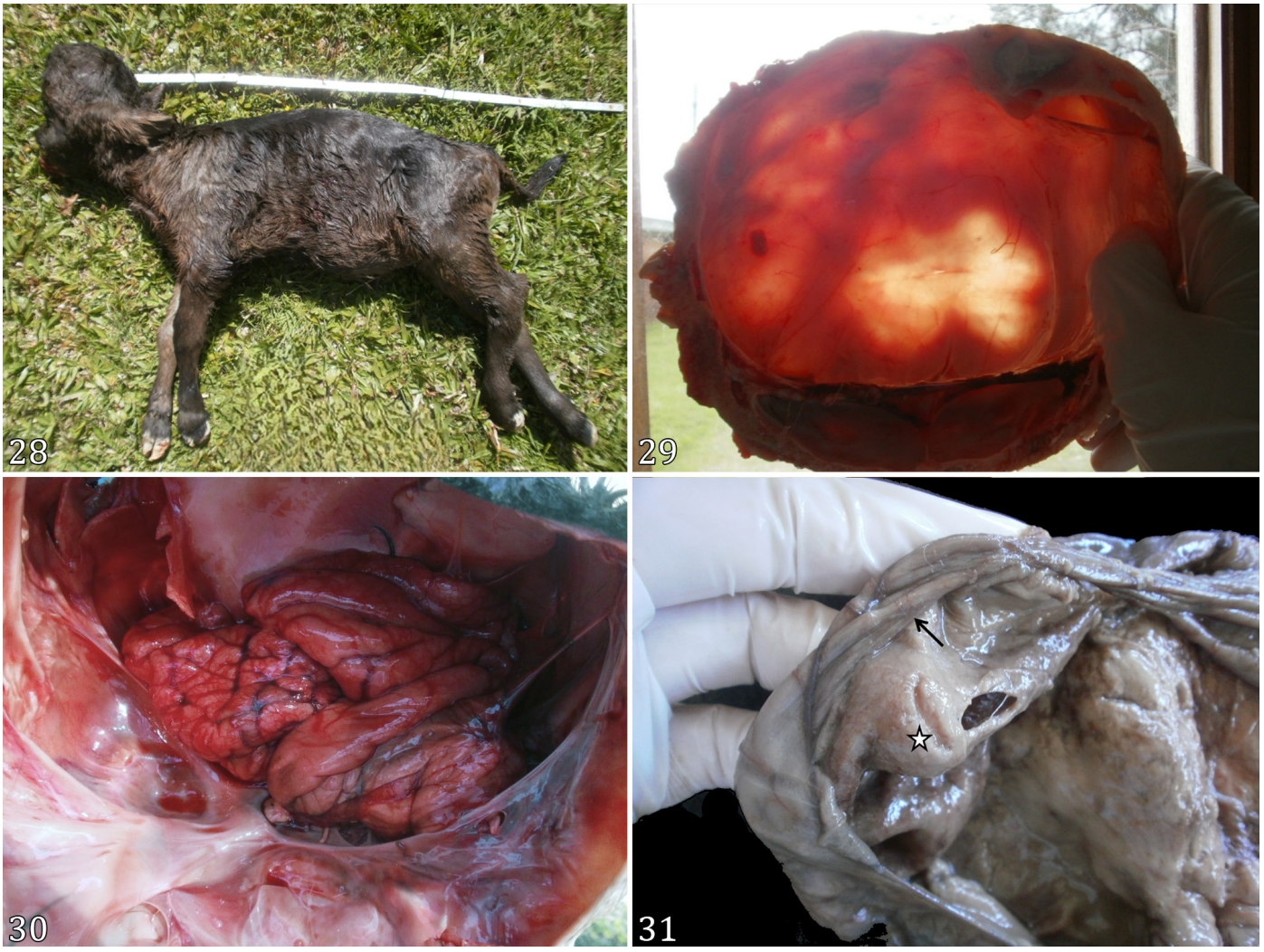

Fig. 28–31. Neuropathic hydrocephalus in Angus calves. (**28**) Stillborn term calf exhibiting macrocephaly and stunted growth (67 cm crown-rump length). (**29**) Transillumination of the skull showing poorly ossified, translucent calvarial bones with markedly enlarged fontanelles. (**30**) Collapse of the cerebral hemispheres upon opening the cranium; note free cerebrospinal fluid pooling within the cranial cavity (hydranencephaly). (**31**) Thin remnants of collapsed cerebral cortex (arrow) and subcortical matter (asterisk), with absence of major cerebral structures, including the thalamus, hippocampus, corpus callosum, and basal nuclei.

Histologically, the dysplastic lesions are characterized by focal disruptions of endochondral ossification. The growth plates appear highly irregular, the cartilage matrix often exhibits reduced staining intensity, and primary spongiosa trabeculae are disorganized, irregular in shape, or absent. A characteristic finding is focal failure of endochondral ossification, characterized by the focal interruption and and islands of hypertrophic cartilage extending into the metaphysis (Fig. 35).

