Reference Point

Dysostoses of the canine and feline appendicular skeleton

Heather A. M. Towle, DVM, and Gert J. Breur, DVM, PhD, DACVS

Dysostoses are a group of congenital bone dysmorphologies characterized by abnormal development of individual bones or part of bones.[1] Such dysmorphologies are caused by failure of a mesenchymal bone model (ie, an anlagen) to form, failure of anlagen to properly transform into cartilage, or failure to convert cartilage into bone.[2] The alterations may be the result of a malformation (intrinsically abnormal developmental process) or a disruption (extrinsic breakdown or an interference with an originally normal developmental process).[3]

There are many reports on congenital bone dysmorphologies in domesticated animals, but such studies are seldom on a large scale. Because many dysostoses are either not diagnosed or not reported, it is impossible to determine the exact prevalence of dysostoses in dogs and cats. However, it is clear that the prevalence of dysostoses in dogs and cats is low. Many dysostoses are obvious, and all can be diagnosed radiographically. The ability to recognize and differentiate between dysostoses is important because many have treatment options and dysostosis often is compatible with a good quality of life. Early diagnosis may be important in preserving the possibility of effective treatment and reducing secondary complications. It also may be important in preventing further propagation of the condition.

Information about canine and feline dysostoses in the veterinary clinical literature is sparse, and most reports are limited to isolated cases. The purpose of this review is to provide a concise guide to the clinical signs, diagnosis, treatment, prognosis, and heritability for each reported appendicular dysostosis. Limb development is briefly described to facilitate understanding of the abnormal developmental embryologic processes that lead to dysostoses. Specific appendicular skeletal dysostoses including amelia, hemimelia, ectrodactyly, polydactyly, and syndactyly, and diagnosis of dysostoses are discussed.

Limb Development

In dogs and cats, limb formation occurs from day 23 of gestation to approximately day 35.[4,5] After this period, skeletal elements only increase in size and obtain their mature morphologic features. All tetrapods have the same patterns of limb formation. Therefore, much of our understanding of limb development obtained from chickens, mice, and humans may be applied to dogs and cats. Limb formation is an intricate process that includes limb bud formation, limb elongation, digit formation, and bone and joint formation.[6,7]

The first visual evidence of canine and feline limb development is formation of a limb bud. Mesenchymal cells are released from the lateral plate of the somatic mesoderm (skeletal precursors) and from somites (muscle precursors).[2,6,7] Somatic mesoderm cells migrate to and multiply beneath the surface ectoderm at the forelimb sites on day 23 of gestation and to the hind limb sites approximately 1 day later. The resulting bulges on the embryo's surface are called limb buds. Recently, it has been discovered that limb bud initiation is governed by **fibroblast growth factor (FGF)**8, FGF10, and Wnt proteins. The location of limb buds and whether a limb bud will develop into a forelimb or hind limb are directed by *Hox*, *Tbx5* (forelimb), *Tbx4* (hind limb), and *Pitx1* (hind limb) genes and retinoic acid.[7,8]

After limb bud formation, a discrete specialized zone called the **apical ectodermal ridge (AER)** forms as the surface ectoderm thickens at its apex on each limb bud. The limb bud at this stage is undifferentiated mesoderm covered by the AER. Elongation and further development of the presumptive limb are largely regulated by the continued interaction between the AER and underlying mesoderm.[6-8] The induction of the AER is probably under control of FGF10 produced by mesodermal cells in the limb below the AER. The maintenance and proliferation of the undifferentiated mesodermal cell mass beneath the AER (progress zone) and the maintenance of their FGF10 expression are regulated by FGF4 and FGF8 synthesis in the AER.[7-9]

The presumptive limb elongates in an orderly fashion. The outgrowing mesoderm forms a superficial, intermediate, and deep layer.[2] The superficial cell mass is exposed to AER signaling and forms the intermediate and deep layer in a proximodistal sequence. The intermediate layer will differentiate into periskeletal tissue (perichondrium, periosteum, joint capsules, and musculotendinous units). The deep layer will give rise to skeletal tissue (bones and cartilage).[2] The development of skeletal and periskeletal tissue is tightly controlled in 3 directions or axes: the proximodistal axis, the craniocau-

From the Department of Veterinary Clinical Sciences, School of Veterinary Medicine, Purdue University, West Lafayette, IN 47907.
The authors thank Drs. J. W. Mauck, D. Griffon, E. F. Richardson, and W. E. Blevins for contributions to the figures.
Address correspondence to Dr. Breur.

dal axis, and the dorsoventral axis. Development in the proximodistal axis is controlled by the AER, and *Hox* and *meis* genes are associated with the specification of the skeletal elements. The craniocaudal development of the limb is under the direction of the *Sonic hedgehog (Shh)* gene and controlled in the **zone of polarizing activity (ZPA)**, a transient population of specialized cells in the limb bud mesoderm. Development in the dorsoventral axis is defined by the *Wnt7a* and *LMX1* genes.[7-9]

The distal end of the elongating limb will flatten, broaden, and differentiate into a forelimb (hand) plate or hind limb (foot) plate.[2,4,7] Within the mesodermal cell mass of the plates, 5 rays that are continuous with the main mesodermal cell mass will develop. These rays will differentiate into the digits. The cells between the rays will die by apoptosis, and interdigital clefts will form.[2,4,7] It has been postulated that the apoptosis signal is controlled by **bone morphogenic proteins (BMPs)** and the *noggin* gene.[7,8]

