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Veterinary Dysmorphology

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1. Introduction

Dysmorphology is a branch of clinical genetics that deals with birth defects on a multidisciplinary basis. It involves knowledge of genetics, embryology, pathology, pediatrics and clinical medicine in order to diagnose birth defects and treat patients. Literally, dysmorphology means "the study of abnormal form". It is a word of Greek origin: *dys*, defect, disorder; *morphé*, form; and *lógos*, word, study. The term was coined by David Smith[1] in the 1960s (Aase, 1990), emphasizing its multidisciplinary aspects to differentiate it from traditional teratology. Due to its multidisciplinary nature, a specialist in dysmorphology works alongside cardiologists, ophthalmologists, neurologists, urologists, orthopedists, imaginologists, pathologists, biochemists and other specialists. It is a field that requires not only medical and biological knowledge but also high level of humanitarian feeling and respect for life, with dedication and perception to reduce the suffering of others. This chapter introduces the fundamentals of dysmorphology and offers an overview of this science in the context of veterinary medicine, with significant examples and emphasis on nosological, pathological, embryological, genetic and clinical aspects. The purpose of this is to provide veterinarians with an approach to congenital defects rather than the usual approach, emphasizing that much can be done instead of simply submitting affected animals to euthanasia. Therapeutic methods and surgical procedures will not be discussed, as each condition requires its own procedures, and these can easily be found in textbooks on medical therapy or surgery and also in scientific journals on veterinarian or human medicine.

[1] David Weyhe Smith (Oakland, 1926 – Seattle, 1981) was an American pediatrician and professor who dedicated his life to children affected by congenital defects, also providing guidance and support to their parents. He was a pioneer of dysmorphology, publishing a large number of articles on this science, of which he was the grand master. One of his books, *Recognizable Patterns of Human Malformation,* became a worldwide classic in the field of human dysmorphology (Wiedemann, 1991), and is now in its sixth edition, updated by Jones (2006). Aase (1990), in a posthumous homage, referred to David W. Smith as "the best and finest man I ever knew".

2. Dysmorphology in veterinary medicine

In veterinary medicine, dysmorphology is still a neglected field of knowledge, but has begun to take shape in line with the advances in veterinary medical genetics. Its basis is derived from human dysmorphology due to current knowledge of the genomic similarities between man and other vertebrates, especially mammals, showing that morphogenesis is evolutionarily conserved throughout the zoological scale. The inductive molecular mechanisms that form the embryonic pattern are identical in all vertebrates (Opitz et al., 2002). Furthermore, veterinary medicine and human medicine share most of the same methods and techniques, both in terms of diagnosis and therapy. However, in the current stage of the development of veterinary dysmorphology, some minute criteria used in human dysmorphology, especially those concerning the extension of concepts, could not always be adopted here.

2.1 Importance

The meaning of dysmorphology in veterinary medicine becomes clear when one considers that congenital defects in animals cause different types of impact: 1) the obvious suffering of the affected individual; 2) the psychological stress for the owners, who are more affectionate towards animals; 3) the abandonment of affected animals by many owners; and 4) the economic loss suffered by breeders, both of companion and production animals. All of these situations are directly linked to the professional work of the veterinarian, meaning different goals in terms of intervention.

2.2 Objectives

The main objectives of veterinary dysmorphology are humanitarian, professional, scientific, preventive and educational. The goal in humanitarian terms is to strive to minimize the suffering of affected individuals and have to do with the perception that animals are sentient beings, i.e., they can feel pain, discomfort, a number of difficulties and other feelings when they are affected by a defect or illness and, consequently, they suffer. The professional goals are to offer qualified assistance to clients who seek guidance and a solution to the congenital health problems of their animals. With these aims in mind more and more people are seeking veterinary clinics and hospitals, especially those dedicated to small animals. The scientific goals have to do with producing knowledge that will result in benefits for the animals themselves and also human beings. The study of spontaneous animal models of human diseases generates knowledge that could not be obtained from human patients for legal and ethical reasons. There are a great number of these animal models recognized today. New medical and molecular biology technology greatly facilitate these studies. The preventive goals are to attempt to advise owners and breeders of animals to help them make decisions and prevent the birth of new individuals with congenital defects. Scientifically based advice is an important step to avoiding the perpetuation of abnormalities, be they of a genetic nature or caused by environmental factors. The educational objectives include raising awareness that veterinarians, like any other professional, should contribute to the development of a better society in every way possible, encouraging ethical values and respect for human beings, animals, nature and life in general.

3. Dysmorphisms: Concept and classification

3.1 Concept

Dysmorphism[2] is the generic name for abnormalities of the form and structure of an animal's body, being used especially for congenital abnormalities, thus constituting an *inborn error of development*. It is important to remember that the adjective "congenital" means born with the individual, independent of the cause. However, it is not synonymous with either "genetic" or "hereditary". Therefore, there are congenital defects that have a genetic cause (the majority) while others have an environmental cause. The word dysmorphism has a broad meaning and can also refer to alterations that are expressed in deviations of size, position, number and even the coloring of one or more parts of the body. Thus, all of the following examples are dysmorphisms: cleft lip and palate (*cheilopalatoschisis*); absence of the cranial vault and cerebral hemispheres (*anencephaly*); very small jaw (*micrognathia*); heart with the apex to the right-hand side (*dextrocardia*); an out of place kidney (*renal ectopia*); one or two missing eyes (*anophthalmia*); extra toes (*polydactyly*); two heads (*dicephaly*); a simple and hyperplasic congenital stain on the skin (*congenital nevus*). Some are extremely serious and lead to death in early life, such as anencephaly; others cause little or no harm to the animal, such as polydactyly (Fig.1).

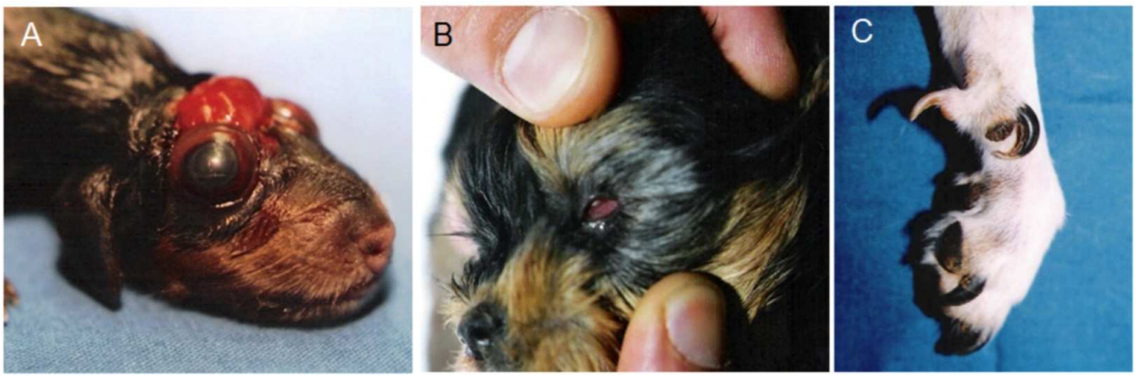


Fig. 1. Examples of dysmorphisms in dogs: A) Anencephaly; B) Anophthalmia; C) Polydactyly.

3.2 Classification

According to the nature of the alteration that causes the dysmorphism and the stage at which it manifests, the phenomenon can be divided into three categories: *malformation, disruption and deformation*. Malformations begin earlier, during the embryonic period, while disruptions appear later. Most deformations begin during the fetal stage, which is when the conceptus grows more rapidly (Kumar & Burton, 2008). If subjacent histological alterations are also considered, a fourth category can be added: *dysplasia*.

[2] Dysmorphism should not be confused with dimorphism, which means the existence of "two different and normal forms" of a given characteristic (from the Greek *di*, two; *morphé*, form), commonly used in the expression "sexual dimorphism" to indicate the natural differences between male and female in a given species.