Diagnosis is confirmed by the combination of growth plate lesions and identification of the *PRKG2* mutation. Skeletal examination should be exhaustive because, although chondrodysplasia is by definition an intrinsic genetic disorder, the lesions are not uniformly detectable throughout the skeleton. Because of allometric growth and the disto-proximal and cranio-caudal maturation gradients of the bovine skeleton, distal growth plates close early, often masking the dysplastic process. Consequently, lesions are most easily identified in late-maturing growth plates, such as

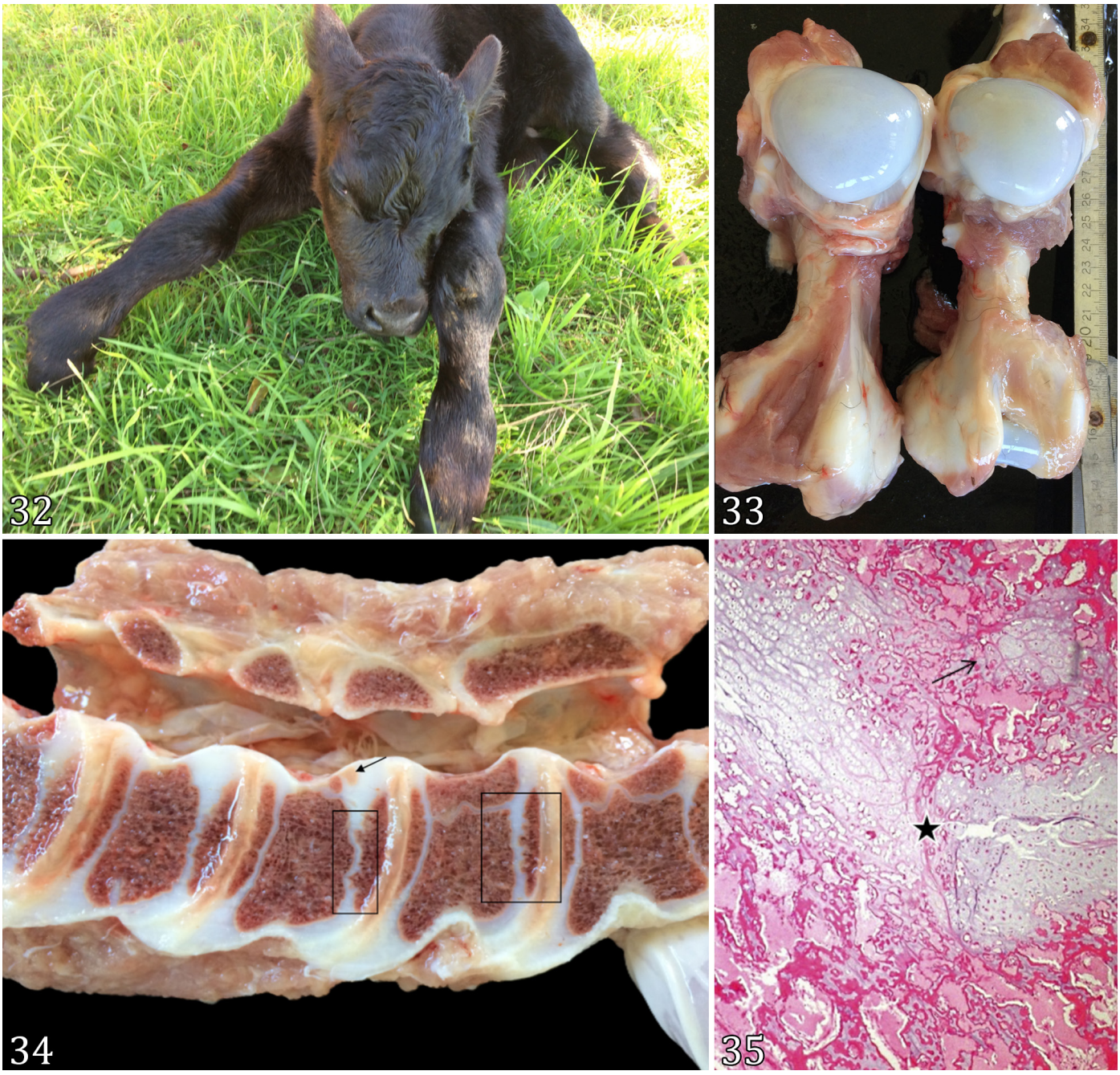

Fig. 32–35. *PRKG2*-associated chondrodysplastic dwarfism in Angus calves. (**32**) Neonatal calf with a domed forehead, enlarged major joints, and bilateral rotation of the forelimbs. (**33**) Paired flared humeri with shortened diaphyses and markedly enlarged epiphyses ("mushroom-like" appearance). (**34**) Sagittal section of the thoracolumbar vertebrae; note shortened vertebral bodies with irregular growth plates (rectangle) and ectopic ossification centers (arrow). (**35**) Histologic section of an irregular vertebral growth plate showing focal disruption of endochondral ossification (asterisk) and focal sequestration of growth plate cartilage (arrow). HE, obj. 100x.

the proximal humerus, the proximal femur, and especially the thoracolumbar vertebral bodies.

The main differential diagnosis is congenital chondrodystrophy of unknown origin (CCUO), a very common condition caused by extrinsic factors such as nutritional, metabolic, infectious, toxic, or hormonal insults (White 2016). In chondrodystrophy, the resulting phenotype is more variable because the skeletal pathology depends on the specific timing of the insult and the growth rate of the bones at the moment of injury. Furthermore, the presence of growth arrest lines (Harris lines) in the metaphysis is a characteristic feature of CCUO (White 2016, Preliasco et al. 2025), a finding that is rare or absent in chondrodysplasias (Rimoin et al. 2013).

