Osteoporosis is a nonspecific term referring to a condition that is characterized by quantitative loss of bone, that is, atrophy of bone. The bone that is present is entirely normal, since the organic and inorganic phases diminish in equal proportion. The reduced amount of bone is manifested by thinning of the cortex or reduced number and caliber of cancerous trabeculae, or more commonly both. Thus, affected bones are thin, porous, and brittle. The volume of bone remains constant, however.

The only bone disease in humans classified as osteoporosis is that condition seen in elderly men and women in which the usual complaint is back pain of insidious or sudden onset, such as following injury, and collapse of vertebral bodies causing kyphosis. It is the most important factor in the incidence of hip disease in the aged. Aegether and Kirkpatrick state "this is the only type of reduction in bone mass that is properly called osteoporosis and the term osteoporosis properly refers to no other bone disease."(1) The cause of osteoporosis is unknown. A reduction in bone mass can be seen in primary hyperparathyroidism, nutritional hyperparathyroidism, renal secondary hyperparathyroidism, pseudohyperparathyroidism, hyperthyroidism, acromegaly, hepatic toxicity, immobilization of a limb, long-term tetraplegia, multiple myeloma, as a result of the administration of certain anticonvulsant drugs, and in hyperadrenocorticism. However, the reduction in bone mass (osteoporosis) is seen only secondarily to the primary condition, hence the term secondary osteoporosis should be used. Primary osteoporosis has not been reported in the dog or cat.

ETIOPATHOGENESIS
Osteoporosis occurs as a result of an imbalance between bone formation and bone resorption. It may occur if bone formation fails to keep pace with normal resorptive processes or if bone resorption exceeds bone production. Thus, generalized osteoporosis may be associated with diseases that affect either the organic matrix or the mineralized matrix of bone. For example, in scurvy due to ascorbic acid deficiency, the mesenchymal cells and osteoblasts are unable to form or maintain the normal amount of intracellular substance. Similarly, protein or copper deficiency, as well as hormonal imbalances involving estrogen and adrenal, thyroid, and pituitary hormones, also induce osteoporosis by a decrease in bone formation. Osteoporosis may also occur in disorders of mineral metabolism, such as fibrous osteodystrophy (hyperparathyroidism) and rickets or osteomalacia, in which the fundamental pathogenic mechanism is excessive osteoclastic resorption or failure in the mineralization of the organic matrix, respectively. However, in these diseases, the osteoporosis usually is accompanied by other microscopic features characteristic of the disease, such as proliferation of fibrous tissue in fibrous osteodystrophy and wide osteoid seams in rickets and osteomalacia. The radiographic appearance of these conditions can be remarkably similar.

Disuse osteoporosis is the term used to describe the type of osteoporosis that is caused by immobilization of the affected bone. Frequently, this is the result of plaster casts or paralysis. The osteoporosis is due to a reduction or cessation of normal muscular activity around the bone, which in turn diminishes the flow of blood through the bone(9)

Osteoporosis has been reported in dogs following gastrectomy. The bone lesion was thought to be related to altered calcium absorption and retention.(2) It has also been reported in dogs as an aging phenomenon(3) and in dogs, cats, and mice fed all-meat diets.(4,12,13,16)
Although there is no substantial evidence that insufficient calcium intake will produce osteoporosis, there is evidence that imbalances in calcium and phosphorus lead to fibrous osteodystrophy in some instances, and osteoporosis in others. However, since osteoporosis often is the earliest lesion detected in fibrous osteodystrophy, in some instances this disparity may be related to early versus late diagnosis. The differences in the lesions that are observed may also be related to the magnitude of the secondary parathyroid response and to whether there is compensation of the hypocalcemia that occurs initially. The age of the animal at the time of the imbalance appears to be a factor in the bone lesion that develops; for example, adult cats and mice fed a beef heart diet developed osteoporosis, whereas kittens fed a low-calcium or beef heart diet developed fibrous osteodystrophy in 6 to 8 weeks.

DIAGNOSIS
The diagnosis of secondary osteoporosis can be made by clinical signs, radiography, and a confirmed diagnosis or association of one of the primary disease conditions. Clinical signs are referable to fractures of the long bones and vertebrae and a reduction in bone mass of the mandible and maxilla. Laboratory findings are referable to the primary disease.