3.2.1 Malformation

This is a morphological defect of an organ, part of an organ, or a larger region of the body, resulting from an intrinsically abnormal developmental process (Spranger, 1982)[3]. This definition highlights that malformations are disorders in the formation of organs and manifest early, i.e., they are *abnormal processes since the time of their origin*. The affected organ can show varying degrees of imperfection or simply not exist. Malformations arise during blastogenesis or organogenesis and are causally heterogeneous and those that appear earlier (blastogenesis) tend to affect more than one region of the body (Opitz et al., 2002). Although they can be induced by environmental factors, they are commonly caused by gene mutations, chromosomal aberrations or a combination of genetic and environmental factors (Kumar & Burton, 2008). Examples: 1) A nonsyndromic cleft lip and palate can be caused by a recessive autosomal mutation in Brittany spaniels (Richtsmeier et al., 1994), Pyrenees shepherds (Kemp et al., 2009) and boxers (Moura et al., 2011); 2) In Rocky Mountain horses ciliary body cysts, iridal hypoplasia, iridocorneal adhesions and megalocornea are caused by codominant autosomal mutation, with cysts expressed in the heterozygotes and multiple ocular anomalies expressed in the homozygotes (Ewart et al., 2000), whose locus was mapped to the long arm of chromosome 6 (Andersson et al. 2008); 3) The trisomy 18 in cattle causes brachygnathia and is lethal (Herzog, 1974); 4) Cardiac malformations usually have a multifactorial etiology, such as a patent ductus arteriosus in poodles (Buchanan & Patterson, 2003); 5) Neural tube closure defects, such as spina bifida and anencephaly, also have a multifactorial etiology, including mutations in genes involved in folate metabolism (De Marco et al., 2011).

3.2.2 Disruption

A disruption is a morphological defect of an organ, part of an organ or a larger region of the body, resulting from a disturbance in an originally normal developmental process (Spranger, 1982)[4]. This definition highlights that the *formation process of the organs was initially normal, but suffered negative interference during its development*, having affected the organ during the embryonic or fetal stage. In a disruption there is damage to structures of the conceptus because of interference in the blood supply, anoxia, infection or mechanical force (Epstein, 2004), affecting several different tissues and the defect does not respect the boundaries imposed by embryonic developmental process (Aase, 1990). In general, disruptions are caused by environmental factors, but genetic factors can predispose to the development of a disruption (Kumar & Burton, 2008). Examples: 1) A number of therapeutic drugs can cause damage to the embryo when used during pregnancy, especially drugs for continuous use, such as the anticonvulsant valproic acid (Jentink et al., 2010); 2) The feline panleukopenia virus has long been known to cause cerebellar hypoplasia and eventually

[3] In the early 1980s, due to divergences and mistaken nomenclature at that time, specialists in congenital defects formed an International Work Group (IWG) to classify and define terms and expressions for morphogenesis disorders. Their recommendations were published in 1982 (Spranger et al., 1982) and adopted by most dysmorphologists and are still in use today, with very few modifications.

[4] The definitions of malformation and disruption used here correspond, respectively, to the *primary malformation* and *secondary malformation* that were previously in use in dysmorphology. In 1982, the IWG restricted the use of malformation to intrinsically abnormal or primary defects (Opitz, 1984).

hydranencephaly in cats (Résibois et al., 2007); 3) The intrauterine infection caused by the blue tongue virus (BTV serotype 8) causes hydranencephaly in cattle (Wouda et al., 2009); 4) A well known cause of disruption in human beings and which has also been found in the rhesus monkey (Tarantal & Hendrickx, 1987), are amniotic bands that can cause constriction of body structures, leading to facial clefts, amputation of fingers and toes or limbs and other abnormalities.

3.2.3 Deformation

This is a defect of the shape or position of part of the body caused by mechanical forces (Spranger, 1982). These forces may be of internal or external origin and are most evident in the bones, cartilage and joints, as soft tissues tend to return to their original form as soon as the force ceases. Deformations set in during the fetal stage and are normally caused by forces that act late in pregnancy (Epstein, 2004). A large number of deformations have a spontaneous resolution after birth, although this normally takes place slowly. Sometimes, however, treatment is necessary to correct a deformation (Aase, 1990). Like disruptions, although later on, deformations also cause damage to previously intact developed structures with no intrinsic tissue abnormality (Kumar & Burton, 2008). Examples: 1) Club foot as a result of too little space in the uterus and muscular hypotonia or joint laxity, impeding movement of the extremities. Among the factors that reduce uterine space are a very large fetus and a reduction in amniotic fluid, a condition known as oligohydramnios; 2) Increased cephalic perimeter in the hydrocephaly[5] due to pressure from the accumulation of cerebrospinal fluid. The first example is caused by an external force (pressure from the uterus) whereas the second one is caused by an internal force (pressure from the cerebrospinal fluid). It is worth bearing in mind, however, that not all deformations are congenital. They can also develop in postnatal life. For example, bones can be bent because of a lack of calcium or the joints can lose alignment because of the laxity of the joints or lack of calcium. These structures become deformed because of the weight of the body.

3.2.4 Dysplasia

Dysplasia is a morphological defect that results from a disorganization of cells (Spranger, 1982) and other components of a tissue, which, in turn, does not have normal architecture. Therefore, dysplasias are disorders of histogenesis and the alterations occur on a microscopic level and are reflected in the imperfect appearance of the organ or other affected regions of the body. Examples: 1) Congenital alopecia and dental abnormalities in dogs with X-linked hypohidrotic ectodermal dysplasia. There is also absence of piloglandular units in the areas of alopecia (Moura & Cirio, 2004). 2) Thoracic and pelvic limbs are short and bent in dogs affected by chondrodysplasia as can be seen in Great Pyrenees dogs (Bingel & Sande, 1994) or in Labrador retrievers (Smit et al., 2011). Figure 2 shows a visual comparison between normal development and the four types of inborn errors of development (malformation, disruption, deformation and dysplasia).

[5] The cause of hydrocephaly is a malformation or disruption that blocks the drainage of cerebrospinal fluid which, in turn, dilates the cerebral ventricles and separates the cranial bones, *deforming* the head.

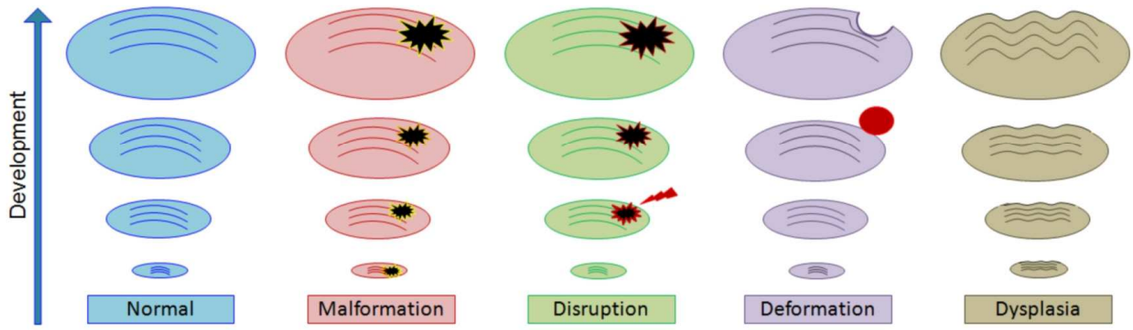


Fig. 2. Types of dysmorphisms compared with normal development.

3.3 Further considerations

Dysmorphisms can also be classified based on criteria other than those presented above. When the medical consequences are considered, they are divided into major and minor dysmorphisms. The former have a significant effect on the quality of life of the affected individual, such as oral clefts, or even impede survival (lethal dysmorphisms), such as anencephaly. The latter have little or no effect on the quality of life of the affected individual and do not require treatment or can be easily treated, such as polydactyly. Dysmorphisms can occur due to increased size or number of body parts and are known as excess dysmorphisms, e.g., extra fingers and toes (polydactyly), duplication of the face (diprosopia) and two heads (dicephaly); or missing body parts, known as reduction dysmorphisms, such as unilateral or bilateral absence of the radius (radial agenesis), missing pinna (anotia) and missing tail (anury). Figure 3 shows some of these defects.