Syndactyly (SN), *LRP4*-related (OMIA 000963-9913). SN ("mule foot") is an autosomal recessive congenital malformation of Holstein-Friesian, AA, and several other breeds, characterized by the partial or complete fusion of the functional digits (III and IV). It is caused by mutations in the *LRP4* gene on bovine chromosome 15 (BTA 15), which is essential for limb bud development and programmed digital separation (Drögemüller et al. 2007). Specific genetic defects vary by breed: a 2-bp deletion in exon 33 in Holstein-Friesian (*syH*), a splicing error in intron 37 in Angus (*syA*), and various missense substitutions in Simmental and Charolais breeds (Drögemüller et al. 2007). In this allelic series, the allele *syH* is dominant over *syA*, whereas both remain recessive to the wild-type *SY* allele. The higher frequency in Holsteins is attributed to the widespread use of carrier sires whose daughters exhibited overdominance with higher milk fat production (Drögemüller et al. 2007).

The mutation exhibits incomplete penetrance, with up to 18% of homozygous calves remaining phenotypically normal (Briano-Rodríguez et al. 2021). It also shows variable expressivity, manifested by different degrees of synostosis and a varying number of affected limbs. SN is significant in Uruguayan Holsteins, where the mutation has been detected in 22% of dairy farms, with a carrier prevalence of 4.2% and an allelic frequency of 0.02 (Briano-Rodríguez et al. 2021).

Fig. 36–39. Syndactyly in Aberdeen Angus calves. (**36**) Calf with syndactyly affecting all four feet and impaired mobility. (**37**) Characteristic truncated, cone-shaped syndactylous forefeet. (**38**) Variable morphology of syndactylous claws, ranging from complete, cone-shaped fusion (left) to incomplete fusion (center) and partial fusion involving the first phalanx (right); note the prominent dewclaw (arrow). (**39**) Pathologic anatomy of the distal metacarpus: the malformed metacarpal trochleae show complete absence of the intertrochlear notch (right) compared with a normal distal metacarpus (left).

In four cases diagnosed in AA and Red Angus in Uruguay, where a G>A mutation in the intron 37/exon 38 splice site of the *LRP4* gene was demonstrated (Romero Velázquez et al. 2015), the pooled morbidity was 1% and the lethality was 100% (Romero Benavente 2017).

Embryologically, SN results from the non-division of the dual digital anlagen (Leipold et al. 1998). The right forelimb is most frequently affected, followed by the left forelimb, right hindlimb, and left hindlimb. In Angus calves, all four feet are generally involved, and the condition is lethal (Fig. 36). These calves exhibit shortened limbs and a severe inward deviation at the fetlock joint (fetlock varus). The claws appear fused into a cone-shaped, truncated structure with the base at the coronary band, resembling a "mule's foot" (Fig. 37). While complete fusion is common, morphology is variable; distal notches or dorsal grooves are often present (Fig. 38). A consistent diagnostic feature is hypertrophy of the lateral dewclaws (Leipold et al. 1998). Affected calves experience significant locomotor difficulties, remaining in prolonged recumbency. The inability to walk and suckle typically results in death within a few days or necessitates euthanasia for welfare reasons. Furthermore, affected individuals are heat intolerant and can develop lethal hyperthermia under heat-stress conditions (Leipold et al. 1998).

The osteology of Angus SN is variable and affects several limb bones, not only the phalanges (Leipold et al. 1969). The primary finding is horizontal synostosis of the paired phalanges. The proximal and middle phalanges are more frequently fused than the distal phalanx, and fusion is more severe in the forelegs. Synostosis also commonly occurs in the carpal bones, while brachydactylous metacarpi and tibiae are frequently observed. Metacarpal trochleae appear malformed, ranging from absence of the intertrochlear notch to a single-ridged trochlea in severe cases (Fig. 39). Metatarsal trochleae and tarsal bones are also affected when all four feet are involved. Additionally, the sesamoid bone count is usually

