# Autosomal recessive genetic disorders of cattle breeds Worldwide- a Review

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ABSTRACT

The present review briefly describes autosomal recessive disorders observed among various breeds of cattle worldwide. These disorders in cattle may occur at very low to low frequency and therefore, carriers are usually not detected in breeding programmes. The autosomal recessive genetic diseases are mostly breed-specific which can be detected by simple techniques like Polymerase Chain Reaction-Restriction Fragment Length Polymorphism (PCR-RFLP) and other molecular tools.

**Key Words:** PCR-RFLP, recessive, disorders, cattle, carriers, autosome

## INTRODUCTION

Every individual has two copies of each gene, one copy on each of the chromosome pair. The genetic diseases are caused by a single error or mutation in genes present in our genome. Some diseases require both copies of a particular gene to be damaged or mutated (recessive diseases), whereas others need only one gene copy altered (dominant diseases). The mutant gene is inherited from one of the parents in order to get the dominant disease. In recessive genetic diseases, the genetic error usually needs to be inherited from both parents to get the disease. Inheritance of the mutant gene from one parent only usually causes the individual to be a carrier of the disease, but without any symptoms.

Normal cells of every individual have two kinds of chromosomes- autosomes and sex chromosomes. There are two sex chromosomes in normal somatic cells, which determine the sex of an individual. The rest of the chromosomes are known as autosomes. The genetic diseases linked with sex chromosomes are known as sex-linked diseases. The other diseases are known as autosomal genetic diseases, which could be recessive or dominant.

Approximately, 1000 recessive defects have so far been recorded in human (Beaudet et al., 1989 and Mckusik, 1990), compared with fewer than 200 in cattle (Houston, 1993). These disorders in cattle may occur at very low to low frequencies and therefore, carriers are usually not detected in breeding programmes. The autosomal recessive genetic diseases are mostly breed-specific. Some of the autosomal recessive genetic diseases in various cattle breeds are briefly described as under:

1. *a-Mannosidosis* is nervous disease in Angus cattle detected in Australia, New Zealand, Europe and US, and Muray Greys cattle in Australia and New Zealand (Jolly, 1993). It was first described in Australia by Whittem & Walker (1957). The disease results in mental retardation, skeleton changes, ataxia, a fine head tremor, aggressive behaviour and premature death.
2. *Alopecia Anemia syndrome* has been identified in the Polled Hereford breed (Steffen et al., 1991). Affected calves are often small at birth with ugly face and protruding tongue and eyes. Hairs are tightly curled or absent, as a result skin of animal appears as wrinkled or aged. Calves are lazy, cannot tolerate environmental stress and are prone to diseases. They survive for a few months after birth. Malformation of the skeleton structure results in reduced RBC production (anemia).
3. *Arachnomelia Syndrome* (spider legs) is a malformation mainly of limbs, back and head in Brown Swiss and Simmental cattle breeds (Buitkamp et al., 2008). The legs are thinner and appear longer than normal which are more fragile and in combination with stiffened joints, they tend to fracture during calving. The fetlock joints are deformed. The skull malformations are characterized by shortened lower jaw, pointer head etc.
4. *Bilateral Convergent Strabismus* with Exophthalmos (BCSE) is a heritable eye defect that occurs in many cattle breeds, e.g., Jersey, German Fleckvieh, German Holstein, and German Brown etc. [Momke and Distl, 2006]. BCSE shows a progressive course and ends up in complete blindness. The onset of the defect cannot be often noticed prior to first breeding. Generally, no signs of the defect are present at birth.
5. *Bovine Chondrodysplastic Dwarfism* in Japanese Brown cattle is characterized by short limbs, joint abnormality and ateliosis. Affected calves show insufficient endochondral ossification with irregularly arranged chondrocytes, abnormal formation of the cartilaginous matrix, and partial disappreance of the epiphysical growth plates. Disproportionate dwarfism has also been reported in other cattle breeds including Dexter, Holstein, Aberdeen-Angus Hereford and Shorthorn breeds (Takeda et al., 2002).
6. *Bovine Chronic Interstitial Nephritis* with Diffuse Zonal Fibrosis (CINF) was diagnosed in Japanese Black (Wagyu) cattle. Bovine CINF is characterized by increased blood urea nitrogen, creatinine, and urinary proteins, leads to death before puberty, usually within the first 6 months or year of life (Kobayashi et al., 2000).
7. *Bovine Citrullinaemia* is a disease of newly born Holstein Friesian calves worldwide (Harper et al., 1986). It is urea cycle disorder in animals. Calves affected with the disease appear normal immediately after birth. However, by the second day of life they become depressed and feed poorly. By the third day, they are often seen aimlessly wandering about their enclosure or standing with their head pressed against a fence or wall. Between day 3 and 5 the disease progresses rapidly. The calves appear to be blind and collapse. Death usually occurs within 12 hours of onset of these clinical signs (Healy et al., 1990; Patel and Singh, 2004; Patel et al. 2006).