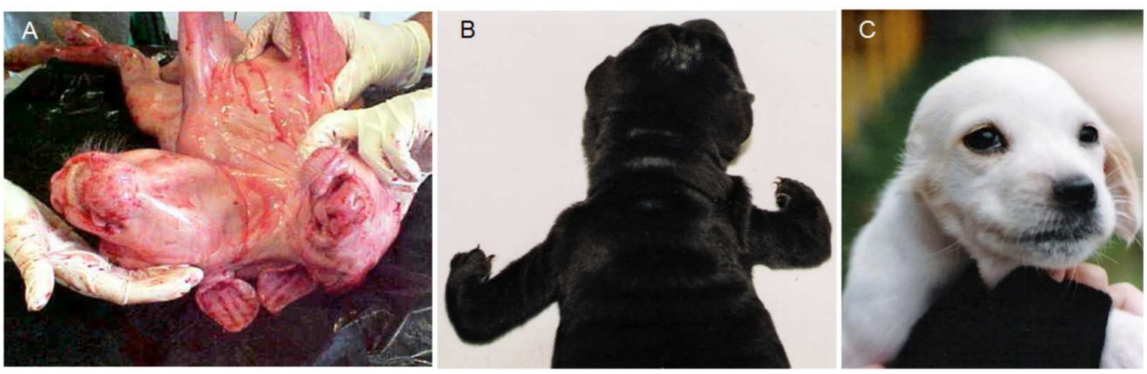


Fig. 3. A) Dicephaly (excess dysmorphism) in extreme premature calf); B) Bilateral radial agenesis in a dog (reduction dysmorphism); C) Anotia in a dog (reduction dysmorphism). Photograph **A** courtesy of Dr. Antonia M. R. B. do Prado and Dr. Joséli Maria Büchele, Laboratory of Anatomy, Faculty of Veterinary Medicine, Pontíficia Universidade Católica do Paraná

4. Epidemiological aspects of dysmorphisms

On its own, a certain type of congenital defect may be rare, but congenital defects as a whole are relatively common in all domestic species and their different breeds and are a significant cause of neonatal and infant mortality and morbidity. Preliminary data suggest that the frequency of dysmorphisms is greater in pigs, followed in descending order by dogs, horses, cattle and cats[6] (Hámori, 1983).

4.1 Frequency, mortality and morbidity

The *frequency* of major dysmorphisms in humans is estimated at 3% of live births (Marden et al, 1964). This number practically doubles by the end of the first year of life, with the identification of defects that manifest later (Kumar & Burton, 2008). In domestic animals, these numbers must be similar or even higher because inbreeding is common in selective breeding both for companion animals and for farm animals, increasing the coefficient of consanguinity. One study (Priester et al, 1970), which included all domestic species, analyzed almost 138,000 individuals and found a rate of 4.68%. However, minor dysmorphisms are not always identified and are seldom included in statistics. The same may occur in the case of major dysmorphisms when they affect internal structures and cause intrauterine or neonatal death and are not always reported. Rates of occurrence vary according to each abnormality and can also vary according to species, breed and geographical location. *Mortality* varies a great deal from one dysmorphism to another. Some are so serious that they cause intrauterine or perinatal death, such as combined heart-lung defects; others are incompatible with life and the affected individual dies soon after birth, as is the case with anencephaly. However, a large number of major dysmorphisms can be corrected surgically or be given some form of treatment, making life viable. Furthermore, minor dysmorphisms have no meaning in terms of mortality. Like mortality, *morbidity* also varies according to the dysmorphism. In many cases, treatment definitively cures the defect and the individual goes on to live a normal life; in other cases, treatment can improve the quality of life, but the individual will have chronic difficulties until the end of his days.

4.2 Risk factors

The artificial selection in breeding to obtain animals with a new or better appearance or for financial gain often means consanguineous unions, increasing the risk of the recurrence of a given defect in future generations. The environment also poses many risk factors during pregnancy, such as: 1) residue from pesticides in water, pasture and other foods; 2) certain toxic plants[7] in the pasture; 3) inadequate conservation of animal feed and other foodstuff

[6] Cats are generally under-represented in samples involving several species. However, veterinarians of small animals often come across congenital defects in purebred cats, which are suggestive of a relatively high rate of dysmorphisms in this species, which is not always reported in journals. They have seen conjoined twins, poliotia, radial agenesis, frontonasal dysplasia, cyclopia, diprosopia, meningocele, anencephaly, spina bifida, hydrocephaly, polydactyly, syndactyly, anal atresia, hypospadias, true hermaphroditism, pseudohermaphroditism and others.

[7] Examples include certain species of the genus *Lupinus* (lupines) that contain teratogenic alkaloids (anagyrine, ammodendrine) that cause a form of congenital arthrogryposis in calves, known as "crooked calf disease". This disease occurs when pregnant cows ingest the plants between the fortieth

which results in mycotoxins; 4) excessive levels of nitrogen-containing food preservatives[8] in low quality animal feed; 5) medicine[9] in the early stages of pregnancy; 6) medicines for continuous use during pregnancy, such as some anticonvulsants; 7) occurrence of certain infectious or metabolic diseases during pregnancy.

5. Etiopathogenesis of dysmorphisms

5.1 Etiology

The *etiological agents* of dysmorphisms can be divided into three large groups: *genetic, environmental and multifactorial*. Although, presumably, any cause of congenital defect is included in one of these groups, a large number of dysmorphsisms have no identified cause and are provisionally separated as a group of *unknown etiology*.

5.1.1 Genetic etiology

In humans, genetic factors are responsible for most dysmorphisms with a known cause (Kumar & Burton, 2008). Considering that mammals in general share most of their genes with humans and that the genes responsible for morphogenesis are highly conserved, the genetic factors must be equally responsible for most of the congenital defects of domestic mammals. These factors are: 1) *dominant autosomal mutations*, such as the fibrillin-1 gene (*FBN 1*), which causes Marfan syndrome in cattle (Singleton et al., 2005). The affected animals have long, thin limbs, laxity of the joints, lens abnormalities, aortic dilation, etc. (Besser et al., 1990); 2) *recessive autosomal mutations*, such as the one that causes anotia, cleft palate and bifid tongue in St. Bernard dogs (Villagómez & Alonso, 1998); 3) *recessive X-linked mutations*, such as the one that occurs in the ectodysplasin A1 and A2 gene isoforms (*EDA-A1* and *EDA-A2*) and causes X-linked hypohidrotic ectodermal dysplasia in dogs (Casal et al. 2005). Affected individuals have imperfect teeth, oligodontia and cutaneous areas with no piloglandular units, as shown in Figure 4 (Moura & Cirio, 2004); 4) *deletions of Y chromosome genes*, such as the one of the sex-determining region Y gene (*SRY*), which determines sex reversal in horses, i.e., it leaves individuals with an male XY karyotype with a female phenotype and ovaries (Raudsepp et al., 2010); 5) *chromosomal aberrations,* such as trysomy of chromosome 30 in horses, which makes them smaller than normal, with a

and hundredth day of pregnancy. The affected calves characteristically have bent extremities and can also have scoliosis, torticollis and cleft palate. Ingestion of toxic plants by farm animals can have a serious economic impact on livestock producers in given geographical areas through death losses, abortions, and birth defects (Lee et al., 2008).

[8] It has not been completely established that *N*-nitroso compounds, such as nitrosamine and its precursors (nitrites and nitrates) naturally cause congenital diseases. Studies in animals indicate that they are highly carcinogenic and at higher levels can be teratogenic, but there is a need for further studies (Griesenbeck et al. 2010). Likewise, mycotoxins should also be considered. Fumonisins (frequent contaminants of corn) and ochratoxin-A (often found in stored grains) experimentally cause craniofacial and neural tube defects in mice (Marasas et al., 2004; Ueta et al. 2010).

[9] An example of routine use in veterinary medicine is griseofulvin, an antifungal drug for animals with dermatomycosis. Scott et al. (1975) observed multiple congenital defects in newborn cats whose mothers orally received high doses of griseofulvin (500-1000 mg, at weekly intervals). There were cerebral defects, skeletal defects, cleft palate, anophthalmia with absence of optic nerves, anal atresia, lack of atrioventricular valves and other defects.

serious angular deviation of the thoracic limbs and polydactyly (Bowling & Millon, 1990); 6) *structural chromosomal aberrations*, such as the translocation between the X chromosome and an autosome described by Schelling et al., (2001) in an intersex Yorkshire terrier.