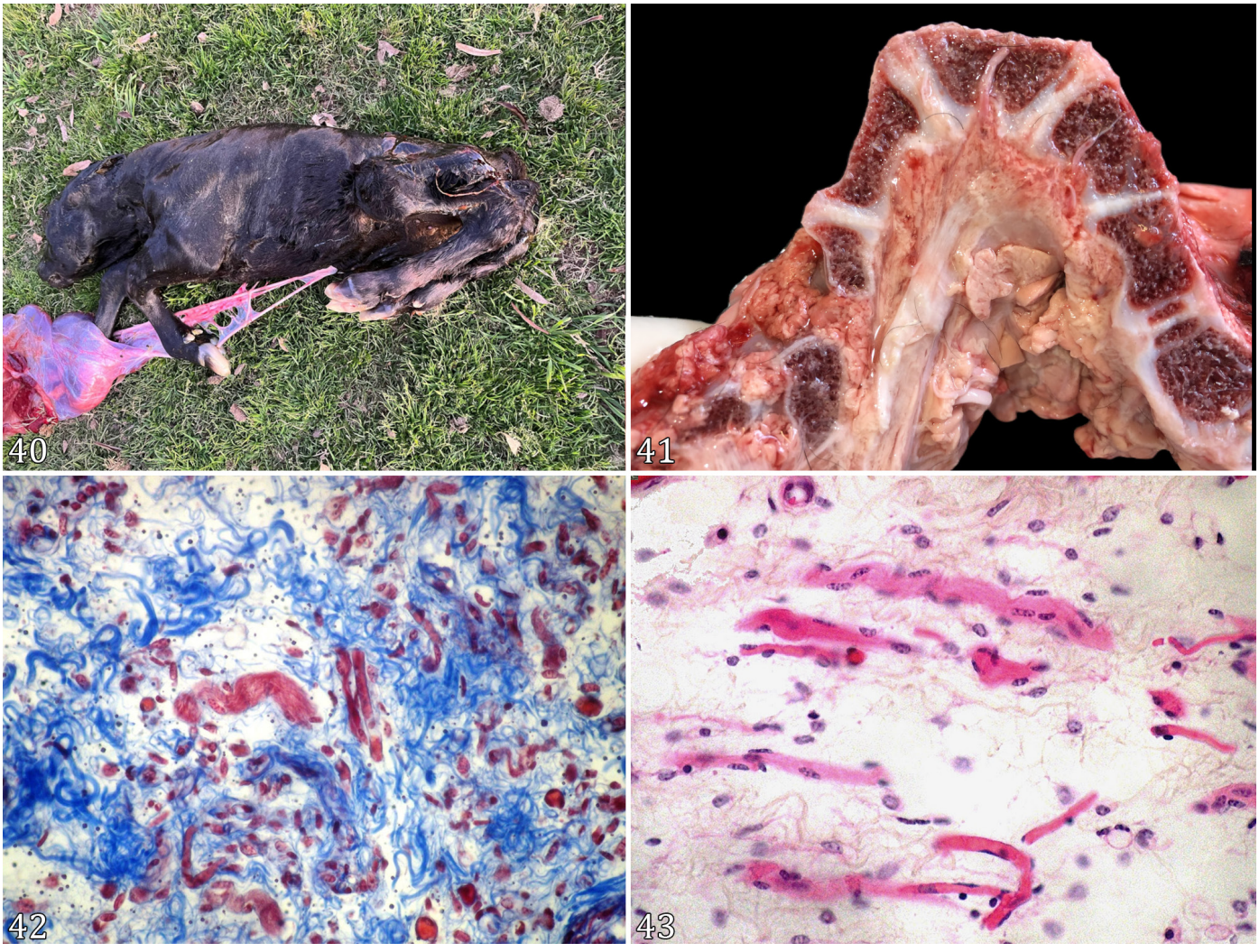

Fig. 40–43. Arthrogryposis multiplex congenita in Aberdeen Angus calves. (**40**) Stillborn calf with contracted, atrophic hindlimbs and an edematous head due to dystocia. (**41**) Sagittal section of the lumbosacral vertebral column showing dorsal curvature (kyphosis), with severe muscle atrophy and normal vertebral growth plates. (**42**) Severe atrophy of skeletal muscle from the hindlimb, with scant residual myofibers embedded within thin collagenous connective tissue. HE, obj. 400x. (**43**) Histopathology of skeletal muscle from the hindlimb showing sparse residual atrophic myofibers stained red and abundant fibrillar connective tissue stained blue. Masson's trichrome, obj. 400x.

reduced. Growth plates typically remain normal. Diagnosis is confirmed by the characteristic phenotype, radiographic detection of osteological anomalies, and identification of the specific *LRP4* mutation.

Arthrogryposis multiplex congenita (AM) (OMIA 002135-9913). AM, also known as "curly calf syndrome," is a hereditary autosomal recessive disorder of the AA breed. It is caused by a 23,363 bp deletion encompassing three genes: *ISG15*, *HES4*, and *AGRN* (Beever & Marron 2011). The *AGRN* gene encodes AGRIN, a proteoglycan essential for neuromuscular junction formation during embryonic development (Agerholm et al. 2016). The pathogenesis of AM centers on the failure of neuromuscular communication. The absence of an essential protein prevents signal transmission between nerves and muscles, leading to fetal akinesia. This lack of movement *in utero* results in the characteristic fixation of joints and severe kyphoscoliosis (Romero et al. 2020).

AM was first reported in the United States and later described in other countries (Whitlock 2010, Windsor et al. 2011). Beever & Marron (2011) estimated a carrier prevalence of 8% among AA bulls. The defect originated in the bull Rito 9J9 of B156 7T26 and spread globally through his descendant, GAR Precision 1680. Following its emergence in 2008, rapid identification of the mutation was achieved through 54K SNP chip technology, revealing that the defect was disseminated not only by GAR Precision 1680 but also significantly by his descendant CA Future Direction 5321 (Whitlock et al. 2021).

In Uruguay, AM was confirmed in a commercial AA herd in 2017 (Romero et al. 2020). Based on 12 registered cases across three commercial herds, the estimated pooled morbidity is 6.0%, and the maternal allele frequency q = 0.12, indicating that approximately 21.1% of the dams are asymptomatic carriers. This suggests a substantial prevalence of the mutant allele within the Uruguayan Angus population (Romero et al. 2020).

Affected calves are significantly underweight (15–25 kg) because of poor muscular development and exhibit arthrogryposis affecting the joints of the limbs, neck, and spine (Fig. 40). Forelimbs are typically fixed in flexion, whereas hindlimbs may be fixed in either flexion or extension without joint ankylosis. Additional features include torticollis, craniofacial bone asymmetry, severe scoliosis, and deviation of the cervical, thoracic, and lumbar vertebral column (Fig. 41). Some cases may exhibit palatoschisis (cleft palate) and mild hydrocephalus (Windsor et al. 2011). The carcass musculature is severely atrophic, pale, and has a sticky consistency. Despite the low fetal weight, the malformation is associated with a high incidence of dystocia and hydroamnion.

Histologically, skeletal muscle is markedly hypoplastic, with a severe reduction in myofiber number and variable fiber diameter (Fig. 42). The few residual myofibers are small and irregular in size and are embedded within abundant endomysial and perimysial collagen (Fig. 43). The normal cytomorphology and number of ventral spinal motor neurons, together with the normal proportion of myelinated fibers in intramuscular nerves (Romero et al. 2020), support the interpretation that muscle atrophy results from failure of the neuromuscular junction (Agerholm et al. 2025). Diagnosis is confirmed by the characteristic phenotype, detailed histology of skeletal muscles and central nervous system, and identification of the specific mutation. The main differential diagnoses include viral teratogenic infections (Akabane virus, bovine viral diarrhea virus, border disease virus, Schmallenberg virus, and bluetongue virus) and plant-associated teratogenesis (*Lupinus* sp., *Conium maculatum*, and *Nicotiana glauca*), which can be differentiated on the basis of epidemiological, gross, and histologic findings.