Shortly after formation of the AER and elongation of the limb, the deep mesodermal layer starts chondrification. Bone and joint formation begin with segmentation of the chondrogenic core. The regions between the formed segments (presumptive bones) are termed interzones (presumptive joints). The interzones will differentiate into 3 zones: the 2 presumptive opposing joint surfaces and an intermediate layer. The joint cavity develops from small spaces in the intermediate layer that coalesce to form the joint cavity. This process is called cavitation. Joint formation is completed by development of synovium and intra- and periarticular structures.[2,4,10] The *Hox* genes and BMPs appear to play an important role in both the aggregation of mesenchymal cells into outlines of the future bones and in the segmentation process.[9,11] Bone morphogenic proteins (BMP2, BMP7, and GDF5) and *noggin* genes are essential for diarthrodial joint formation.[7,8,11]

In general, the morphologic developmental aberrations that result in dysostoses are well understood, and more genes responsible for these aberrations are rapidly being identified. On the basis of chick, mice, and human studies, mutations are suspected to play a role in canine and feline dysostoses, although none have been identified. Environmental factors have also been implicated in development of dysostoses. Such environmental factors may include drugs; maternal disease; faulty maternal diet; modified-live vaccines; radiation; and trauma to the mother, embryo, or placenta.[12,13]

Appendicular Dysostoses

Amelia—Amelia is the congenital absence of 1 or more limbs. Monobrachia refers to the agenesis of 1 forelimb and monopodia refers to the agenesis of 1 hind limb. Abrachia indicates the absence of both forelimbs, and apodia indicates the absence of both hind limbs.[14] Amelia is caused by failure of limb bud formation or limb outgrowth and elongation. For instance, chick embryos homozygous for the *limbless* mutation initiate limb bud formation, but the AER fails to form and the limb subsequently regresses. In this mutation, the actual defective gene is not known yet, but *En-1* (homeobox gene-*engrailed-1*), *Wnt7a* (signaling molecule), and *Lmx-1* (homeobox gene) have been implicated.[6,10]

The diagnosis of amelia can be made by physical examination. Radiographs may be used to differentiate between true amelia and proximal terminal transverse hemimelia (discussed later in this report). Affected dogs and cats that have been documented in the veterinary literature all had concurrent life-threatening conditions. Amelia was reported in a colony of Beagles with concurrent blepharophysmosis, bulldog head, and a kidney syndrome, histologically similar to Balkan nephropathy in humans. Affected dogs often died spontaneously soon after birth or were euthanatized.[15] The mode of inheritance of this trait has not been reported.

Hemimelia—Hemimelia is a congenital complete or partial absence of 1 or more bones. All appendicular bones can be affected, and many different permutations of this condition have been recognized **(Figures 1 and 2)**. Hemimelia is called terminal if all or part of the middle and distal bones of a limb are absent. If all or part of the middle bones of a limb are absent, with the proximal and distal portions being present, the hemimelia is called intercalary. Each of these 2 main groups can be subdivided: transverse hemimelia refers to complete absence of 1 or more bones across the limb's width, and longitudinal hemimelia indicates absence of 1 or more bones along the preaxial (medial) or postaxial (lateral) side of a limb.[16,17]

Hemimelia results from a lack of AER-mesodermal interaction during limb outgrowth. Transverse bone deficiencies may arise because of timed, massive failure of the AER-mesodermal interaction. Intercalary bone deficiencies may be caused by more localized failure of AER-mesodermal interactions or failure of the bone anlagen to differentiate from mesenchymal tissue into

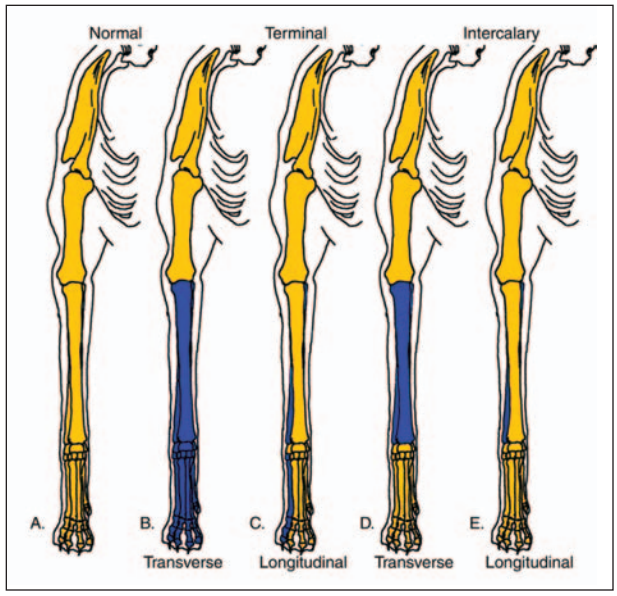

Figure 1—Illustration of the classification of hemimelia. A—Normal development of appendicular bones. B and C—Terminal hemimelia: absence (dark gray) of all or part of the middle and distal bones of a limb. D and E—Intercalary hemimelia: absence of all or part of the middle bones of a limb (dark gray), with the proximal and distal portions present (light gray). Terminal and intercalary hemimelia can be subdivided into transverse (complete absence of 1 or more bones across the limb's width [B and D]) and longitudinal hemimelia (absence of 1 or more bones along the medial or lateral side of a limb [C and E]).