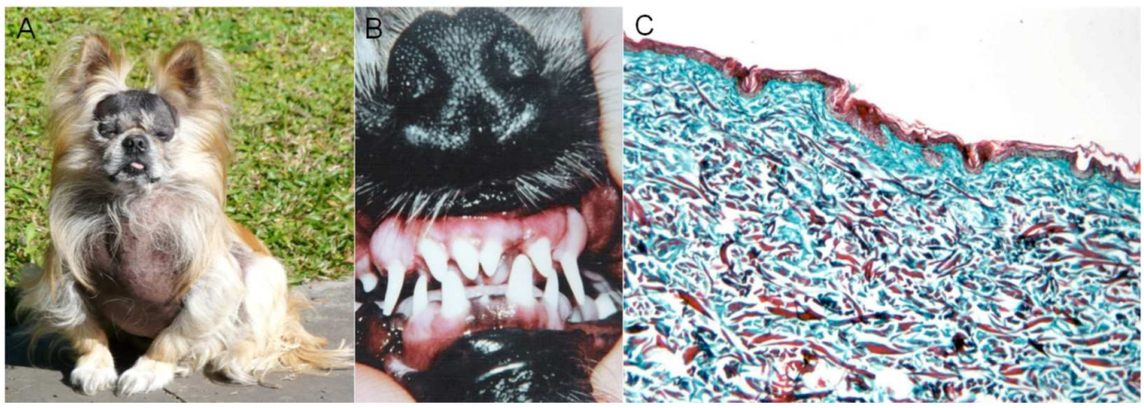


Fig. 4. X-linked hypohidrotic ectodermal dysplasia: A) Congenital absence of hair (congenital alopecia); B) Dental defects (conical teeth and oligodontia); C) Microphotograph of the skin (from an alopecic area) showing absence of hair follicles, sebaceous glands and sweat glands. Shorr stain, X10 objective. Photograph **C** courtesy of Dr. Silvana M. Cirio, Laboratory of Pathology, Faculty of Veterinary Medicine, FEPAR.

5.1.2 Environmental etiology

The environment can be a source of numerous potential teratogens, an important cause of congenital defects in both humans and animals because their presence is not always obvious or the harmful effect of certain products is unknown to the public at large, which increases the risk of maternal exposure to them. *Environmental teratogens* are agents in the *environment* that can negatively impact embryonic development, causing congenital defects. Many chemical products and medicines have been considered potentially teratogenic for decades. Some have been confirmed as such and others have been refused, while the potential of others is doubtful or has been mistakenly confirmed (Koren & Nickel, 2010; 2011). In principle, the risk of a defect is related to the frequency and degree of maternal exposure (Holmes, 2011). Agents that are commonly considered as potentially teratogenic can be separated into four groups: 1) *environmental contaminants,* such as mercury[10], lead, polychlorinated biphenyls, organochlorines and dioxins. There is also considerable doubt

[10] Mercury does not cause gross birth defects, but rather lesions in the central nervous system which cause psychomotor retard, convulsions and other neurological signs (Lancaster, 2011). The sad history of *Minamata disease* was first reported in 1953, but its cause was identified only three years later: a chemical plant discharged water containing inorganic mercury into Minamata Bay in Japan, and this was transformed into organic mercury (methylmercury) by marine microorganisms. Contaminated fish and clams with mythylmercury were consumed as food by the inhabitants of the town of Minamata and this was the source of poisoning which, in the case of pregnant women, affected the fetus, causing *congenital Mimata disease* (Moura, 1993). The number of people affected by the disease was officially established as 2,252, of whom 1,043 had already died 36 years later (Harada, 1995).

concerning their real effect on teratogenic processes. For example, dioxins have been held responsible for a variety of defects. However, that scientific data have so far only confirmed a link to spina bifida (Ngo, 2010); 2) *medicines*[11] such as phenytoin, valproic acid, coumarins and antibiotics; 3) *physical agents* such as heat and radiation[12]; 4) *infectious agents* such as viruses, bacteria and protozoa. Thus, teratogens are of a chemical (dioxins, drugs), physical (heat, radiation) and biological nature (microbes). Non-infectious maternal diseases can also cause dysmorphisms: diabetes mellitus, iodine deficiency, uterine myomas, autoimmune diseases, etc. Uterine dysmorphisms and abnormalities in the extra-embryonic membranes can also cause fetus defects.

5.1.3 Multifactorial etiology

The joint action of several genes (polygenic inheritance) can also play a significant role in the occurrence of dysmorphisms. Deleterious alleles of the different genes play an additive effect until they reach a threshold at which the defect occurs. Environmental factors usually add to this mechanism. Thus, an individual with a given genotype becomes more susceptible to developing a defect, which can be unleashed when environmental forces are at play (multifactorial inheritance). Neural tube closure defects (anencephaly, spina bifida) and conotruncal defects (truncus arteriosus, tetralogy of Fallot) generally have a multifactorial etiology.

5.2 Pathogenesis

The process that gives rise to an abnormal form is a *morphogenetic disturbance* and is known as dysmorphogenesis. The mechanisms involved in dysmorphogenesis are complex, compromising a number of the embryonic developmental phenomena (division of cells, cellular migration, cell adhesion, differentiation, etc.), including cell signaling pathways, e.g., the Sonic hedgehog pathway. They can also include hypoxia resulting from blocked

[11] The tragic history of thalidomide is a warning that the use of medicine during pregnancy should be strictly limited to what is absolutely necessary and should be taken only with medical advice. Thalidomide was launched in 1956, initially as a sedative. By the early 1960s it had become a popular medicine to control morning sickness during pregnancy and could be purchased without a prescription. The following year, Australian obstetrician *William McBride* and German pediatrician *Widukind Lenz* independently saw the link between thalidomide in the early stages of pregnancy and *phocomelia*. The children born with this defect had short limbs close to their bodies and malformed fingers and toes. The abnormality could affect one limb, both arms or all four limbs and often affected internal organs such as the heart and duodenum, constituting a pattern of abnormalities that became known as *thalidomide embryopathy*. It is estimated that there were 8,000 to 10,000 cases worldwide (von Moos et al. 2003). However, thalidomide has been used successfully to treat diseases such as cancer, leprosy and auto-immune diseases.

[12] The *Chernobyl nuclear accident* (Ukraine), in 1986, is a blatant and relatively recent example of the catastrophic effect of *ionizing radiation* on living beings. A number of disorders, including a variety of *malformations*, were registered in animals, from fish to mammals, and even in invertebrates. Congenital defects of the mouth, anus, legs and head were reported in domestic animals. Until today, in animal populations of the contaminated region, there is *transgenerational genomic instability* and *gene mutation rates* are significantly high. In some areas of Europe, the radionuclide levels remain high in mammals, birds, amphibians and fish (Yablokov, 2009).

circulation or non-formation of blood vessels like that caused by antiangiogenic drugs, such as thalidomide and retinoids (Holaday & Berkowitz, 2009). They manifest at the histological level in different ways, such as aplasia, hypoplasia, dysplasia, atrophy, hypertrophy, etc. To follow, we present the fundamental concepts of the developmental field theory, the knowledge of which facilitates the understanding of dysmorphogenesis.

5.2.1 Developmental fields

Developmental field is, initially, the entire embryo in the early stages of its development and, later, it is a region or part of the body of the embryo which responds as a unit to embryonic induction and gives rise to multiple or complex anatomic structures (Spranger et al., 1982; Opitz et al., 2002). Developmental fields are systems that control the progressive differentiation of the structure and size, and also the temporal and spatial distribution of the complex organ components. To understand better the developmental field concept, it is important to remember the meaning of the terms *blastogenesis*, *organogenesis*, *morphogenesis*, *histogenesis* and *phenogenesis* in the context of dysmorphology. *Blastogenesis* is the set of events of embryonic development from fertilization to the end of gastrulation, i.e., it includes phenomena such as the formation of the morula, blastocyst, ectoderm, endoderm, mesoderm, neural tube and midline, in addition to cardioangiogenesis, mesonephrogenesis and curving of the embryo, which then takes the shape of a C (Opitz et al., 2002). At the end of the gastrulation, *organogenesis* begins. This is the set of events that lead to the formation of the organs and other parts of the body (*morphogenesis*) and includes the differentiation of the cells and tissues (*histogenesis*). On average, the duration of blastogenesis is similar in the majority of mammals, but the duration of the phenomena that follow varies from one species to another, especially the fetal period, which is reflected in the duration of pregnancy. The development that ranges from the fetal period and postnatal period to puberty is called *phenogenesis* (Opitz et al., 2002). During the fetal period, phenogenesis is characterized by growth and maturation, preparing the individual for birth. The *primary developmental field* is the field represented by the entire embryo in the early stages of blastogenesis. The initial phenomena of this period include pattern formation, generating components known as **progenitor fields**, which are the primordia of all final structures (Davidson, 1993; Martínez-Frías et al., 1998), as they give rise to the heart, central nervous system and limb buds (Opitz et al. 2002). When the components of a field remain contiguous, they constitute a *monotopic field*, in other words, a developmental field related to the formation of a single area of the body. However, there are fields in which the components separate from one another to give rise to distant final structures among themselves, which are known as *polytopic fields*. Thus, a polytopic field has to do with the formation of structures situated in different areas of the body (Opitz, 1982). *Secondary developmental fields* are the fields formed by the subdivision of progenitor fields, and each of them originates a determined final structure during organogenesis (Martínez-Frías et al., 1998).