TREATMENT
Secondary osteoporosis is treated by correcting the primary problem or condition.

DISUSE OSTEOPOROSIS
Disuse osteoporosis is a bony loss in an individual bone or limb or in the entire body caused by lack of normal body stress. As seen in veterinary medicine, it usually relates to the bone beneath a rigid plate or to the bones immobilized by an external cast.

Radiographically, affected bones will be more radiolucent and may appear obviously different from other bones in the same animal. Care must be taken in such animals to prevent pathologic fractures in the osteoporotic bones.

Animals with this disease show elevated serum calcium and phosphorus levels and may be excreting abnormally large quantities of urinary calcium. The etiology and etiopathogenesis of disuse osteoporosis are known. With the lack of normal stresses, bones are remodeled by osteoclasts and new bone is not formed to replace it, thus the resulting bony loss. The process is reversible, and normal bone will be replaced when normal stress is reapplied to the affected bones.

OSTEOPETROSIS
Osteopetrosis is a rare congenital and familial developmental abnormality of skeletal growth of man and animals. The formation and production of the growth plate cartilage cells and matrix and the primary trabeculae are normal. Bone length and shape are relatively normal. There is, however, marked retardation of the remainder of the enchondral ossification cycle which includes bone maturation, resorption of immature bone, bone remodeling and cortex formation beyond the primary trabecular stage. The accumulation and persistence of cores of calcified cartilage, osteoid and primitive bone in the medullary cavities results in abnormally dense bone and has led to the radiographic diagnosis of this disease by such synonyms as osteosclerosis fragilis, marble bones and chalk bones.

HISTORY
Osteopetrosis has been reported in the dog only twice. In 1970, Riser reported the results of postmortem radiographic and histologic examination of bones obtained from three dachshund pups. These pups were the only clinically abnormal members of a litter of five and had been put to sleep at 8 weeks of age because they were unable to stand. A single case was described in 1979 by Lees and Sautter in which a one-year-old male Australian shepherd with consanguineous parents presented with a severe nonregenerative anemia associated with osteopetrosis.

ETIOPATHOGENESIS
Osteopetrosis has been described in three mutant strains of rats, four mutant strains of mice, and in rabbits, dogs, cattle, and humans. In humans, rats, mice, and rabbits, the disease is inherited as an autosomal recessive trait. Investigations in both dogs and cattle suggest a genetic basis for the condition in these species as well. The characteristic
feature of the disease is excessive accumulation of bone and mineralized cartilage throughout the skeletal system (Figs. 55-1 and 55-2). Often, the accumulation of mineralized cartilage is evident before birth. The most prominent and dense lesions occur in the metaphysis of the humerus, femur, and tibia. Although the basic lesions are similar in the various animal species, the disease varies in intensity within and among species.

The basic pathogenetic mechanism of osteopetrosis is abnormal osteoclastic function. Functional defects that have been observed in osteopetrotic animals include decreased activity of lysosomal and oxidative enzymes and partial or complete absence of ruffled borders. In many osteopetrotic animals, the number of osteoclasts is severely reduced. In addition, bone formation is abnormally excessive in all of the mouse mutants. Owing to the failure in osteoclastic remodeling, the mineralized cartilage spicules of the physis and the primary trabeculae of the metaphysis are not resorbed, causing the medullary cavity to be filled with large-caliber, cancellous trabeculae containing central cores of cartilage (Fig. 55-3). Except for occasional increase in width, the growth plate is normal. Failure of osteoclastic remodeling in the ossification groove gives the long bones a tubular shape rather than the normal funnel shape. Severe myelophthisic anemia and extramedullary hematopoiesis have been observed in humans, dogs, and some laboratory animal mutants.(8,21) Incisors and molars fail to erupt in osteopetrotic rats, mice, and rabbits because of lack of resorption in the dental crypts. Odontomata are regularly observed in long-lived mutants as a result of continued growth of the entrapped tooth germ.(21) The ia rat is the only known animal with congenital osteopetrosis that recovers spontaneously from the skeletal abnormality, with remission beginning at about 3 weeks of age.