8. *Bovine Ferrochelatase Deficiency* or Bovine Protoporphyria in Charolais cattle is an acute photosensitivity evident from birth and characterized by alopecia, ulceration etc. (Ruth et al., 1977 and Jenkins et al., 1998). A common symptom is very painful photosensitivity, manifesting itself as a burning and itching sensation on the surface of the skin. At times the itching sensations are almost unbearable. Although it is not life threatening, the condition may reduce productivity.
9. *Bovine Hereditary Zinc Deficiency* is also known as lethal trait in cattle. Zinc is an essential nutrient and plays a critical role in the function of many biological processes as a cofactor of many enzymes, transcription factors and other critical molecules in animals. Symptoms of zinc deficiency in animals are similar across various species and include diarrhea, skin lesions, immunodeficiency, and growth retardation (Liuzzi and Cousins, 2004).
10. Bovine Leukocyte Adhesion Deficiency (BLAD) was identified in North American Holstein and was exported to other national HF populations (Kerhli et al., 1990; Patel et al., 2007). Animals with BLAD are characterized by recurrent pneumonia, ulcerative and granulomatous stomatitis, enteritis with bacterial overgrowth, periodontitis, loss of teeth, delayed wound healing, persistent neutrophilia and death at an early age (Nagahatta et al., 1987; Patel and Singh, 2003).
11. *Bovine Spinal Dysmyelination* (BSD) in cattle (Bos taurus) is a congenital neurodegenerative disease characterized by pathological changes of the myelin sheaths in the spinal cord. Main clinical signs of BDS are manifested at birth and include lateral recumbency with opisthotonos, body tremor, and spastic extension of the limbs. Attempt to rise and limb movements are absent. The occurrence of BSD is a longstanding problem in the American Brown Swiss (ABS) breed and in several European cattle breeds upgraded with ABS (Nissen et al., 2001).
12. *Brachygnathia Inferior* (parrot mouth) is a condition in Simmental breed where the incisor teeth meet the maxillary pad behind its anterior angle. It is often referred to as undershot jaw. In cattle it has been demonstrated under adverse grazing conditions to be economically important (Moller and James, 1975). Griffith et. al. (1989) observed cleft palate, brachygnathia inferior and mandibular oligodontia in a HF calf.
13. *Bull dog or Achondrosplasia* is a congenital lethal genetic disease in Dexter breed of cattle. Affected calves are usually aborted before the seventh month of gestation, with extreme shortening of limbs and vertebral column, gross craniofacial defects (relatively large head with retruded muzzle, cleft palate and protruding tongue), and a large abdominal hernia (Harper et al., 2008). It is also very rarely reported in African cattle (Carmichael, 1933) and Holstein (Berger and Innes, 1948).
14. *Cardiomyopathy Progressive Disease* in bovine has been observed in many countries in Holstein and Red Holstein as well as Simmental x Red Holstein crossbred (Furuoka et al., 2001). Affected animals show all the signs of congestive heart failure. Other typical signs include an increased pulse rate, gallop-rhythm of the heart and distension of the jugular veins and milk veins.