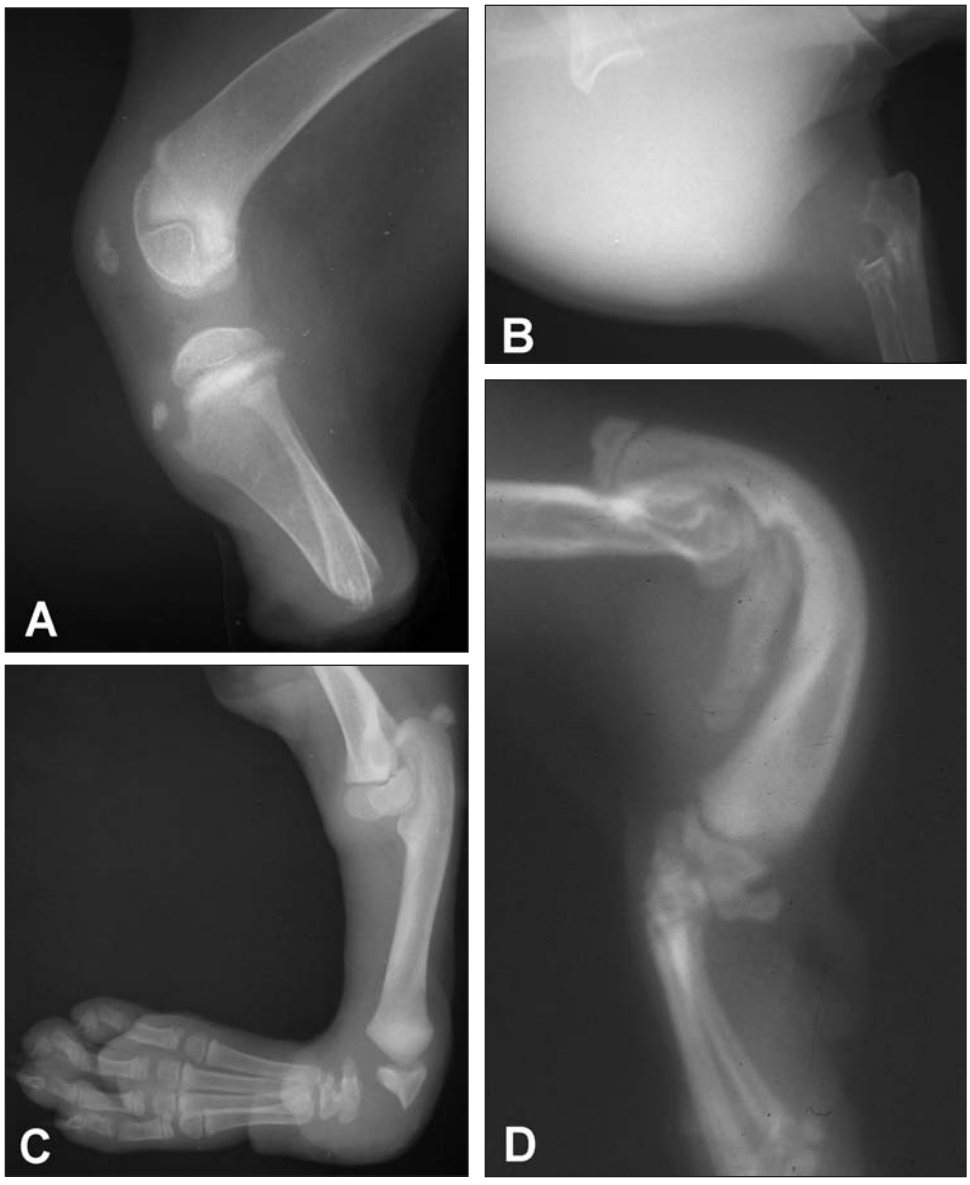

Figure 2—Radiographic views of limbs of animals with hemimelia. A—Terminal transverse hemimelia in a 9-week-old male Labrador Retriever. The distal aspects of the tibia and fibula and all bones distad are absent. B—Intercalary transverse humeral hemimelia in a mixed-breed dog. The entire humerus is absent. C—Preaxial complete intercalary longitudinal radial hemimelia in an 11-week-old Pit Bull Terrier. Notice absence of the radius with functional adaptation of the ulna (thickening of the cranial ulnar cortex). D—Preaxial partial intercalary longitudinal radial hemimelia with ulnar deformity in an 8-month-old female domestic shorthair cat. The radius is partially absent, and the ulna has a secondary deformity (abnormal shape and bowing).

cartilage or from cartilage into bone.[2] Although the exact trigger is not known, chick embryo studies[7,10] have revealed that *En-1, Wnt7a*, FGF-2, and *Lmx-1* may play a role in the development of hemimelia.

Both terminal[18-20] and intercalary[13,20-22] forms of canine[13,20,22] and feline[13,20,23] hemimelia have been reported. Most reported hemimelias are single case reports and appear nonhereditary. An exception is bilateral terminal preaxial pectoral limb hemimelia in Chihuahuas, which is characterized by multiple zeugopodial (radius, ulna, tibia, and fibula) and autopodial (manus and pes) deficiencies. This trait in Chihuahuas is autosomal recessive.[20]

Preaxial longitudinal intercalary radial hemimelia is the most common type of hemimelia in dogs and cats.[24,25] This condition is usually unilateral, but bilateral absence may occur.[25] The entire radius or part of it may be absent, whereas parts of the ulna are sometimes missing as well. It has been suggested that radial hemimelia in Siamese and domestic shorthair cats may be a hereditary trait,[26] but there is no such evidence in dogs.[13,21,22]

The clinical signs and findings of hemimelia vary and depend on the type of hemimelia. If only a non–weight-bearing bone such as the fibula or ulna is missing, the condition may go unnoticed.[13] Radial hemimelia is usually noticed soon after birth. Clinical signs may consist of a marked varus and flexion deformity of the elbow and carpus because the ulna is unable to support the animal's weight and the flexor muscles are not balanced by extensor muscles. Over time, the flexor muscles may become permanently contracted.[22,27] The ulna is the main weight-bearing bone and may assume a larger than normal diameter.[27] Other clinical signs may include signs of pain upon palpation over the distal ulna, lack of forelimb flexion or extension, bone deformity, and severe muscle atrophy and muscle contraction over the entire length of the forelimb.[22,27] Concom- itant fractures may also be present.[22] Radiographs of the affected limb may be used to confirm the diagnosis (Figure 2).[13]