5.2.2 Congenital defects and developmental fields

Malformations, disruptions and dysplasias are the result of disorders that occur in one of more developmental field. If they result from alterations that occur during blastogenesis, when the progenitor fields are formed, they are *primary field defects;* if they are the result of

alterations that occur during organogenesis, after the formation of the progenitor fields, they are *secondary field defects*. Those that are localized, i.e., the affect only one structure or part of the body, which was differentiated during organogenesis, are *monotopic field defects*; those affecting structures situated in different parts of the body are *polytopic field defects* and originate in the early stages of blastogenesis (Martínez-Frías, 1998).

5.2.3 Heterogeneity, pleiotropy and sequence

Developmental fields are embryonic morphogenetic units and, thus, respond to an inductive stimulus as an epimorphically hierarchical self-organizing unit that is temporally synchronized and spatially coordinated (Opitz, 1982). Consequently, a given abnormal phenotype can originate as a response of a field to different causes. This becomes clearer if we remember that different fields can share parts of the same cell signaling pathway involved in embryonic development. For example, the *Sonic hedgehog cell signaling pathway* is composed of genes that codify proteins that act as intercellular signals in many development processes. Mutations in these genes can result in malformations such as holoprosencephaly, syndactyly, polydactyly, heart defects, kidney defects and anal atresia, or even in neoplasias such as meningioma and squamous cell carcinoma (Cohen Jr, 2004). A congenital defect can be the result of mutations in different genes, chromosomal aberrations or the action of mutagenic agents or teratogens, i.e., it is *causally heterogeneous*. Evidently, the meaning of this is that defects that are clinically the same can have a genetic or environmental cause (Fig. 5). A defect caused by an environmental factor, but which is the same as another caused genetically, is known as a *phenocopy*.



Fig. 5. Cleft lip and palate in dogs are phenotypically and etiologically heterogeneous. They can be unilateral (A) or bilateral (B). They can affect the entire extension of the palate or only the primary palate (C). They can have a multifactorial origin or a monogenic autosomal recessive origin, or be caused by environmental factors (phenocopy).

On the other hand, the same gene can give rise to a series of morphogenetic events that are necessary for the formation of different final structures. This genetic phenomenon in which a gene is responsible for several different phenotypic characteristics is known as *pleiotropy* and is also one of the phenomena that can occur in dysmorphogenesis. For example, a mutation in the gene that codifies ectodysplasin, a protein that regulates the initial

epithelial-mesenchymal interaction necessary for the formation of ectodermal derivatives, causes X-linked hypohidrotic ectodermal dysplasia, which occurs in humans, cattle, mice and dogs, and is characterized by defects in the teeth and in the skin (absence of piloglandular units) and other ectodermal derivatives (Moura & Cirio, 2004). In addition to heterogeneity and pleiotropy, another phenomenon may be behind multiple abnormalities: they may be the consequence of only one initial defect that provokes the occurrence of new events in a chain reaction, characterizing a *dysmorphogenetic sequence*. For instance, micrognathia can unleash retroglossoptosis which, in turn, causes cleft palate and respiratory distress, a condition known as Pierre Robin sequence (Mackay, 2011).

5.2.4 More frequently affected systems and selected examples of abnormalities

Cardiovascular system: communication between the pulmonary trunk and the aorta artery (*patent ductus arteriosus,* Fig. 6-A); communication between the atria (*atrial septal defect*) or between the ventricles (*ventricular septal defect*); combination of pulmonary stenosis with a ventricular septal defect, hypertrophy of the right ventricle and an overriding aorta, i.e., the aorta is positioned directly over a ventricular septal defect (*tetratology of Fallot*); imperfect mitral valve and support structures (*mitral dysplasia*); imperfect tricuspid valve and support structures (*tricuspid dysplasia);* right or left atrium divided by a membrane, leaving it with two chambers (*cor triatriatum*); absence of communication between the right atrium and ventricle (*tricuspid atresia*); lack of differentiation of the origins of the pulmonary trunk, aorta and coronary arteries, forming a common arterial trunk (*truncus arteriosus*).

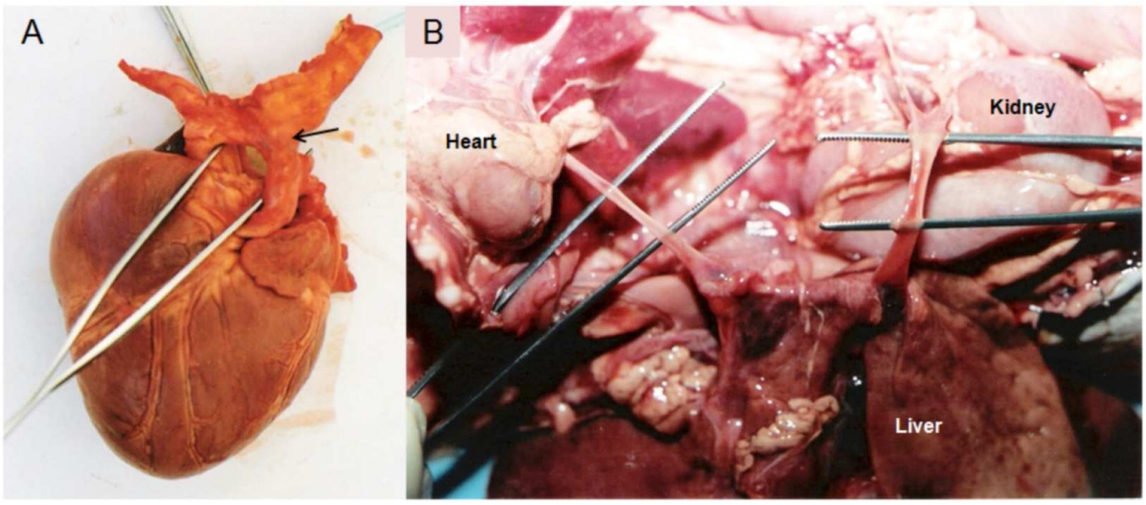


Fig. 6. Examples of abnormalities of the cardiovascular system: A) Patent ductus arteriosus (arrow); B) Abnormality of the caudal vena cava in a dachshund dog with Caroli disease. Note that this vein (raised by forceps) does not have normal morphology. Photograph **B** courtesy of Dr. Marconi R. de Farias, Companion Animal Veterinary Hospital, Faculty of Veterinary Medicine, Pontifícia Universidade Católica do Paraná.

Musculoskeletal system: missing jaw (*agnathia*); shorter-than-normal jaw (*brachygnathia*); abnormally small jaw (*micrognathia*); incompletely formed vertebra (*hemivertebra,* Fig. 7-A and B); missing vertebrae in the lumbar and sacral region (*lumbosacral agenesis*); absence of

the radius (*radial agenesis*, *radial hemimelia*) which may be unilateral or bilateral; absence of one or more limbs (*amelia*); fused digits (*syndactyly*); missing digits and respective metacarpal bones (*ectrodactyly,* Fig. 7-C); existence of extra digits (*polydactyly*); presence of one or more supernumerary limbs (*polymelia*); shorter-than-normal bones due to deficient endochondral ossification (*chondrodysplasia*); incongruence of the elbow joint (*elbow dysplasia*); incongruence of the coxofemoral joint (*hip dysplasia*); congenital joint immobility (*arthrogryposis*); paraumbilical defect in the abdomen with evisceration (*gastroschisis*, Fig. 7-D); congenital umbilical hernia containing viscera (*omphalocele*); congenital cleft of the thoracic wall (*thoracoschisis*), with exteriorization of the heart (*ectopia cordis*).



Fig. 7. Examples of abnormalities of the musculoskeletal system: A) Newborn foal with serious scoliosis as a result of spinal defects (hemivertebrae); B) Radiograph of the foal shown in A, revealing the hemivertebrae (arrow); C) Ectrodactyly in a poodle dog (left thoracic limb); D) Gastroschisis in a newborn Siberian husky; E) Pituitary dwarfism in a German shepherd at the age of 4 years; F) Duplication of the left hind paw of a newborn Rottweiler (polypodia). Photographs **A** and **B** courtesy of Dr. Pedro V. Michelloto Junior, Equine Veterinary Hospital, Faculty of Veterinary Medicine, Pontifícia Universidade Católica do Paraná.