15. *Chediak-Higashi Syndrome* (CHS) is a disorder associated with bleeding tendency and characterized by insufficient platelet that affects several species including Japanese black (Wagyu) cattle (Yamakuchi et al., 2000). CHS is manifested clinically by partial oculocutaneous albinism, photophobia, an increased susceptibility for infection, and a hemorrhagic tendency. Histological examination of skin, hair, and eyes has revealed that the basis for the partial albinism is a clumping of melanin granules (Prieur and Collier, 1978).
16. *Complex Vertebral Malformation* (CVM) has been reported in aborted, premature born, stillborn and neonatal HF calves (Steffen, 2001). Typical signs of CVM are shortened neck and forelimbs, bilateral, symmetrical, moderate traction of the carpal joints, severe contraction and slight lateral rotation of the fetlock joints. The hind limbs show marked bilateral, symmetrical contraction of the fetlocks, with medial rotation of distal limbs. Elongation of the tarsus is also present in both limbs. Vertebral abnormalities are confined to fusion of the last two cervical vertebrae and distortion of the first three thoracic vertebrae, giving a slight scoliosis at that point.
17. *Congenital Myasthenic Syndrome* (CMS) has been reported in Red Brahman calves in South Africa. It is characterized by loss of function and subsequent impairment of neuromuscular transmission. Clinical signs are similar to Pompe's disease, with the exceptions that the onset of the disease is earlier and progression much faster. Muscular weakness develops at 3 to 4 weeks of age, and progresses within weeks to the point where the calf can no longer rise unassisted. Life expectancy is less than 6 months (Thompson et al., 2003).
18. *Curly Calf Syndrome* or Arthrogryposia (Rigid joints) in Angus cattle breed is characterized by congenital fixation of multiple joints of all the four legs, with presence of cleft plate (Greene et al., 1973). It can cause calves to be stillborn with twisted spines.
19. *Deficiency of Uridine Monophosphate Synthase* (DUMPS) was observed in early 80's in HF animals (Robinson et al., 1984). The enzyme, Uridine Monophosphate Synthase (UMPS) is found in all body cells which synthesize pyrimidine that is required for DNA replication during mitotic cell division. The embryos homozygous for DUMPS do not survive to birth rather die early in gestation, as embryos appear to be aborted or reabsorbed approximately 40 days after conception, leading to repeat breeding problems (Patel et al., 2006).
20. *Double Muscling or Muscular Hypertrophy* (MH) in cattle is visibly distinct muscular hypertrophy, commonly known as double muscling, occurs with high frequency in the Belgian Blue and Piedmonte cattle breeds (Grobet et al., 1997). These breeds produce extraordinary amounts of meat but critics call Belgian blues 'monster cows' and some countries have advocated eliminating the strain as it usually cause dystocia.