Early recognition and treatment of radial hemimelia may facilitate prevention of muscle contracture, bone deformity with subsequent varus deformity, or limb disuse. If a limb deformity can be reduced, we recommend stabilization of the radiocarpal joint in a normal weight-bearing position with a fortified Robert Jones or Spica bandage in animals younger than 4 to 5 months.[28] The splint is applied to prevent further bone and limb deformity, promote ankylosis of the radiocarpal joint in a weight-bearing position, and prevent disuse. After this period, the animal is reevaluated to

determine whether further treatment is indicated. If the limb function is acceptable and the deformity minimal, no further care is indicated. If limb function is unacceptable because of the severity of the deformity, additional conservative or surgical treatment may be considered. Such conservative management consists of supportive care. Because this condition by itself is not painful, animals usually do not require pain medication. Conservatively treated animals with radial hemimelia usually have a good quality of life. Surgical treatment may consist of declawing of selected digits (if the affected limb is rotated and nails get caught in carpet, for instance), reconstruction (carpal arthrodesis and repair of the radial defect), or amputation.[13,21,27-30] Fusion of the defect and carpal arthrodesis has been accomplished successfully by use of an autogenous rib graft stabilized with a small Kirschner wire or Steinman pin.[21,29] Amputation has been suggested for unilateral hemimelia for medical reasons (ulceration or fracture) or cosmesis. A thorough physical examination should be performed before amputation is performed because there are often multiple congenital abnormalities.[13] With early diagnosis and appropriate treatment, most animals with unilateral and even bilateral hemimelia will have a good quality of life.

Ectrodactyly—Ectrodactyly (also split-hand deformity, cleft hand, lobster-claw deformity, oligodactyly, or hypodactyly) is congenital digital cleft formation extending between the metacarpal bones (**Figure 3**).

The cleft is associated with hypoplasia or absence of 1 or more bones in the adjacent area of the distal portion of the limb.[31] Most feline and canine cleft metacarpal deformities that have been reported are between the first and second metacarpal bones, but clefts between other metacarpals may occur.[31] The elbow joint may be incongruent or luxated.[31-33] Carpal bones are often severely hypoplastic or missing, and the ulna may be short. One or more digital rays (metacarpal bone and associated phalanges) may be absent as well. Syndactyly (incomplete separation of interdigital clefts) and digital contractures may be present.[31,34]

It has been reported that the development of ectrodactyly in the *Dylaplasia* mouse is associated with massive aberrant cell death of the forelimb (hand) plate's AER. There is evidence that in this animal model, ectrodactyly is associated with abnormal expression of the *FGF8* gene.[35]

In cats, ectrodactyly may be inherited as an autosomal dominant defect with variable expression and no apparent breed or sex predilection.[36] There is no evidence that this trait is heritable in dogs.[33]

All reported cases of ectrodactyly in dogs and cats are unilateral and affect only the forelimb. Clinical signs vary from mild deformity and lameness to severe deformity and non–weight-bearing lameness. The defect is present at birth, but the lameness and deformity may become more severe with age. The malformed limb may be shorter than the contralateral normal limb. It may also be abducted at the elbow and supinated at the carpus, leaving the carpal dorsum as the weight-bearing surface.[37] Carpal laxity may be present during manipulation. Palpation may reveal the absence of 1 or more digits, metacarpal bones, and carpal bones. Radiography will confirm the diagnosis and help determine the extent of the malformations so that a treatment plan can be developed.[31,37]

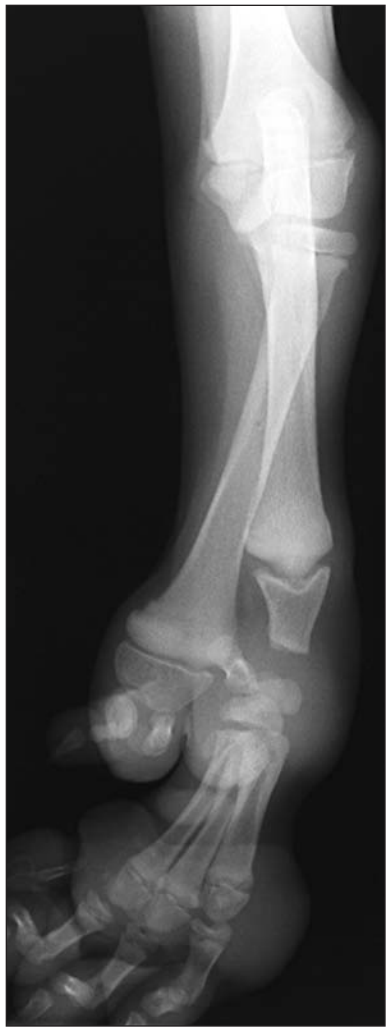

Figure 3—Dorsopalmar radiographic view of the forelimb of a 10-week-old female Labrador Retriever with ectrodactyly. Notice soft tissue separation between the second and third metacarpal bones. The first metacarpal bone is hypoplastic and the second is absent. Radial overgrowth in relation to the ulna is evident. The separation of the carpal bones has occurred between the intermedioradial and ulnar carpal bones. There is also evidence of flexure contracture of the digits.

As in hemimelia, early diagnosis is important regarding prognosis. Early recognition and treatment with a splint until the animal is 4 to 5 months of age may help prevent muscle contracture, bone and limb deformity, and limb disuse and promote ankylosis of the radiocarpal joint.[28] If limb function is acceptable and the deformity is minimal after this treatment, no further care is indicated. If limb function is unacceptable, further conservative or surgical treatment may be considered. Such conservative management may be indicated in mild cases or if the owner does not desire surgical treatment. It usually provides the animal with a good quality of life, and pain medication is usually not needed. The animal may be treated surgically by amputation or reconstruction. Reconstruction may include carpal and metacarpal stabilization with bone grafting; reconstruction of antebrachium, manus, and soft tissues; and ulnar lengthening.[30,32,33] The choice of treatment is determined by the extent of the malformations, and multiple corrective surgeries may be required. Reconstructive surgery has resulted in improved limb function, so it may be a viable treatment option.[33] However, amputation is often selected as the primary method of treatment because of progressive degenerative joint disease or cosmetic reasons or because the limb is a hindrance to the animal.[30,33]

