

**ANIMAL MODEL
OF
HUMAN DISEASE**

Osteopetrosis, Albers-Schönberg
Disease, Marble Bone Disease

Animal Model: Osteopetrosis in
Angus and Hereford Calves

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Biologic Features

Osteopetrosis in cattle is defined as a generalized congenital skeletal defect due to continuous formation of bone but lack of resorption and failure of remodeling.¹⁻⁶ It has been described as a frequently occurring congenital disease in red and black Angus calves and more recently it has been described in two Hereford calves. The condition in Angus calves was recognized grossly by small body size, brachygnathia inferior, impacted molar teeth, and dense long bones lacking bone marrow cavities. In addition, Angus calves affected with osteopetrosis were prematurely born from 253 to 272 days of gestation and were dead at birth or died shortly after birth.^{3,4}

Radiographs of longitudinal bisection of long bones, vertebra, cranium, cranial base, and other bones readily established the presence of a dense overgrowth of bone narrowing or filling of the marrow cavity and lack of differential density (Figures 1 to 3).^{3,4}

Additional gross findings were flattened and rectangular cerebrum and compressed cerebellum. Two Hereford calves affected with osteopetrosis presented similar gross features but had, in addition, extremely thickened cranial bones which revealed numerous cysts upon radiographic examination or cross longitudinal sectioning of bones (Figure 4). Furthermore, bone cysts ranging in size from a few millimeters to 0.5 cm and multiple fractures were present in long bones.⁵

Macerated bones of Angus calves were characterized by being smaller

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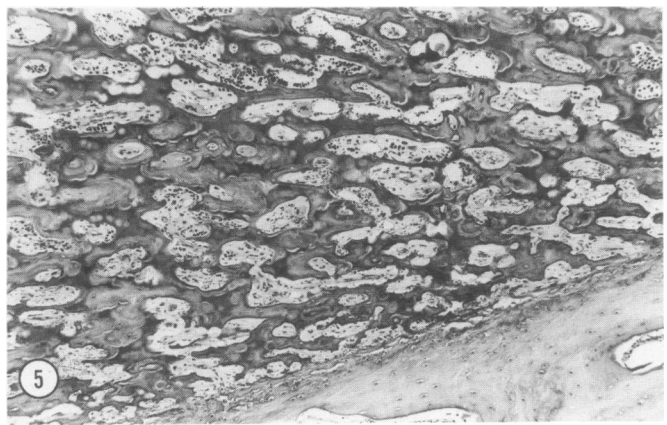
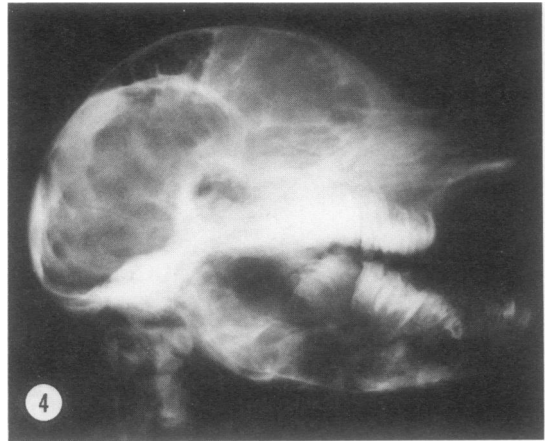
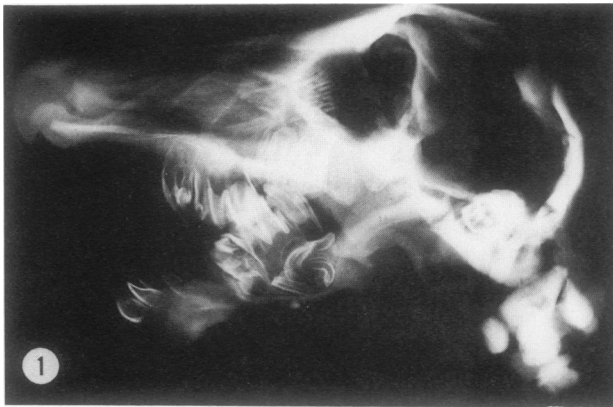


Figure 1—Radiograph of Angus calf aborted at 256 days of gestation affected with osteopetrosis. Note dense cranial base, impacted molar teeth, and brachygnathia inferior. **Figure 2**—Radiograph of long bones affected with osteopetrosis of an Angus calf aborted at 256 days of gestation. Notice lack of differential density between bone cortex and bone marrow cavities. **Figure 3**—Longitudinal bisection of a humerus from an Angus calf aborted at 262 days of gestation showing dense endochondral bone cones filling and the bone marrow cavity. **Figure 4**—Osteopetrosis in a neonatal Hereford calf. Notice the extremely thickened and cystic cranial bones. **Figure 5**—Photomicrographs of bone from an aborted Angus calf afflicted with osteopetrosis. Note laminar cortical bone and chondroosseous bone filling the bone marrow cavity of first phalanx. (H&E, $\times 100$)

than controls and revealing agenesis or hypoplasia of major nutrient foraminae.^{1,3}

Hereford and Angus calves afflicted with osteopetrosis have similar histologic changes in osseous tissue. The epiphyseal plates were relatively normal. Vascularity of the metaphysis was sparse.³

The endochondral bone cones were comprised of irregular, hypercalci-fied primitive woven bone interspersed with cartilage tissue and sparse lamellar bone.^{1,3}

The primitive nature of the epiphyseal trabeculae was underlined by basophilia in many areas and numerous cementing lines and a wide chondroid core (Figure 5). The Hereford calves had radiographically evident "cysts" in bones which were areas of necrosis upon histologic examination. Osteoclasts were rare but seemed normal although inactive. The remaining spaces in bone were occupied by a loose mesenchymal tissue.⁵

Vessel walls were mineralized in thalamus, meninges, choroid plexus, and cerebellum. Liver and spleen revealed extramedullary hematopoiesis. Thyroid and parathyroid and C cells appeared normal upon histologic examination.¹

Comparison With Human Disease

Osteopetrosis in Angus and Hereford calves shares many gross and microscopic features with osteopetrosis in human babies. In both man and animals this hereditary disorder in its malignant form appears to result from autosomal recessive inheritance.^{2,7} The term malignant refers to changes *in utero* and early death. The benign form in man, which has a dominant autosomal mode of transmission, has not been recognized in cattle.

Potential of This Model

Size and availability of cattle heterozygous for osteopetrosis would allow surgical, genetic, clinical, and clinicopathologic studies of comparative value.

Availability

A small herd of Angus cattle heterozygous for osteopetrosis has been assembled in the Animal Resources Facility of the College of Veterinary Medicine at Kansas State University, Manhattan, Kansas.

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