21. *Ehlers-Danlos Syndrome* (EDS) or Dermatosparaxix is a heterogeneous group of heritable disorder of connective tissue characterized by articular hypermobility, skin hyperextensibility, and tissue fragility affecting skin, ligaments, joints, blood vessels, and internal organs. The disease has been observed in Holstein, Belgium Blue, Charolais, Hereford, Simmental and crossbred cattle (Scott and Miller, 2003), and Drakensberger cattle in South Africa (Holm et al., 2008).
22. *Factor XI Deficiency Syndrome* is inherited bleeding disorder of HF worldwide (Brush et al., 1987). Factor XI is one of more than a dozen proteins involved in blood clotting. Prolonged oozing of blood following dehorning and castration may also be observed. Affected cows frequently have pink coloured colostrums or milk. Affected animals are more susceptible to diseases such as pneumonia, mastitis and metritis (Liptrap et al., 1995; Patel et al., 2008).
23. *Goiter* is an autosomal recessive disease of Afrikander cattle, was reported in a number of herds during 1950's, is characterized by the production of abnormal thyroglobulin (Tg) and the coexistence in the thyroid of normal-sized (Recketts et al., 1985).
24. *Hydrocephalus* (water head) commonly found in beef cattle especially Polled and Horned Hereford, is an abnormal expansion of cavities (ventricles) within the brain that is caused by the accumulation of cerebrospinal fluid. Excess fluid is present in the brain, which may result in a bulging forehead. Calves are usually born dead or die shortly after birth. Environmental as well as recessive genetic factors can develop this disease (Greene and Leipold, 1974).
25. *Hypotrichosis* or Hairlessness exists in several beef breeds of cattle. Complete or partial loss of skin hair is characteristic of this disease. Calves are usually born with hair but that grow a short curly coat of hair with increasing age (Hutt and Saunders, 1953). Affected calves are prone to environmental conditions; cold, wet and hot and that is why skin infections are more prevalent.
26. *Maple Syrup Urine Disease* (MSUD) was commonly diagnosed in Polled Hereford calves in Australia in mid 1980's (Harper et al., 1989) and is also found in Polled Shorthorns (Healy et al., 1992). MSUD occurs from metabolism error, is characterized by accumulation of the branched chain amino acids and their respective keto acids. Within 12-48 hours, affected calves develop central nervous system depression, lethargy and a scruffy unclean coat, progressing to coma and death within 48-72 hrs. (Fries and Ruvinsky, 1999). The calves were reported to be normal at birth, and then develop a progressive neurological disease
27. *Marble Bone* or Osteopetrosis affects Angus, Hereford and Aberdeen Angus calves (Greene et al., 1974; Ojo et al., 1975; Leipold et al, 1970). It is defined as a generalized congenital skeletal defect due to continuous formation of bone but lack of resorption and failure of remodeling. The calves are usually born dead 2 to 4 weeks early. Bones are solid and do not contain marrow, making them brittle and easily broken.
28. *Myoclonus* (neuraxial adema) is inherited as a recessive trait in Polled Hereford cattle. At birth affected calves are unable to stand because of myoclonic jerks to skeletal muscles in response to external stimuli; affected calves are not viable (Pierce et al., 2001).
29. *Myopathy of the Diaphragmatic Muscles* in Holstein-Friesian cattle is a muscular disease in which the muscle fibers do not function, resulting in muscular weakness (Furuoka et al., 1995). This also leads to degenerative changes in the diaphragmatic and other thoracic muscles.
30. *Myophosphorylase Deficiency* reported in Limousin and Charolais cattle, is a glycogen storage disease. To date, 5 of glycogen storage diseases have been identified in animals (types I, II, III, VII and VIII). Myophosphorylase deficiency is type V glycogenosis in which cattle show exercise intolerance and may have increased serum activities of skeletal muscle-origin enzymes (Angelos et al., 1995). The disease may be life threatening under extensive management systems, but carriers can survive to breeding age if managed under intensive system (Bilstrom et al., 1998).
31. *Ocular Disorder* is a vision-impairing disease, observed in a local Japanese Black cattle population (Ihara et al., 2005).
32. *Pink Tooth* or Congenital Porphyria is a rare cattle hereditary disease of Shorthorn, Hereford, Holstein etc. in which defective hemoglobin formation results in production of an excess of Type I porphyrins in the nuclei of developing normoblasts. Affected cattle exhibit a syndrome of effect manifested early in life. The usual symptoms are discoloured (pink to reddish brown) teeth and urine. Dermal lesions on unpigmented areas may be present when the animals are subjected to sunlight. Anemia and unthriftness may also be observed. Discoloured bones are also observed upon post mortem examination. The condition has been recognized in the USA, Canada, Denmark, Jamaica, England, South Africa, Australia, and Argentina (Franco et al., 1992). It has also been reported in Holstein (Madden et al., 1958).
33. *Platelets Bleeding Disorder* involves impaired aggregation of platelets and has been diagnosed in Simmental cattle (Searcy et al., 1990). Although the disorder does not necessarily manifest clinically early in life, it eventually results in prolonged bleeding from relatively minor trauma, and animals either die or are severely debilitated. Even with wimple processes such as dehorning or castration, animals may have periodic bouts of bleeding that can cause death (Mapletoff et al., 2000).
34. *Polydactyly* (extra toes) in various breeds (Simmental, Holstein etc.) of cattle in which one or both front feet are usually affected, but all four may have the outer dewclaw develop into an extra toe (Johnson et al., 1981 and Vermunt et al., 2000). At least two sets of genes are involved in the inheritance of this trait.
35. *Pompe's Disease* / Generalized Glycogenosis Glycogen storage disease, type II is a fatal glycogen storage disease in cattle whereby excess glycogen is built up in muscle tissue and nerve cells, which interferes with normal function.