Polydactyly—Polydactyly is the congenital presence of 1 or more extra digits. The extra digit often does not

contain a full complement of bones. If the extra digit is on the medial side of the limb, the condition is called preaxial polydactyly, and if on the lateral side of the limb, the condition is called postaxial polydactyly. Multiple dewclaws are an example of preaxial polydactylism[25,38,39] (**Figure 4**). The dewclaw represents the first digit that was lost during evolution in most canine species.[25,38,39]

It has been suggested that *shh* and *msx-1* genes are involved in the development of polydactyly along with retinoic acid.[7] In most dog breeds, preaxial polydactyly is inherited as an autosomal dominant trait with variable expression.[25,38,40] However, preaxial hind limb polydactylism in Saint Bernards and Collies is presumed to be an autosomal recessive trait.[40,41] In Saint Bernards, the condition is also associated with palate agenesis, anotia (congenital absence of 1 or both external ears), incomplete bifid tongue, and an extra thoracic vertebra and rib.[41] A similar syndrome has been described in Australian Shepherds. Male dogs affected with this syndrome may also have cleft palate, syndactyly, shortened tibia or fibula, brachygnathism, and often scoliosis. Females are not as severely affected and lack the cleft palate, brachygnathism, and scoliosis. The defect is lethal to males, and it has been suggested that the syndrome is inherited as an X-linked lethal trait or a sex-influenced autosomal trait.[42,43]

In cats, polydactyly is also considered an autosomal dominant trait with variable phenotypic expression. Clinically normal cats typically have 5 digits on each front paw and 4 digits on each hind paw. However, cats with more digits are not unusual, and the number of additional digits is variable. This feature is found in both male and female cats.[38]

For the most part, polydactyly is of no clinical importance. However, there is the possibility that the extra digit may become infected, ingrown, or catch and tear at the adjoining skin. In that case, amputation of the extra digit is an effective treatment.[38] Digit amputation also has been performed to make dogs more competitive for show exhibits. Prognosis is considered excellent to good.

Syndactyly—Syndactyly is the congenital lack of differentiation between 2 or more digits.[18] In humans, it is classified as simple or complex and as complete or incomplete.[44] In simple syndactyly, the interconnection between adjacent digits consists only of skin and fibrous tissue. Complex syndactyly occurs when the bones are fused. Complex syndactyly is called complete when the digits are connected throughout their entire length and incomplete when the digits are not connected throughout their entire length (**Figure 5**).[44,45] Syndactyly has been reported in dogs[45,46] and seen as a single defect and in combination with ectrodactyly.[31,46] It also has been reported in combination with other severe defects in a family of Australian Shepherds. This trait was lethal to males and inherited as an X-linked lethal trait or a sex-influenced autosomal trait.[42,43]

Syndactyly results when the mesenchyme between radial swellings fails to break down and allows complete separation of digits, fibrous tissue, or skin in utero.[2,7,45,46] Syndactyly in humans has been associated with a mutation of the *Hoxd-13* gene.[7,8]

Animals with simple syndactyly may have lameness because as the digits attempt to spread during weight bearing, the thin skin on the dorsum of the paw is stretched taut.[45] Complex syndactyly is usually without clinical signs. The diagnosis is based on orthopedic and radiographic evaluation.

The treatment of choice for simple syndactyly is surgical separation of the weight-bearing digits. By use of large dorsal and palmar skin flaps, the digits can be separated and an interdigital commissure can be created. Full-thickness skin grafts can be harvested to cover the exposed axial and abaxial surfaces of the digits.[45] No treatment has been recommended for complex syndactyly.

Diagnosis of Dysostoses

The diagnostic approach to dysostoses is straightforward. The physical examination should be preceded by a detailed history. The age at which the defect became visible should be determined. To expose a possible genetic background, the clinician should ask whether there were other affected littermates or affected puppies or kittens from previous litters (including male-to-female ratio) and whether other related dogs or cats were affected.[47,48] If possible, information on the first and second trimester of the animal's gestation should be obtained to determine possible causative environmental factors (eg, drug exposure, maternal disease, or radiation).[12,13] A complete nutritional history should be established as well. A thorough physical examination

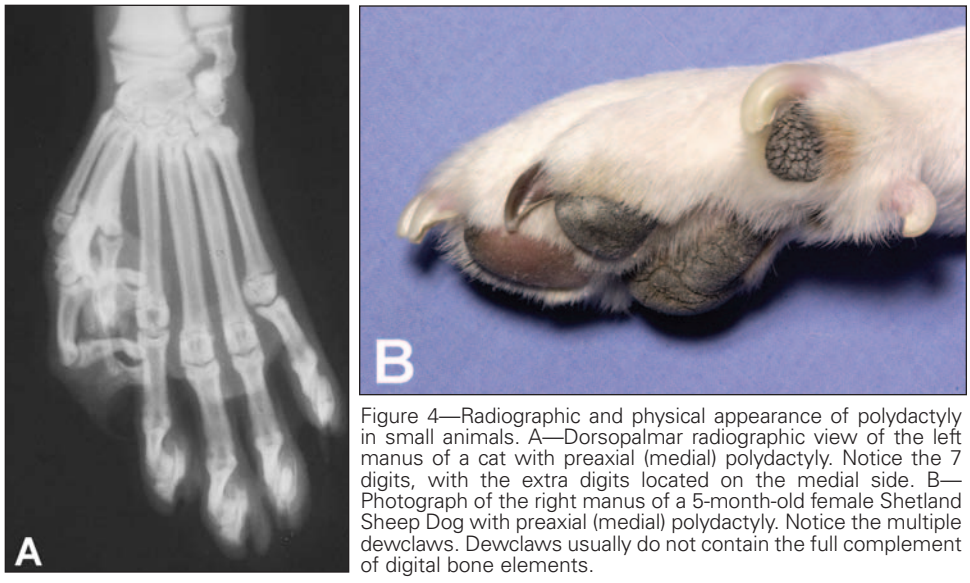

Figure 4—Radiographic and physical appearance of polydactyly in small animals. A—Dorsopalmar radiographic view of the left manus of a cat with preaxial (medial) polydactyly. Notice the 7 digits, with the extra digits located on the medial side. B—Photograph of the right manus of a 5-month-old female Shetland Sheep Dog with preaxial (medial) polydactyly. Notice the multiple dewclaws. Dewclaws usually do not contain the full complement of digital bone elements.