CONCLUSIONS

Inherited diseases in beef cattle in Uruguay represent a significant but often silent cause of reproductive and neonatal loss. These losses are closely linked to the intensive use of specific high-performance lineages in commercial herds.

This review demonstrates that although clinical and pathological examinations remain the cornerstone of diagnosis, molecular tools are indispensable for identifying asymptomatic carriers.

To safeguard the productivity and international standing of Uruguayan beef, it is imperative to transition from sporadic case reporting to a systematic national program of genomic surveillance in breeding stock. Genomic screening of breeding animals is essential to identify asymptomatic carriers and to guide breeding strategies aimed at eliminating these mutations from the population.

Acknowledgments.- The authors thank the staff of the División de Laboratorios Veterinarios "Miguel C. Rubino" (DILAVE, MGAP, Uruguay), as well as the veterinarians and producers who submitted samples and provided confidential field information to the national diagnostic system over the years. Their collaboration made possible the compilation and interpretation of the long-term records used in this review.

Conflict of interest statement.- The authors declare that they have no competing interests.

Credit author statement.- Fernando Dutra-Quintela: Conceptualization, methodology, investigation, data curation, pathology diagnosis, supervision, writing, review and editing. Carolina Briano-Rodríguez: Molecular diagnosis, genetic analysis, investigation, validation, writing – review and editing. Agustín Romero-Benavente: Investigation, pathology diagnosis, data curation, original draft, writing and review.

Data availability statement.- The data supporting the findings of this study are derived from the UNIRADD database of the División de Laboratorio Veterinario "Miguel C. Rubino" (DILAVE, MGAP, Uruguay). Due to institutional and confidentiality restrictions, the complete database is not publicly available. Data supporting the conclusions of this article may be made available by the corresponding author upon request.

Editor-in-Chief.- Fabiano José Ferreira de Sant'Ana.

REFERENCES

Agerholm JS, Drögemüller C, Steffen DJ, Jacinto JGP. An overview of developmental disorders leading to dystocia in cattle. Reprod Domest Anim 2025; https://doi.org/10.1111/rda.70083

Agerholm JS, Hewicker-Trautwein M, Peperkamp K, Windsor PA. Virus-induced congenital malformations in cattle. Acta veterinaria Scandinavica 2015; https://doi.org/10.1186/s13028-015-0145-8

Agerholm JS, McEvoy FJ, Menzi F, Jagannathan V, Drögemüller C. A *CHRNB1* frameshift mutation is associated with familial arthrogryposis multiplex congenita in Red dairy cattle. BMC Genomics 2016; https://doi.org/10.1186/s12864-016-2832-x

Agerholm JS. Inherited disorders in Danish cattle. APMIS 2007; https://ikv.ku.dk/research-files/vro/Doktorafhandling_-_Inherited_Disorder.pdf

American Angus Association. Neuropathic hydrocephalus (NH) fact sheet. 2019. Accessed Feb 27, 2026. https://www.angus.org/pub/nh/nhfactsheet.pdf

Baird JD, Wojcinski ZW, Wise AP, Godkin MA. Maple syrup urine disease in five Hereford calves in Ontario. Can Vet J 1987; https://pmc.ncbi.nlm.nih.gov/articles/PMC1680602/pdf/canvetj00584-0081.pdf

Bedwell S. Performance matters: what to know about MD. Hereford World 2020;111(2):10-11.

Beever JE, Marron BM. Screening for arthrogryposis multiplex in bovines. Mansfield: Agrigenomics Inc.; 2011. (United States patent 20110151440 A1).

Beever JE. A review of dominant and recessive traits. Hereford World 2007:70-71.

Beever JE. Research update on hydrocephalus. 2009. Accessed Feb 27, 2026. https://www.angus.org/Pub/NH/Research_Update_Hydrocephalus.pdf

Briano-Rodríguez C, Romero A, Llambí S, Sica AB, Rodriguez MTF, Giannitti F, Caffarena RD, Schild CO, Casaux ML, Dutra-Quintela F. Lethal and semi-lethal mutations in Holstein calves in Uruguay. Ciência Rural 2021; https://doi.org/10.1590/0103-8478cr20200734

Craig LE, Dittmer KE, Thompson KG. Bones and joints, p.38–39. In: Maxie MG. Jubb, Kennedy and Palmer's Pathology of Domestic Animals. 6th ed. Vol. 1. St. Louis: Elsevier; 2015.

Dennis JA, Healy PJ. Definition of the mutation responsible for maple syrup urine disease in Poll Shorthorns and genotyping Poll Shorthorns and Poll Herefords for maple syrup urine disease alleles. Res Vet Sci 1999; https://doi.org/10.1053/rvsc.1998.0296

Drögemüller C, Leeb T, Harlizius B, Tammen I, Distl O, Höltershinken M, Gentile A, Duchesne A, Eggen A. Congenital syndactyly in cattle: four novel mutations in the low density lipoprotein receptor-related protein 4 gene (*LRP4*). BMC Genet 2007; https://doi.org/10.1186/1471-2156-8-5

Dutra F, Baroni L, Techera M, Quinteros C. Osteopetrosis letal hereditaria (enfermedad de los huesos demármol) en terneros Aberdeen Angus en Uruguay. Veterinaria (Montevideo) 2012; https://revistasmvu.com.uy/index.php/smvu/article/view/201/131

Dutra F, Baroni L. Epidermólisis bullosa hereditaria en terneros Hereford en Uruguay. In: XXXV Jornadas Uruguayas de Buiatría, Paysandú; 2007. p.270-271.