Pompe's disease was first recorded in Shorthorn cattle (Richards et al., 1977) and later in Brahman cattle (O'Sullivan et al., 1981) in Australia. Affected calves suffer from progressive muscular weakness. The animals become lethargic, display poor growth and are most affected during stress of weaning, poor nutrition and crowding. Death occurs within the first year of life.

36. *Renal Dysplasia* in Japanese black cattle is manifested by signs of chronic renal insufficiency from an early age (Ohba et al., 2000). The kidneys of affected animals are atrophic and of granular appearance. Histologically, they exhibit interstitial fibrosis with inflammatory cell infiltration, clusters of atrophic and cystic tubules, and thickening of tubular and Bowman's basement membranes (Kawanura et al., 1997). Renal dysplacia is unrelated to bovine chronic interstitial Nephritis with diffuse zonal fibrosis (CINF) in Japanese Black cattle (Sugiyama et al., 2007). The condition is also recently reported in Limousin calf (Castro et al., 2007).
37. *Spastic Syndrome* (crampiness) is a chronic condition occurring in adult cattle. Animals of several breeds including Holstein can be affected (Sponenberg et al., 1985; Tenszen, 1998). The disease is characterized by intermittent bilateral spasms of the skeletal muscles of the pelvic girdle, including muscles of the rump.
38. *Spinal Muscular Atrophy* in Holstein-Friesian calves exhibited locomotion difficulties starting at the age of 15 days, and progressed to paraparesis and tetraparesis in 2 weeks. The neuropathological examination showed degeneration and loss of motor neurons in the spinal cord, together with astrocytosis (Pumarola et al., 1997). This is also found in Brown Swiss cattle (Troyer et al., 1992).
39. *Syndactyly* or Mule Foot is an autosomal recessive genetic disorder results in the painful fusion of the hooves and reduced mobility in Holstein cattle (Charlier et al., 1996). Mule foot most often affects the front foot that has also been observed in the Angus breed (Leipold et al., 1998).
40. *Tibial Hemimelia* is a congenital abnormality present in Shorthorn and Galloway cattle that is characterized by severe and lethal deformities in newborn calves. These deformities can range from bilateral shortening or malformation of the tibia with joint fusion to completely absent tibia. Other defects include abdominal hernia due to incomplete fusion of the pelvic symphysis and meningoceles (Lapointe et al., 2000; Oja et al., 1974).
41. *Weaver Syndrome* or Bovine Progressive Degenerative Myeloencephalopathy (PDME) is also an autosomal recessively inherited neurological disease mainly found in Brown Swiss breed. PDME was first observed in American Brown Swiss in 1973 and since then has been observed in other parts of the world (Corradi et al., 1998; Patel et al., 2008). Clinical signs for the disease usually begin at 6 to 8 months of age and include weakness in hindquarters when getting up, uncoordinated movement of hind limbs, abnormal gait and staggering.
42. *White Heifer Disease* is a congenital reproductive abnormality in white female offspring (heifers) in Belgian Blue and Shorthorn cattle (Bennett et al., 1973; Seitz et al., 1999). The white color is inherited as a recessive trait which is associated with defects in the female reproductive tract (Muellerian system). These heifers are usually sterile.
43. *β- Mannosidosis disorder* occurs in Salers breed and is caused by deficiency inactivity of lysosomal acidic β- mannosidosis enzyme, resulting in an accumulation of mannose rich oligosaccharides in various tissues. It is characterized by weakness, incoordination, head-swaying, splaying of the front legs, and a poor sucking reflex. Affected calves are usually born alive, but exhibit severe neurological abnormalities. It is neurological disease in which calves after birth never get up and eventually die (Bryan et al., 1993).

## CONCLUSION

Precisely genetic disorders cause physical or functional anomalies with negative impact on viability. The old adage that prevention is better then cure is pertinent. As molecular characterization of many of these diseases has appeared in recent years, it is possible to discover heterozygous carriers and cull them from breeding programmes to avoid risk of spreading these diseases among future bulls and bull mothers.

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