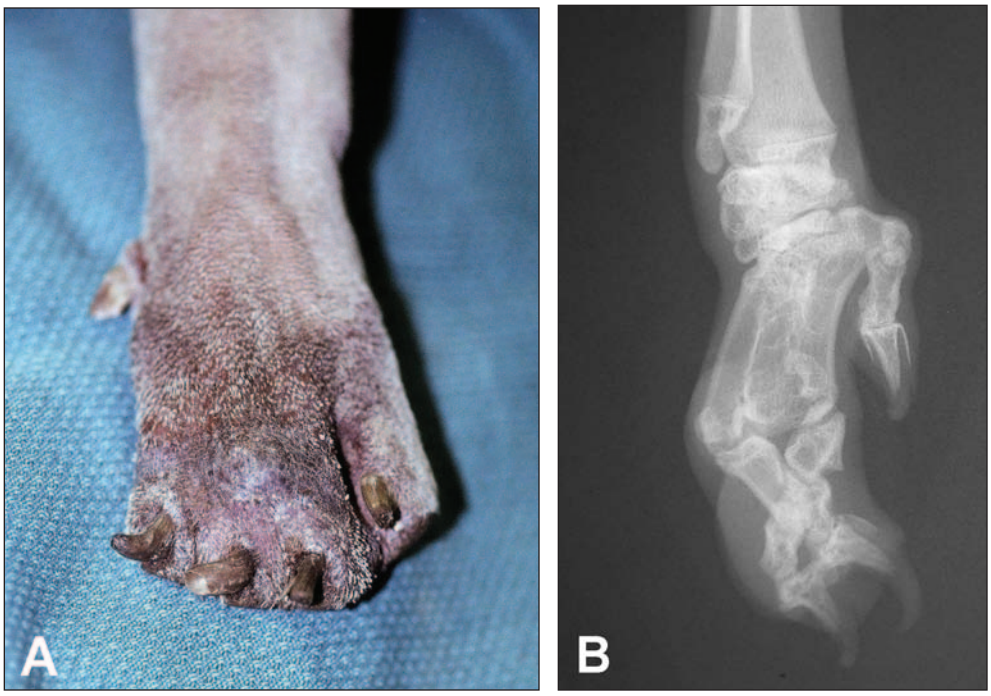

Figure 5—Physical and radiographic appearance of syndactyly in small animals. A—Photograph of the dorsal aspect of the left manus of a dog with simple complete syndactyly. Notice lack of separation between the second and third and third and fourth digits. Only a small degree of separation between the fourth and fifth digits is evident. The nails on all digits are deformed or twisted. (Adapted from Richardson EF, Wey PD, Hoffman LA. Surgical management of syndactyly in a dog. *J Am Vet Med Assoc* 1994; 205:1149–1151. Reprinted with permission). B—Dorsopalmar radiographic view of a 1.5-year-old male domestic shorthair cat with complex complete syndactyly of multiple metacarpal bones. Note interconnection between adjacent metacarpal bones.

should be performed in all animals in which a dysostosis is diagnosed because they may occur in combination with other congenital abnormalities. Because dysostoses are bone deformities, they can easily be visualized radiographically. Therefore, the diagnosis of most dysostoses is rather simple and based on clinical and radiographic findings. Occasionally, interpretation of the collected data, especially for ectrodactyly, may prove challenging. Although the mode of inheritance of most dysostoses is unknown, some have a proven hereditary background **(Appendix)**.

Discussion

All major dysostoses (amelia, hemimelia, ectrodactyly, polydactyly, and syndactyly) have been reported in dogs and cats. However, some rare dysostoses infrequently seen in humans have not been reported in dogs and cats. For instance, canine or feline dimelia (duplication of the whole or part of a limb)[49] has not been reported. Thus, the documentation of feline and canine dysostoses is not complete yet.

The different types of dysostoses reflect aberrations during different stages of limb formation. Amelia may be defined as a disruption of limb bud or AER formation. The hemimelias, ectrodactyly and syndactyly, represent abnormal development along the proximodistal limb axis,[7] whereas polydactyly may be classified as dysmorphologies along the craniocaudal axis. Regulators of individual stages of limb formation have been implicated in dysostoses associated with these stages. For instance, in humans, syndactyly has been associated with a mutation of a *Hox* gene (*Hoxd-13*), a gene directing specification of skeletal elements of metacarpals and digits along the proximodistal limb axis.[7] Although mutations of many dysostoses have been identified, pathophysiologic mechanisms of associated dysmorphologies are not well understood. Mutations in dogs and cats resulting in dysostosis have not been reported yet.

In none of the reported dysostoses was an environmental cause reported. This may suggest that most dysostoses diagnosed in pets are malformations (intrinsically abnormal developmental process) and not disruptions (extrinsic breakdown or an interference with an originally normal developmental process).[3] Few of the reported dysostoses appeared to be hereditary. Therefore, most canine and feline dysostoses may be mutations.[50-52] Although in most dysostoses, particularly hemimelia and ectrodactyly, a hereditary background cannot be determined, it is important that breeding of these animals should be discouraged and that they be spayed or castrated to ensure that the trait is not passed on to offspring.