Dutra F, Castro A, Mayol C, Quinteros C. Cardiomiopatía congénita asociada al pelaje crespoen terneros Polled Hereford en Uruguay. Veterinaria (Montevideo) 2011; https://www.revistasmvu.com.uy/index.php/smvu/article/view/189/120

Dutra F, Romero A, Quinteros C, Kelly L. MSUD (Maple Syrup Urine Disease) en terneros polled hereford y cruzas polled Hereford x Shorthorn en Uruguay. Veterinaria (Montevideo) 2015; https://revistasmvu.com.uy/index.php/smvu/article/view/114/60

Dutra-Quintela F. Enfermedad del ternero Guasón o Joker (mandibulofacial dysostosis, OMIA 002288-9913) – Primer diagnóstico. Archivo Veterinario del Este 2022; https://doi.org/10.13140/RG.2.2.12828.16008

Dutra-Quintela F. Monstruosidades y enfermedades genéticas de los bovinos en Uruguay. Su importancia y significado. In: XLIV Jornadas Uruguayas de Buiatría, Centro Veterinario Paysandú; 2016. p.42-50.

Espasandin AC, Franco J, Oliveira G, Bentancur O, Gimeno D, Pereyra F, Rogberg M. Impacto productivo y económico del uso del cruzamiento entre las razas Hereford y Angus en el Uruguay. In: XXXIV Jornadas Uruguayas de Buiatría, Paysandú; 2006. p.41-51.

Fine J-D, Bruckner-Tuderman L, Eady RAJ, Bauer EA, Bauer JW, Has C, Heagerty A, Hintner H, Hovnanian A, Jonkman MF, Leigh I, Marinkovich MP, Martinez AE, McGrath JA, Mellerio JE, Moss C, Murrell DF, Shimizu H, Uitto J, Woodley D, Zambruno G. Inherited epidermolysis bullosa: updated recommendations on diagnosis and classification. J Am Acad Dermatol 2014; https://doi.org/10.1016/j.jaad.2014.01.903

Ford CA, Stanfield AM, Spelman RJ, Smits B, Ankersmidt-Udy AEL, Cottier K, Holloway H, Walden A, Al-Wahb M, Bohm E, Snell RG, Sutherland GT. A mutation in bovine keratin 5 causing epidermolysis bullosa simplex, transmitted by a mosaic sire. J Invest Dermatol 2005; https://doi.org/10.1111/j.0022-202X.2005.23610.x

Garrick DJ. The nature, scope and impact of genomic prediction in beef cattle in the United States. Genet Sel Evol 2011; https://doi.org/10.1186/1297-9686-43-17

González N, Uzal FA, Videla N, Pierangelini DM, Chamoles N, Lager IA, Jeffrey M, Belak K, Mueller J. Enfermedad de la orina con olor a jarabe de arce (leucinosis) en terneros en Argentina. Rev Med Vet 1997;78(4):243-248.

Greenwood PL. Review: an overview of beef production from pasture and feedlot globally, as demand for beef and the need for sustainable practices increase. Animal 2021; https://doi.org/10.1016/j.animal.2021.100295

Guillenea AC, Lema M, Gimeno D, Ravagnolo O, Espasandín AC. Additive and non-additive effects for mature weight in beef cattle. Arch Latinoam Prod Anim 2020; https://revista.alpaenlinea.org/index.php/alpa/article/view/2795/1285

Harper PAW, Healy PJ, Dennis JA. Maple syrup urine disease (branched chain ketoaciduria). Am J Pathol 1990; https://shre.ink/3ADx

Harvey RJ, Topf M, Harvey K, Rees MI. The genetics of hyperekplexia: more than startle. Trends Genet 2008; https://doi.org/10.1016/j.tig.2008.06.005

Healy PJ, Dennis JA, Windsor PA, Pierce KD, Schofield PA. Genotyping cattle for inherited congenital myoclonus and maple syrup urine disease. Aust Vet J 2002; https://doi.org/10.1111/j.1751-0813.2002.tb11301.x

Hirigoyen DJ, Campoy D, Rubianes E, Rodríguez M. Salud animal en Uruguay: gasto, pérdidas e inversión en I+D. Montevideo: Informe CCSISA; 2023.

INAC. A journey through the Uruguayan beef chain: 2024 annual sustainability report. Montevideo: Instituto Nacional de Carnes; 2024.

Jacinto JGP, Häfliger IM, Veiga IMB, Drögemüller C, Agerholm JS. A *de novo* mutation in *KRT5* in a crossbred calf with epidermolysis bullosa simplex. J Vet Intern Med 2020; https://doi.org/10.1111/jvim.15943

Jacinto JGP, Markey AD, Veiga IMB, Paris JM, Welle M, Beever JE, Drögemüller C. A *KRT71* loss-of-function variant results in inner root sheath dysplasia and recessive congenital hypotrichosis of Hereford cattle. Genes 2021; https://doi.org/10.3390/genes12071038

Jaurena M, Durante M, Devincenzi T, Savian JV, Bendersky D, Moojen FG, Pereira M, Soca P, Quadros FLF, Pizzio R, Nabinger C, Carvalho PCF, Lattanzi FA. Native grasslands at the core: a new paradigm of intensification for the Campos of southern South America to increase economic and environmental sustainability. Front Sustain Food Syst 2021; https://shre.ink/3Adq