Nervous system: absence of the upper parts of the brain and skull (*anencephaly,* Fig.1-A); retroflection of the head and partial or total absence of the cervical vertebrae associated with serious defects of the central nervous system (*iniencephaly*); stenosis of the aqueduct of Sylvius or another part of the brain's drainage system, leading to accumulated cerebrospinal fluid in the cerebral ventricles (*hydrocephaly*, Fig. 8-A); meningeal herniation, i.e., a protrusion of the meninges at some point of the spine (*meningocele*, Fig. 8-B); meningeal herniation containing a segment of the spinal cord (*meningomyelocele*); meningeal herniation containing part of the brain (*meningoencephalocele*); absence of the major connection between the two cerebral hemispheres (*agenesis of the corpus callosum*); failed development of the prosencephalon (forebrain), compromising the separation of the cerebral hemispheres and causing defects in the midline of the face (*holoprosencephaly*); absence of brain gyri (*lissencephaly*); presence of small and multiple brain gyri (*polymicrogiria*); enlargement of the brain gyri (*pachygiria*); lower than normal development of the cerebellum (*cerebellar hypoplasia*).

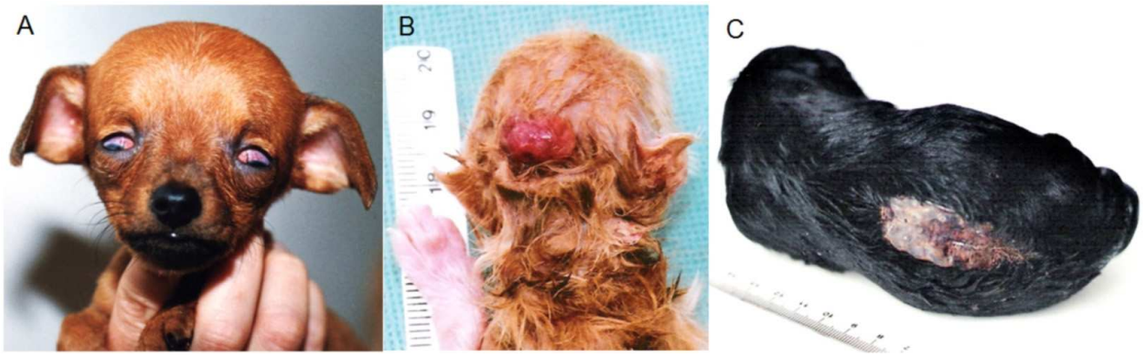


Fig. 8. Examples of abnormalities of the central nervous system: A) Hydrocephaly in a dachshund puppy ; B) Meningocele in a newborn Persian kitty; C) Spina bifida occulta with neural involvement in a newborn Rottweiler puppy.

Genitourinary System: missing kidney (*renal agenesis*) that can be unilateral or bilateral; disorganized renal tissue (*renal dysplasia*); cysts in the kidneys (*polycystic renal disease*); fusion of the kidneys by one of the poles, generally the lower, with a silhouette forming in the shape of a horseshoe (*horseshoe kidney*); proximal bifurcation of the renal pelvis (*bifid renal pelvis*); ureter flowing into an organ other than the bladder, commonly in the urethra or the vagina and even the uterus (*ureteral ectopia*); failure to close the urachus (*patent urachus*); urethral opening located on a point of the ventral side of the penis, scrotum or perineum (*hypospadias*, Fig. 9-A); urethra with a connection to the rectum (*urethrorectal fistula*); cystic tumors formed of tissue from different embryonic germ layers that are strangers to the affected organ (*teratoma*). They are more frequent in ovaries and testicles, but can occur in the prostate or in organs from other systems; absence of vagina (vaginal agenesis); larger-than-normal clitoris (*clitoromegaly*, Fig. 9-B); much smaller-than-normal penis (*micropenis*); testicle retained in the abdomen or inguinal canal (*cryptorchidism*), which can be unilateral or bilateral; presence of a membrane that totally or partially closes the vaginal opening (*persistent hymen*); presence of a fibrous ligament between the gland and the foreskin (*persistent penile frenulum*). In domestic mammals, unlike human beings where the hymen and the penile frenulum are characteristics found in adults, there is a regression of these structures during development.

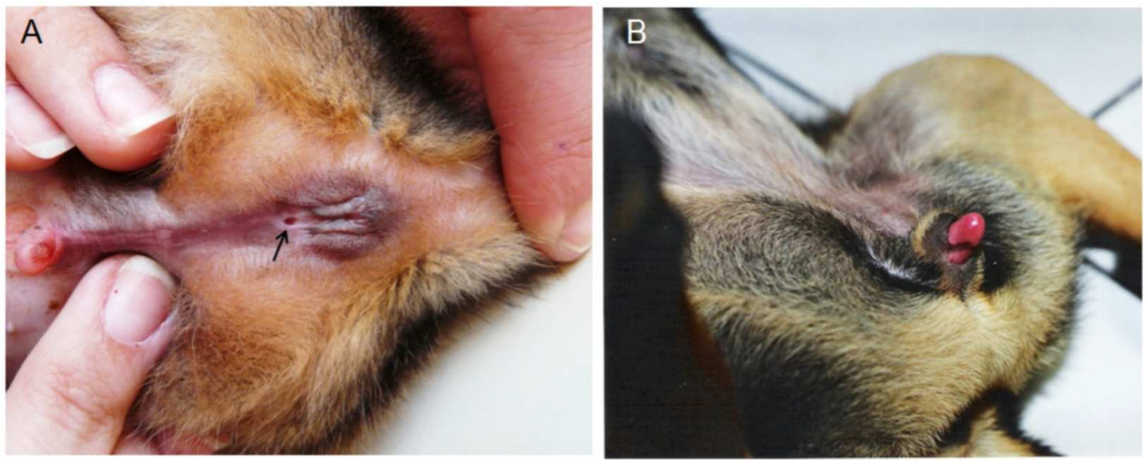


Fig. 9. Examples of abnormalities of the genitourinary system: A) Perineal hypospadias in a dog. Observe the urethral opening (arrow) located in the perineum, near the anus; B) Ambiguous genitalia in a dog with XX true hermaphroditism.

6. Clinical presentation of dysmorphisms

Dysmorphisms can affect an individual as a *single defect* (Fig. 10-A and B) or a set of defects (*multiple congenital anomalies*). The latter include syndromes, developmental field defects, associations and sequences. All arise from disorders in one of more developmental field.

6.1 Single defect

A *single defect* (*isolated defect*) affects only one specific part of an organ or a single organ or a local region of the body. Single defects include an eyelid coloboma, a cleft palate, a patent ductus arteriosus and a hypospadias. Most congenital defects are single and their etiology is often multifactorial. A given type of single defect may be viewed as part of certain syndromes, pointing out that different causes can affect the same developmental field, leading to the same result (Aase, 1990). Single defects are monotopic defects, which are the result of a disturbance in a single monotopic primary field or in a secondary field.

6.2 Multiple congenital anomalies

The occurrence of two or more defects in one or more parts of the body of the same individual is characterized as a *multiple congenital anomaly* (Fig. 10-C). However, the concomitant occurrence of anomalies does not define the etiology. A given pattern of defects may indeed have a specific etiology or may be caused by a variety of possible agents that affect the same developmental fields or a same monotopic or polytopic field.

6.2.1 Syndrome

A syndrome is a *set of defects* that occur simultaneously in the same individual and result from the *same cause*. Therefore, the pattern of defects must be repeated in all affected individuals. Syndromes are defined after several cases have been described, enabling one to determine which defects actually compose the syndrome and which are accidental. Strictly

speaking, however, the cause is not always known, but it is presumed. Generally, syndromes are considered as having resulted from a disorder in more than one developmental field (Spranger, 1982). Examples: 1) Hurler Syndrome (mucopolysaccharidosis I), a recessive autosomal syndrome in which there is a deficiency of alpha-L-iduronidase. Affected dogs have corneal opacity, facial dysmorphism, joint abnormalities, aortic dilation and thickened heart valves (Traas et al., 2007); 2) Hunter Syndrome (mucopolysaccharidosis II), an X-linked recessive syndrome in which there is iduronate-sulfatase deficiency. Affected dogs have a course facial appearance, macrodactyly, corneal dystrophy and neurological alterations (Wilkerson, 1998).