The treatment of dysostoses may cause an ethical dilemma for the attending veterinarian. Clearly, euthanasia appears justified in animals with severe multiple defects[43] or systemic complications.[18] Other defects like ectrodactyly and hemimelia may affect the animal's ability to function normally. However, animals with these conditions treated conservatively with reconstructive surgery or amputation usually have a good quality of life. Therefore, treatment appears ethically justified, particularly if euthanasia is the alternative. Other dysostoses such as polydactyly only have cosmetic consequences that may interfere with competitive show exhibits. For instance, with polydactyly, the attending veterinarian may be asked to surgically remove the extra digit so that the animal can compete in good standing. Such a treatment may pose a similar ethical dilemma as with other cosmetic surgeries such as ear cropping and tail docking.[53] Leading ethicists and veterinary professional societies have attempted to provide guidance for the repair of inherited defects to the practicing veterinarian.[53,54] The AVMA deems performance of surgical procedures for the purpose of concealing genetic defects of animals to be shown, raced, or bred unethical. The AVMA further recom-

mends that correction of inherited defects for medical purposes should be accompanied by a procedure to make the animal incapable of reproduction.[54] Alternatively, the owner can be requested to sign a consent form for surgical repair of inherited defects that includes a statement that following the corrective surgery, the animals will not be entered or exhibited in any breed shows.[54,55]

Appendix

Dysostoses with demonstrated heritable etiology in dogs and cats.

Species	Disease	Breed	Mode of inheritance
Dog	Hemimelia	Chihuahua	Unknown
	Polydactyly, syndactyly	Australian Shepherd	X-linked lethal or sex-influenced automosal
	Polydactyly	Great Pyrenees	Autosomal dominant
	Polydactyly	Collie	Autosomal recessive
	Polydactyly	Saint Bernard	Autosomal recessive
Cat	Hemimelia	Domestic shorthair	Autosomal
	Hemimelia	Siamese	Autosomal
	Ectrodactyly	Domestic shorthair	Autosomal dominant