Jolly RD, Wills JL, Kenny JE, Cahill JI, Howe L. Coat-colour dilution and hypotrichosis in Hereford crossbred calves. N Z Vet J 2008; https://doi.org/10.1080/00480169.2008.36812

Kaiser L. The gene gurus have been busy this decade:recessive defect, mutations and DNA-based tests. Periodical 2009. Accessed Feb 27, 2026. http://kaisercattle.com/pdf/Deadcows.pdf

Kelly L, Dutra F, Llambí S, Rivero R, Moraes J, Trenchi G, D'Agosto S, Peraza P, Ravagnolo O, Dalla Rizza M. Diagnóstico molecular de enfermedades hereditarias bovinas en el Uruguay. Veterinaria (Montevideo) 2012; https://shre.ink/3Akj

Koltes JE, Mishra BP, Kumar D, Kataria RS, Totir LR, Fernando RL, Cobbold R, Steffen D, Coppieters W, Georges M, Reecy JM. A nonsense mutation in cGMP-dependent type II protein kinase (PRKG2) causes dwarfism in American Angus cattle. Proc Natl Acad Sci USA 2009; https://doi.org/10.1073/pnas.0904513106

Konovalova E, Romanenkova O, Kostyunina O, Gladyr E. The molecular bases study of the inherited diseases for the health maintenance of the beef cattle. Genes 2021; https://doi.org/10.3390/genes12050678

Leipold HW, Adrian RW, Huston K, Trotter DM, Dennis SM, Guffy MM. Anatomy of hereditary bovine syndactylism. I. Osteology. J Dairy Sci 1969; https://doi.org/10.3168/jds.S0022-0302(69)86766-4

Leipold HW, Huston K, Dennis SM. Bovine congenital defects. Adv Vet Sci Comp Med 1983;27:197-271. PMid:6417989.

Leipold HW, Schmidt GL, Steffen DJ, Vestweber JGE, Huston K. Hereditary syndactyly in Angus cattle. J Vet Diagn Invest 1998; https://doi.org/10.1177/104063879801000304

MacNeil MD. Invited Review: research contributions from seventy-five years of breeding Line 1 Hereford cattle at Miles City, Montana. J Anim Sci 2009; https://doi.org/10.2527/jas.2009-1909

Marcolongo-Pereira C, Schild AL, Soares MP, Vargas Jr SF, Riet-Correa F. Defeitos congênitos diagnosticados em ruminantes na Região Sul do Rio Grande do Sul. Pesq Vet Bras 2010; https://doi.org/10.1590/S0100-736X2010001000003

Mason CA, Kirby RS, Sever LE, Langlois PH. Prevalence is the preferred measure of frequency of birth defects. Birth Defects Res A Clin Mol Teratol 2005; https://doi.org/10.1002/bdra.20211

Mauldin EA, Peters-Kennedy J. Integumentary system, p.511-736. In: Maxie MG. Jubb, Kennedy, and Palmer's Pathology of Domestic Animals. 6th ed. Vol. 1. St. Louis: Elsevier; 2015.

Meyers SN, McDaneld TG, Swist SL, Marron BM, Steffen DJ, O'Toole D, O'Connell JR, Beever JE, Sonstegard TS, Smith TPL. A deletion mutation in bovine *SLC4A2* is associated with osteopetrosis in Red Angus cattle. BMC Genomics 2010; https://doi.org/10.1186/1471-2164-11-337

MGAP. Datos preliminares basados en la declaración jurada de existencias DICOSE–SNIG 2025. Ministerio de Ganadería, Agricultura y Pesca; 2025. Accessed Feb 27, 2026. https://www.gub.uy/ministerio-ganaderia-agricultura-pesca/datos-y-estadisticas/datos/datos-preliminares-basados-declaracion-jurada-existencias-dicose-snig-2

Morrow CJ, McOrist S. Cardiomyopathy associated with a curly hair coat in Poll Hereford calves in Australia. Vet Rec 1985;117(12):312-313. PMid:4060539.

Murgiano L, Wiedemar N, Jagannathan V, Isling LK, Drögemüller C, Agerholm JS. Epidermolysis bullosa in Danish Hereford calves is caused by a deletion in *LAMC2* gene. BMC Vet Res 2015; https://doi.org/10.1186/s12917-015-0334-8

Navajas EA, Baldi F. Beef cattle genetic evaluations in South America. Puerto Varas: Interbeef Meeting; 2016. p.141-149. ICAR Technical Series 21.

O'Toole D, Swist S, Steadman L, Johnson GC. Neuropathology and craniofacial lesions of osteopetrotic Red Angus calves. Vet Pathol 2012; https://doi.org/10.1177/0300985811412621

OMIA. Online Mendelian Inheritance in Animals. University of Sydney; 2026. Accessed Feb 27, 2026. https://omia.org/home

Preliasco M, Cabrera V, Romero A, Briano C, Armua J, Pieruccioni F, Rodríguez B, Auscarriaga J, Domínguez F, Bonjour L, Dutra F. Condrodistrofia congénita de origen desconocido: reporte de dos brotes en Uruguay. In: LII Jornadas Uruguayas de Buiatría, Paysandú; 2025. p.144-146. Accessed Feb 27, 2026. https://buiatriapaysandu.uy/img/publicaciones/buiatria2025.pdf

Quigley K, Mee JF. Bovine congenital defects recorded in a national survey of dairy and beef herds over ten years (2014–2023). Reprod Domest Anim 2025; https://doi.org/10.1111/rda.70067

Ravagnolo O, Lema M, Aguilar I, Calistro SA. Ayudas para Manejar la Información. In: Catálogo de Padres Hereford 2021. Montevideo: Sociedade de Criadores de Hereford Uruguay, INIA; 2021. 93p.