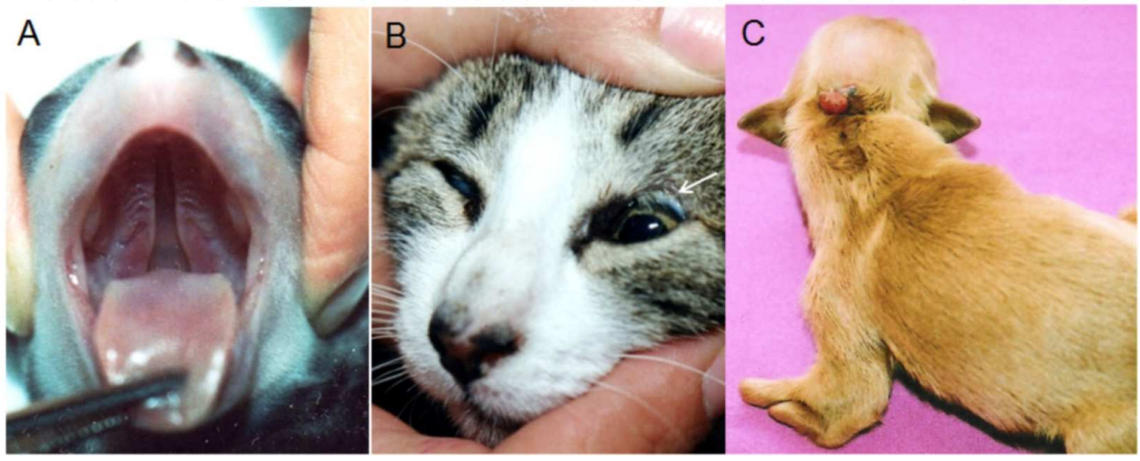


Fig. 10. Examples of single defect: A) Dog with cleft palate; B) Eyelid coloboma (arrow) in a cat; C) Example of a multiple congenital anomaly in a dog (meningocele and peromelia).

6.2.2 Developmental field defects

Developmental field defects are resulting from a *dysmorphogenetic response* of a developmental field (Hersch et al., 2002) and are causally heterogeneous. This means that the *same field reacts in a similar way to different factors*. They may be multiple anomalies that affect an area of anatomically related structures, being monotopic field defects; or they may be anomalies in different areas of the body, being polytopic field defects. Holoprosencephaly in its different degrees is a monotopic field, such as semilobar holoprosencephaly in Morgan horses (Kock et al., 2005), and may be associated with otocephaly, as reported by Martínez et al., (2006) in a Rottweiler dog. Lumbosacral agenesis in its different degrees is a polytopic field defect and has been described in a number of domestic species, such as sheep (Denis, 1975), cattle (Jones, 1999; Son et al., 2008), pigs (Avedillo & Camón, 2007) and dogs (Araújo et al., 2008).

6.2.3 Association

Association is a *combination of two or more defects* in the same individual and occurs in the population more frequently than could be expected merely at random, but it does *not have a specific cause*. Like syndromes, associations must be defects involving more than one developmental field (or only one polytopic field), but are etiologically heterogeneous.

Example: VACTERL (or VATER) is an acronym for the non-random co-occurrence of vertebral anomalies (V), anal atresia (A), cardiac malformations (C), tracheoesophageal fistula (TE), renal anomalies (R) and limb defects (L). The presence of two of these anomalies in the same patient is considered sufficient for diagnosis (Källén et al., 2001), although other researchers are of the opinion that at least three are required (Martínez-Frías, 1994; Faivre et al., 2005). The defects that compose VACTERL association originate during blastogenesis and the existence of a characteristic pattern of abnormalities caused by different factors suggests a dysmorphogenetic response from a primary developmental field (Hersch et al., 2002). For this reason, Martínez-Frías & Frías (1999) consider it a primary, polytopic developmental field defects. In animals, the first record of a spontaneous occurrence of VACTERL association was made by Moura et al. (2010) in a female cat with costovertebral defects, anal atresia, heart and kidney defects, bilateral radial agenesis and persistent cloaca, but no tracheoesophageal fistula.

6.2.4 Sequence

This is a set of defects in an individual and results from an *initial defect* (malformation, disruption, dysplasia or deformation) that interferes in the development process, *leading to additional defects*. For example, as the result of a persistent right aortic arch, a ring is formed around the thoracic esophagus, causing an increased diameter of the esophagus in the cervical segment (a pouch is formed cranially to the point of constriction). A bilateral elbow dysplasia can cause a luxation of the elbows, which leads to medial rotation of the forearms, deforming the carpus. Micrognatia causes retroglossoptosis, which in turn can cause a cleft palate and respiratory distress (Pierre Robin sequence).

6.3 Further considerations

The same dysmorphism can appear in isolation or be part of syndromes or associations. Single defects or multiple defects of the same area (monotopic defects) without anomalies in other areas of the body are often called *nonsyndromic defects* to distinguish them from the same defects in an individual affected by a syndrome. A given defect can be a manifestation of the same anomaly expressed in different degrees, as is common in the developmental field defects. Any degree of expression of these cases is part of the total spectrum of a multiple anomaly. For instance, a single upper central incisor or an iris coloboma may be a minimum clinical sign of the total spectrum of holopresencephaly (Fig. 11-A), which at the most serious degree includes anomalies such as cyclopia, proboscis, absence of optic nerves and cleft lip and palate (Spranger, 1982; Jones, 2006). Dysmorphisms that affect the right and left side of the body (*symmetrical dysmorphisms*) are more likely to have a genetic cause than those that affect only one side (*asymmetric dysmorphisms*). However, this is not a rule (Turnpenny & Ellard, 2007). When a dysmorphism is extenal it is easily observed, especially if it is a major dysmorphism. Internal dysmorphisms, in turn, can only be confirmed by imaging tests, endoscopic viewing or a postmortem examination. Nevertheless, affected individuals will show clinical signs (Fig.11-B and C) at some time during their development, enabling a diagnosis using the aforementioned examinations. Internal congenital defects must be on the list of possible diagnoses in stillborn and critically ill newborn animals, although they may look normal externally. Internal

congenital defects too must be considered a possible cause of clinical conditions identified in the first months of life. Although most of these defects are identified in the first six months, there are cases that manifest clinically later on and are diagnosed in adult life. For example, many cases of dogs with pulmonic stenosis show no clinical signs for years (Ware, 2011).

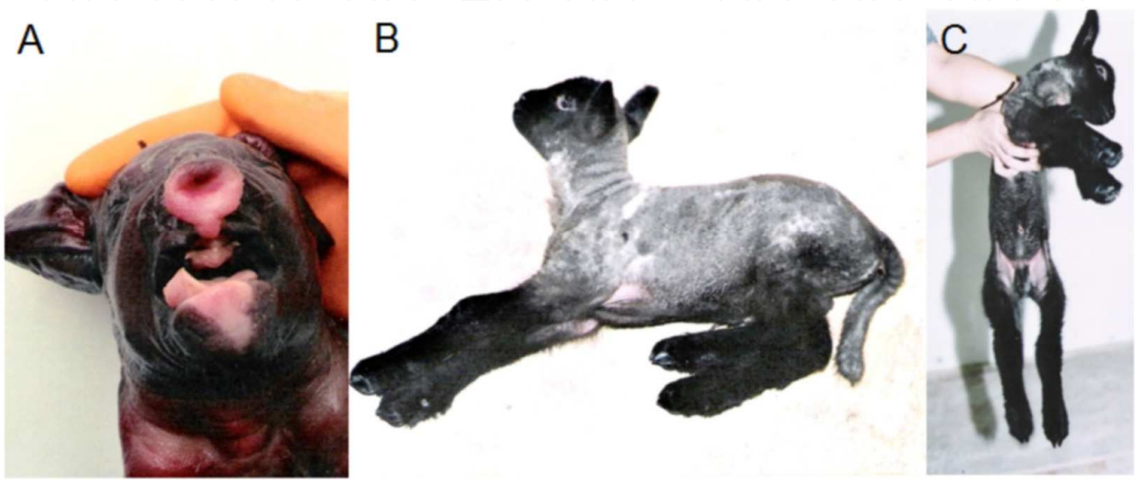


Fig. 11. A) Holoprosencephaly in a pig; B and C) Clinical signs of cerebellar disorder in a lamb (backward contraction of the neck, thoracic limbs in hyperextension and flexed pelvic limbs) as a result of cerebellar hypoplasia.