References

1. Breur GJ, Lust G, Todhunter RJ. Genetics of canine hip dysplasia and other orthopaedic traits. In: Ruvinsky A, Sampson J, eds. *The genetics of the dog*. Wallingford, UK: CAB International, 2001;267–298.
2. Ogden JA, Grogan P. Prenatal skeletal development and growth of the musculoskeletal system. In: Albright JA, Brandt RA, eds. *The scientific basis of orthopaedics*. Norwalk, Conn: Appleton & Lange, 1987;47–89.
3. Spranger J, Benirschke K, Hall JG, et al. Errors of morphogenesis: concepts and terms. Recommendations of an international working group. *J Pediatr* 1982;100:160–165.
4. Evans HE. Prenatal development. In: Miller ME, ed. *Miller's anatomy of the dog*. 3rd ed. Philadelphia: WB Saunders Co, 1993;32–97.
5. Ruvinsky A. Developmental genetics. In: Ruvinsky A, Sampson J, eds. *The genetics of the dog*. Wallingford, UK: CAB International, 2001;431–459.
6. Noden D, de Lahunta A. Limb development. *The embyrology of domestic animals: developmental mechanisms and malformations*. Baltimore: The Williams & Williams Co, 1985;196–210.
7. Gilbert SF. Development of the tetrapod limb. *Developmental biology*. 7th ed. Sunderland, Mass: Sinauer Associates Inc, 2003;523–546.
8. Arias AM, Stewart A. Patterns in three dimensions. *Molecular principles of animal development*. Oxford, UK: Oxford University Press, 2002;363–400.
9. Karsenty G. Genetic control of skeletal development. In: Cardew G, Goode JA, eds. *The molecular basis of skeletogenesis*. Chichester, UK: John Wiley & Sons, 2001;6–17.
10. Upholt WB. Homeobox genes and limb development. In: Buckwalter JA, Ehrich MG, Sandell LJ, et al, eds. *Skeletal growth and development: clinical issues and basic science advances*. Rosemont, Ill: American Academy of Orthopaedic Surgeons, 1998;71–85.
11. Kingsley DM. Genetic control of bone and joint formation. In: Cardew G, Goode JA, eds. *The molecular basis of skeletogenesis*. Chichester, UK: John Wiley & Sons Ltd, 2001;213–222.
12. Gilbert SF. Medical implications of developmental biology. *Developmental biology*. Sunderland, Mass: Sinauer Associates Inc, 2003;683–719.
13. Lewis RE, Van Sickle DC. Congenital hemimelia (agenesis) of the radius in a dog and cat. *J Am Vet Med Assoc* 1970;156:1892–1897.
14. Hiraga A, Abe M, Iwasa K, et al. Anatomical findings of apodia in a calf. *J Vet Med Sci* 1991;53:1125–1127.
15. Earl FL. Dogs: developmental abnormalities. In: Benirschke K, Garner F, Jones T, eds. *Pathology of laboratory animals*. New York: Springer-Verlag Inc, 1978;1874–1886.
16. O'Rahilly R. Morphological patterns in limb deficiencies and duplications. *Am J Anat* 1951;89:135–193.
17. Frantz CH, O'Rahilly R. Congenital skeletal limb deficiencies. *J Bone Joint Surg* 1961;43-A:1202–1224.
18. Schultz VA, Watson AG. Lumbosacral transitional vertebra and thoracic limb malformations in a Chihuahua puppy. *J Am Anim Hosp Assoc* 1995;31:101–106.
19. Johnson TC. What is your diagnosis? Congenital bilateral radius hemimelia in a cat. *J Am Vet Med Assoc* 1978;173:1019–1020.
20. Alonso RA, Hernandez A, Diaz P. An autosomal recessive form of hemimelia in dogs. *Vet Rec* 1982;110:128–129.
21. Pederson NC. Surgical correction of a congenital defect of the radius and ulna of a dog. *J Am Vet Med Assoc* 1968;153: 1328–1331.
22. Ahalt BA, Bilbrey SA. Radial agenesis with secondary contractual deformity of the right forelimb. *J Small Anim Pract* 1997; 38:539, 571.
23. Swalley J, Swalley M. Agenesis of the radius in a kitten. *Feline Pract* 1978;8(5):25.
24. Richardson DC. Radial agenesis. *J Vet Orthop* 1979;1:39–42.
25. Jezyk PF. Constitutional disorders of the skeleton in dogs and cats. In: Newton CD, Numamaker DM, eds. *Textbook of small animal orthopaedics*. Philadelphia: Lippincott Williams & Wilkins, 1985;637–654.
26. Hoskins JD. Congenital defects of cats. *Compend Contin Educ Pract Vet* 1995;17:385–405.
27. Chambers JN. Developmental and congenital problems of the antebrachium and adjacent joints. In: Bojrab MJ, Smeak DD, Bloomberg MS, eds. *Disease mechanisms in small animal surgery*. Philadelphia: Lea & Febiger, 1993;834–840.
28. Breur GJ. Diagnosis and treatment of dysostoses and osteochondrodysplasias. *Voorjaarsdagen* 2003;17–18.
29. Betts CW. Agenesis of the radius. In: Bojrab MJ, Wingfield WE, Olds RB, eds. *Pathophysiology in small animal surgery*. Philadelphia: Lea & Febiger, 1981;650–653.
30. Johnson AL. Growth deformities. In: Olmstead ML, ed. *Small animal orthopedics*. Columbus, Ohio: Mosby Year Book Co, 1995;293–309.
31. Carrig CB, Wortman JA, Morris EL, et al. Ectrodactyly (split-hand deformity) in the dog. *Vet Radiol* 1981;22:123–124.
32. Keller WG, Chambers JN. Antebrachial metacarpal arthrodesis for the fusion of deranged carpal joints in two dogs. *J Am Vet Med Assoc* 1989;195:1382–1384.
33. Innes JF, McKee WM, Mitchell RAS, et al. Surgical reconstruction of ectrodactyly deformity in four dogs. *Vet Comp Orthop Traumatol* 2001;14:201–209.
34. Montgomery RD, Milton JL, Mansfield PD, et al. Ectrodactyly. *J Am Vet Med Assoc* 1989;194:120–121.
35. Seto ML, Nunes ME, MacArthur CA, et al. Pathogenesis of ectrodactyly in the *Dactylaplasia* mouse: aberrant cell death of the apical ectodermal ridge. *Teratology* 1997;56:262–270.
36. Searle AG. Hereditary "split-hand" in the domestic cat. *Ann Eugen* 1953;17:279–282.
37. Frey M, Williams J. What is your diagnosis? Ectrodactyly in a dog. *J Am Vet Med Assoc* 1995;206:619–620.
38. Foley C, Lasley J, Osweiler G. Bones and joints. In: *Abnormalities of companion animals: analysis of heritability*. Ames, Iowa: Iowa State University Press, 1979;87–106.
39. Shively M. First metacarpal bone or proximal phalanx. *J Am Vet Radiol Soc* 1978;19:50–52.
40. Erickson F, Saperstein B, Leipold H, et al. Congenital defects of dogs—part 3. *Canine Pract* 1977;4(6):40–53.
41. Villagomez DF, Alonso RA. A distinct Mendelian autosomal recessive syndrome involving the association of anotia, palate agenesis, bifid tongue, and polydactyly in the dog. *Can Vet J* 1998;39: 642–643.
42. Freeman LE, Sponenberg DP, Schabdach DG. Morphologic characterization of a heritable syndrome of cleft lip/palate, polydactyly, and tibial/fibular dysgenesis in Australian Shepherd dogs. *Anat Histol Embryol* 1988;96:444–450.
43. Sponenberg DP, Bowling AT. Heritable syndrome of skeletal defects in a family of Australian Shepherd dogs. *J Hered* 1985; 76:393–394.
44. Swanson AB. A classification of congenital limb malformations. *J Hand Surg* 1976;1:8–22.

45. Richardson EF, Wey PD, Hoffman LA. Surgical management of syndactyly in a dog. *J Am Vet Med Assoc* 1994;205:1149–1151.
46. Dallman MJ, Brown RE. Syndactyly in the dog. *Canine Pract* 1980;1:21–24.
47. Patterson DF, Aguirre GA, Fyfe JC, et al. Is this a genetic disease? *J Small Anim Pract* 1989;30:127–139.
48. Thrusfield M. Is it hereditary?: 3. Identifying hereditary disease. *J Small Anim Pract* 1988;29:719–726.
49. O'Rahilly R, Muller F. The skeletal system and the limbs. *Human embryology and teratology*. New York: Wiley-Liss, 2001; 357–394.
50. Thrusfield M. Is it hereditary?: 2. Types and characteristic patterns of hereditary disease. *J Small Anim Pract* 1988;29:667–678.
51. Oberbauer AM, Sampson J. Pedigree analysis, genotype testing and genetic counseling. In: Ruvinsky A, Sampson J, eds. *The genetics of the dog*. Wallingford, UK: CAB International, 2001; 461–485.
52. Gelehrter TD, Collins FS, Ginsburg D. *Principles of medical genetics*. 2nd ed. Baltimore: The Williams & Wilkins Co, 1998; 48.
53. Rollin BE. *An introduction to veterinary medical ethics: theory and cases*. Ames, Iowa: Iowa State Press, 1999;112–114.
54. AVMA. Principles of veterinary medical ethics of the American Veterinary Medical Association (AVMA) (2003 Revision). *2004 AVMA membership directory and resource manual*. AVMA: Schaumburg, Ill: 2004;40–42.
55. Wilson JF. *Law and ethics of the veterinary profession*. Yardley, Pa: Priority Press, 1993;343–344.