Rimoin D, Lachman R, Unger S. Chondrodysplasias, p.1-44. In: Rimoin DL, Pyeritz RE, Korf B. Emery and Rimoin's Essential Medical Genetics. Philadelphia: Elsevier; 2013.

Rivero R, Kautz S, Gomar MS, Barros SS, Gimeno EJ. Enfermedad de almacenamiento lisosomal en terneros del norte de Uruguay. Veterinaria (Montevideo) 2001; https://revistasmvu.com.uy/index.php/smvu/article/view/416/273

Robarge ME, Beever JE, Lenz SD, Lynch CJ, Wigle WL. Maple syrup urine disease in a Central Indiana Hereford herd. Case Rep Vet Med 2015; https://doi.org/10.1155/2015/204037

Romero A, Briano C, Quintela FD. Arthrogryposis multiplex congenita in Aberdeen Angus cattle in Uruguay. Pesq Vet Bras 2020; https://doi.org/10.1590/1678-5150-PVB-6636

Romero Benavente A. Genotipado para MSUD, osteopetrosis y sindactilia en bovinos de carne de la región este de Uruguay. Tesis de Maestría, Universidad de la República, Uruguay; 2017. 47p.

Romero Velázquez A, Romero Benavente A, Montenegro M, Artigas R, Briano C, Dutra F, Arruga MV, Llambí S. Identificación de la mutación A/G en el exón/intrón 37 del gen *LRP4* asociada a sindactilia en un ternero Aberdeen Angus en Uruguay (primer reporte). Proceedings XLIV Congreso Argentino de Genética. J Basic Appl Genet 2015; https://shre.ink/3hW3

Romero-Benavente A, Briano-Rodríguez C, Dutra-Quintela F. Hypotrichosis congenita (*KRT71* mutation) in Hereford cattle in Uruguay. Pesq Vet Bras 2023; https://doi.org/10.1590/1678-5150-PVB-7327

Rousseaux CG, Klavano GG, Johnson ES, Shnitka TK, Harries WN, Snyder FF. "Shaker" calf syndrome: a newly recognized inherited neurodegenerative disorder of horned Hereford calves. Vet Pathol 1985; https://doi.org/10.1177/030098588502200202

Rousseaux CG, Ribble CS. Developmental anomalies in farm animals II. Defining etiology. Can Vet J 1988; https://pmc.ncbi.nlm.nih.gov/articles/PMC1680752/pdf/canvetj00566-0032.pdf

Salmela E, Niskanen J, Arumilli M, Donner J, Lohi H, Hytönen MK. A novel *KRT71* variant in curly-coated dogs. Anim Genet 2019; https://doi.org/10.1111/age.12746

Sieck RL, Fuller AM, Bedwell P, Ward J, Sanders S, Xiang S-H, Peng S, Steffen D, Petersen JL. 17 A *de novo* recessive mutation causative of mandibulofacial dysostosis in Hereford cattle. J Anim Sci 2021; https://doi.org/10.1093/jas/skab054.047

Sieck RL, Fuller AM, Bedwell PS, Ward JA, Sanders SK, Xiang S-H, Peng S, Petersen JL, Steffen DJ. Mandibulofacial dysostosis attributed to a recessive mutation of *CYP26C1* in Hereford cattle. Genes 2020; https://doi.org/10.3390/genes11111246

Simpson MA, Cook RW, Solanki P, Patton MA, Dennis JA, Crosby AH. A mutation in *NFκB* interacting protein 1 causes cardiomyopathy and woolly haircoat syndrome of Poll Hereford cattle. Anim Genet 2009; https://doi.org/10.1111/j.1365-2052.2008.01796.x

Singh K, Rohilla A. Retrieval of ossicles by Cobbler's cut. Eur J Anat 2018; https://www.eurjanat.com/v1/data/pdf/eja.170129ks.pdf

Strauss KA, Puffenberger EG, Carson VJ. Maple syrup urine disease. In: Adam MP, Bick S, Mirzaa GM, Pagon RA, Wallace SE, Amemiya A. GeneReviews®. Seattle: University of Washington; 2020. Accessed Feb 27, 2026. Available from: https://www.ncbi.nlm.nih.gov/books/NBK1319/

White PJ. Could a trace mineral deficiency be associated with congenital chondrodystrophy of unknown origin (CCUO) in beef cattle in Australia? J Anim Physiol Anim Nutr 2016; https://doi.org/10.1111/jpn.12335

Whitlock BK, Beever JE, Steffen DJ. Heritable congenital defects in cattle, p.863-875. In: Hopper RM. Bovine Reproduction. 2nd ed. Hoboken: John Wiley & Sons; 2021.

Whitlock BK. Heritable birth defects in cattle. In: Applied Reproductive Strategies in Beef Cattle Conference Proceedings, Nashville, TN 2010; https://shre.ink/376B

Wight-Carter M. Inherited and BVD-induced osteopetrosis in calves. Kansas Vet Q 2006;9:2-3.

Windsor P, Kessell A, Finnie J. Neurological diseases of ruminant livestock in Australia. V: Congenital neurogenetic disorders of cattle. Aust Vet J 2011; https://doi.org/10.1111/j.1751-0813.2011.00826.x

Windsor P. Abnormalities of development and pregnancy, p.168-194. In: Noakes DE, Parkinson TJ, England GCW. Veterinary Reproduction and Obstetrics. 10th ed. Amsterdam: Elsevier; 2018.