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It has been demonstrated that resorption of bone and mineralized cartilage is restored in grey-lethal (gl) and microphthalmic (mi) mice by parabiotic union. The corrective influence of such a temporary circulation between normal and osteopetrotic litter mates is attributed to a population of competent osteoclasts derived from mononuclear cells present in the normal circulation.(17) Subsequently, infusion of normal spleen or bone marrow cells into irradiated osteopetrotic litter mates was shown to reverse the disease.(11,18,19) Further, osteopetrosis was induced in lethally irradiated, normal gl and mi strains of mice by infusion of spleen cells from osteopetrotic litter mates.(20) It was concluded, therefore, that resorption of bone matrix is controlled by migratory mononuclear cells derived from the spleen or bone marrow.

However, it has not been established whether the migratory cells provide new osteoclasts directly or cells that influence osteoclastic function indirectly.(17) The possibility that deficiencies of the immune system, such as T-cells, may secondarily affect bone is under investigation. Attention is also focused on factors that control differentiation of the osteoclast, elucidation of the homing phenomenon, and determination of the fate of the osteoclast.
HISTOLOGY
Histologic changes present in osteopetrosis have been described by Riser.(14)

Histologically, the shape of the epiphyses, growth plates, metaphyses and diaphyses were of normal proportions except for the long bones which were fractured. In the bones studied, immature trabecular bone was present the full length of the medullary cavity and it was estimated that twice as much trabecular tissue was present than is normal. The cortex was absent.

Ossification of epiphyses was occurring and the resulting epiphyseal trabeculae were more numerous and wider than normal. The cartilage of the growth plate was of the same width and had the same pattern of development as the cartilage cells of a normal Dachshund of the same age; the calcified matrix of the primary trabeculae streaked down from the cartilage plate in a normal manner. Osteoblasts osteoid, fiber and lamellar bone are all present in their normal position. Osteoblasts seem to attach to the trabeculae, depositing osteoid and bone. Osteoclasts were also present. Bone marrow cells occupied the spaces between the trabeculae. The trabeculae from the growth plates extended through the metaphyses and into the diaphyses in a conical or V-shaped arrangement. There was a distinct line of separation between the enchondral trabeculae which extended from the distal to proximal growth plate and the membranous trabeculae which were formed by the periosteal layer. Trabeculae that formed from the diaphyseal periosteum filled the spaces outside the conical arrangement formed by the endochondral trabeculae. There was not evidence of formation of a cortex nor a medullary cavity in any of the long bones.

DIAGNOSIS
Clinical diagnosis is difficult to describe when only four cases of a disease have been reported. What is known, however, is that osteopetrotic bone is brittle and may result in pathologic fracture. The obliteration of normal bone marrow spaces is likely to result in a nonregenerative anemia.

Radiography demonstrates increased radiodensity in the medullary and cancellous portions of all bones of the axial and appendicular skeletons. The trabecular pattern normally found on radiographs of cancellous portions of bones cannot be readily distinguished. Increased radiodensity in the normally radiolucent medullary portions of the long bones blends into the dense medullary portions of the bones and causes the inner margins of the cortices to become indistinct. The shape and size of bones remain normal (Figs. 55-4 and 55-5).

FIG. 55-4 Radiograph of the femur, tibia, and fibula of a dachshund with osteopetrosis. The bones are more dense than normal. What appears to be a cortex in the femur was proven histologically to be membranous bone formed by the diaphyseal periosteum. The remainder of the femur has a "watch glass" structure that presents as normal enchondral bone ossification arising from the proximal and distal growth plates. Fracture calluses are seen in the midshaft of the tibia and fibula. (Riser WH, Frankhauser R: Osteopetrosis in the dog: A report of three cases. J Am Vet Radiol Soc 11:29, 1970)

FIG. 55-5 A dorsoventral radiograph of the lumbar vertebrae from a dog with osteopetrosis. There is a conical formation of enchondral bone produced from each vertebral growth plate. The lateral cones of bone are membranous bone produced by the periosteum. This gives the vertebrae the appearance of consisting of four conical segments. (Riser WH, Frankhauser R: Osteopetrosis in the dog: A report of three cases. J Am Vet Radiol Soc 11:29, 1970)

TREATMENT
Because the etiology is unknown, treatment can be directed only at symptomatic correction of problems. Of greatest concern in the mature animal is treatment of the anemia by transfusion.
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