7. Medical history, physical examination and management of dysmorphic patients

In dysmorphology, the clinical activities that lead to the diagnosis (medical history, physical examination, complementary examinations, etc.) and the therapeutic procedures are that same as those of clinical medicine and/or surgery, with the inherent aspects of each specialty and any adaptations that each dysmorphic condition may require. In any situations, a correct diagnosis is very important for making the best decision. It has implications in terms of prognosis and possible treatment. All procedures should be noted according to well defined criteria in order to obtain a complete and consistent record, whose importance in terms of diagnosis and therapy transcends each case, enabling comparisons with new cases and generating innovations. The following topics introduce some general observations concerning these aspects.

7.1 Medical history

A detailed and solid medical history is one of the pillars of the diagnosis. It should include information about the environment in which the mother lives or lived, maternal diseases

(metabolic disorders, infectious diseases, etc.), the mother's food, any medication given to the mother during pregnancy, and particularities of pregnancy and labor. Whenever possible, the veterinarian should seek not only similar cases but also different defects between sibs of the affected animal and other relatives. A pedigree should be drawn that is as complete as possible to facilitate the genetic analysis and enable the identification of an inheritance pattern when there is one.

7.2 Physical examination

The physical examination of a dysmorphic patient follows clinical principles, as in any specialty, and should be detailed. In addition to obvious defects, other abnormalities that the animal may have should be sought, even if they are only minimal. All anatomical regions and organic systems should be examined. All inspection and palpation should be done carefully in order not to miss any minor anomalies. One should always remember that the animal hair coat may make it difficult to see an anomaly but palpation contact facilitates detection. Minor anomalies, which may at first appear irrelevant, may help in the diagnosis. One should also remember that external defects, even if there is only one, may be a sign of an internal defect, meaning that specific examinations are required to locate them. The more minor defects at patient has, the greater the chance that it will also have major defects. Measurements of various segments of the body should be made routinely as they help to recognize patterns or define patterns of congenital malformations. An examination of normal relatives could also be useful.

7.3 Diagnostic tests

In many cases the diagnosis can be obtained with a minimum number of diagnostic tests. However, in other cases, a large number of tests is required, which significantly increases the cost, which often makes a more in-depth evaluation impossible in veterinary medicine. Some tests can only be conducted at universities, research centers or large private clinics. Imaging tests (simple X-ray, contrast X-ray, tomography, magnetic resonance imaging, ultrasound, endoscopy) are especially useful, as are karyotype analyses, biochemical examinations and, when available, DNA tests. The affected animals that do not survive should be submitted to a detailed postmortem examination. This examination provides diagnostic information and can help to develop treatment strategies for future cases.

7.4 Care and treatment

Therapy varies according to the type of defect. Very serious dysmorphisms often make life impossible, while less serious types often require no treatment. When treatment is possible, it can vary from methods that improve the quality of life of the patient to full correction of the defect. For instance, in the first case, a system of wheels for a dog that was born with no pelvic limbs (nowadays, there are "wheelchairs" for dogs and cats that are sold commercially); in the second case, a surgery to correct a cleft lip and palate or to correct a patent ductus arteriosus. There are cases where simple care is all that is required, such as giving a dog with oligodontia soft and previously cut food.

8. Prevention of dysmorphisms

Preventing dysmorphisms involves three main points: *genetic counseling, screening* and *monitoring during pregnancy*. The former two apply when the defect is hereditary or is influenced by genetic factors. The latter is useful in any situation.

8.1 Genetic counseling

The basic recommendation in the case of genetic diseases in animals is that affected individuals should not breed and that normal couples with affected descendents should not breed again. However, owners of normal animals that have had affected descendents are not usually willing to follow this advice. With this in mind, when there is a correct diagnosis and the genetic nature of the defect is known, other decisions are possible, but the risk of recurrence should be taken into consideration. To avoid autosomal recessive phenotypes, an important strategy is never to mate individuals who are known to be heterozygotes one with another, such as those who have already had an affected descendent. For recessive X-linked phenotypes, daughters of affected individuals are all carriers (heterozygotes) and should not be mated, even when the males are normal. When there is a family history of a recessive defect and the zygosity of an individual is unknown, consanguineous unions should be avoided.

8.2 Screening

When breeding small or large animals, identifying heterozygotes (recessive phenotypes and dominant phenotypes with reduced penetrance) can be an economically advantageous procedure and allows people to make appropriate preventive decisions concerning the mating of such individuals. For several recessive heredopathies commercial DNA tests are now available, significantly reducing costs. For instance, there is a test for arthrogryposis multiplex in cattle; for pulmonary hypoplasia with anasarca (PHA) in Dexter cattle; for polycystic kidney disease in cats, for Sly disease (mucopolysaccharidosis VII) in dogs; for hereditary microphthalmia in sheep. In abnormalities in which there is incomplete dominance between the mutant and normal allele, the heterozygotes can be identified visually because they have an abnormal phenotype, although it is less serious than that of homozygotes for the mutant allele. For example, there is a type of chondrodysplasia in cattle, common in the Dexter breed, in which the heterozygotes have shorter than normal limbs. If two chondrodysplasic individuals breed, there is a 50% risk of recurrence of the parents' phenotype (heterozygotes) and a 25% risk of a very serious and lethal chondrodysplasia, popularly known as a "bulldog calf", when the affected animals have very short limbs and spine, and their heads somewhat resemble that of a bulldog.

8.3 Monitoring during pregnancy

Several aspects deserve attention during pregnancy: 1) Care should be taken not to expose the pregnant animal to teratogens in the environment (mercury, herbicides, toxic plants, organochlorides, etc.); 2) The animals should not be given medicine with teratogenic potential; 3) They should not be submitted to radiographic examinations. If this cannot be avoided, the abdomen of the pregnant animal should be protected with a lead apron or the

examinations should be conducted in the later stages of the pregnancy; 4) Examinations that use radioactive contrast (scintigraphy) should not be conducted; 5) Care should be taken concerning the quality and conservations of animal food. Feed that is exposed to dampness could lead to contamination by mycotoxins; 6) Food should be supplemented with folic acid[13]; 7) Pregnant animals that suffer from diabetes should be monitored. In humans, diabetes mellitus is a significant risk factor when it comes to congenital defects. This may also be the case in animals.

9. Ethical aspects in veterinary dysmorphology

When a dysmorphic animal is born, its owners can have many different reactions: pity, fear or repulsion, to name a few. They also make different decisions: some will care for the animal, while others may abandon it or kill it. Those who seek a veterinarian wish to give the animal to a new owner, treat it or sacrifice it. What will be done depends on the moral and ethical principles of each owner and each veterinarian. The most common argument is that, to avoid a life of suffering, the affected animal should be euthanatized. In this case, some points have to be considered: 1) In the case of serious malformations that are incompatible with life or when there are no technical resources to treat the animal properly, the ethical choice is undoubtedly to shorten the suffering; 2) Many cases that initially seem to be incompatible with life can be fully resolved with adequate treatment, while in other cases the animal may not even require surgery to live well, as long as it received proper care and affection. This includes some cases of conjoined twins. Unlike humans, animals have no awareness of their appearance and do not suffer because of it and can live happy lives if their owner gives them care and affection; 3) If the defects are not extensive, there are owners who decide not to submit their animal to surgery when they realize that it is living well and is not suffering and they develop an emotional tie and grow used to its different appearance; 4) There are cases when medical treatment is enough to make the animal comfortable, even though it may not completely cure the deficiency; 5) There are people who cannot bear the idea of looking after dysmorphic animals, while others do not mind and feel gratified when they see that they are keeping the animal alive. These latter are often willing to adopt animals with deficiencies; 6) The treatment and monitoring of dysmorphic animals generates technical and scientific knowledge that results in improved efficiency and quality of medical and nursing care for new cases in both animals and humans. However that may be, the decisions reflect the socioeconomic and cultural status of each society.

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[13] Supplementing food with folic acid has been recommended to prevent neural tube defects and cleft lip and palate in humans. This food supplement for pregnant Boston terriers, a breed of dog that is particularly susceptible to cleft lip and palate, significantly reduced the occurrence of these abnormalities in controlled studies (Elwood & Colquhoum, 1997; Guilloteau et al., 2006).

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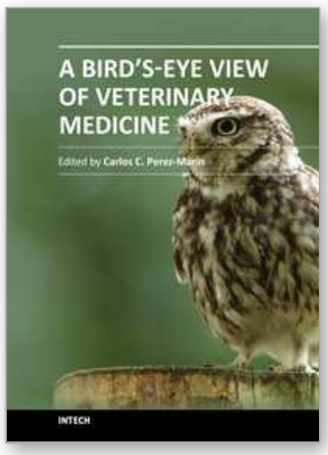
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