This is to certify that the

thesis entitled
Relationships of Nutrition and Management Factors to Incidence of Equine Developmental Orthopedic Disease: A Field Survey

presented by

Mary Amelia Williams

has been accepted towards fulfillment
of the requirements for

Master of Science degree in Large Animal Clinical Sciences

Howard D. Stowe

Howard D. Stowe

Major professor

Date November 10, 1989

RELATIONSHIPS OF NUTRITION AND MANAGEMENT FACTORS TO INCIDENCE OF EQUINE DEVELOPMENTAL ORTHOPEDIC DISEASE: A FIELD SURVEY

By

Mary Amelia Williams

A THESIS

Submitted to
Michigan State University
in partial fulfillment of the requirements
for the degree of

MASTER OF SCIENCE

Department of Large Animal Clinical Sciences

1989

ABSTRACT

RELATIONSHIPS OF NUTRITION AND MANAGEMENT FACTORS TO INCIDENCE OF EQUINE DEVELOPMENTAL ORTHOPEDIC DISEASE: A FIELD SURVEY

By

Mary Amelia Williams

Data were collected from two hundred Quarter Horse weanlings on sixty Michigan horse farms. The degree of developmental orthopedic disease (DOD) in each weanling was determined by visual and radiographic assessment. The sum of both assessments produced a total weanling score (TWS). Values for TWS were regressed against dietary nutrient concentrations; serum concentrations of minerals, vitamin A and vitamin E; physical characteristics; and various management factors.

The TWS tended to be associated with lower ration mineral concentrations, and were inversely related ($p < 0.05$) to dietary copper, serum vitamin E ($p < 001$), and degree of exercise ($p < 0.002$), were positively correlated with TWS.

This survey suggests that dietary copper, serum vitamin E, and exercise are associated with the incidence of DOD in weanling horses.

DEDICATION

This thesis is dedicated to the loving memory of my parents John Dalton and Thelma Conomos Williams.

ACKNOWLEDGMENTS

To my advisor, Howard D. Stowe, for his kindness and wisdom, and to my committee members Christopher M. Brown, Joseph Rook, and John Shelle for their support and encouragement.

To Russ Stickle who generously gave his time for radiographical interpretations.

To my friends Benjamin J. Darien, Nancy Goyert, Carolyn Schlick, Scott Vaughan, and James Q. Robinson, for their enthusiasm and greatly appreciated assistance.

Table of Contents

LIST OF TABLES

Table Page

LIST OF FIGURES

Figure Page

Figure Page

CHAPTER I

INTRODUCTION

Knowledge has been accumulating over the past decade about several bone diseases which commonly occur in young, healthy, rapidly growing horses. Most affected animals are large and well-built for their age. Originally referred to as metabolic bone disease, this process has now been designated as developmental orthopedic disease (DOD).[1] Because many aspects of the pathogenesis of this disease complex are similar, DOD presently includes osteochondrosis, osteochondritis dissecans, subchondral bone cyst, physitis, flexure deformities, angular limb deformities, and cervical vertebral malformation.

These bone and cartilage diseases commonly cause serious debility in young horses. Several researchers have reported an increasing incidence in DOD, both in Europe[2] and the United States,[3] and have estimated as much as a tenfold increase of this disease in the past decade. A 1985 review of 380 equine cases presented, for musculoskeletal problems, to the Large Animal Clinic of the College of Veterinary Medicine, Michigan State

University, indicated 13% (forty-nine) represented a form of DOD.

While veterinary surgeons are left with the dilemma of treatment, the matter of DOD prevention is equally important. Other investigators[3] have implicated nutritional factors in the etiology of DOD in Ohio and Kentucky, but there was virtually no organized information on feeding practices and management of weanling horses in Michigan. Therefore, a field investigation was designed to gather such information and also to assess the incidence and degree of DOD present on these farms. The objectives of this survey were to create a base of information from which to evaluate the relationships between this disease complex and such controllable factors as nutrition and management. The knowledge gained is intended to provide a basis for advising clients in the prevention of DOD.

CHAPTER II

LITERATURE REVIEW

Diseases of bone and cartilage are of primary interest to those responsible for the management and feeding of brood mares and foals.

These diseases are clinically different; however, several are considered related due to similar histopathological appearances and include:

1. Osteochondrosis
2. Subchondral bone cyst
3. Osteochondritis dissecans
4. Physitis
5. Angular limb deformity
6. Acquired flexure deformity
7. Cervical vertebral malformation

None of these conditions has a single etiology. Genetics, trauma, nutrition, growth rate, and endocrine imbalances have all been suggested as contributing factors.

Originally referred to as metabolic bone disease, these conditions have now most recently been renamed

developmental orthopedic disease (DOD).[1] Description of this disease and the proposed etiologies are discussed.

A. Developmental Orthopedic Disease (DOD)

Osteochondrosis

Limb bones develop from a cartilage model. The process of transition from cartilage to bone (endochondral ossification) begins early in fetal life (in some bones of foals as early as 90 days post-conception).[4] Osteochondrosis, by definition, is the failure of cartilage transition to bone and can occur at any point until growth ceases. Normal bone formation begins within the center of the cartilaginous model and continues toward either end. This forms the tubular shaft or diaphysis of the bone, leaving a bulbous cartilage expansion at both ends. A secondary center of ossification forms in the cartilage ends or epiphyses at a genetically determined time. The diaphysis and epiphyses remain separated from each other by a proliferative disc of cartilage (metaphyseal physis) Continued growth of the metaphyseal physis adds length to the bone as the animal matures. A similar physis (epihyseal physis) is located adjacent to the articular surface cartilage and provides for enlargement of the epiphysis[5] (Figure 1).

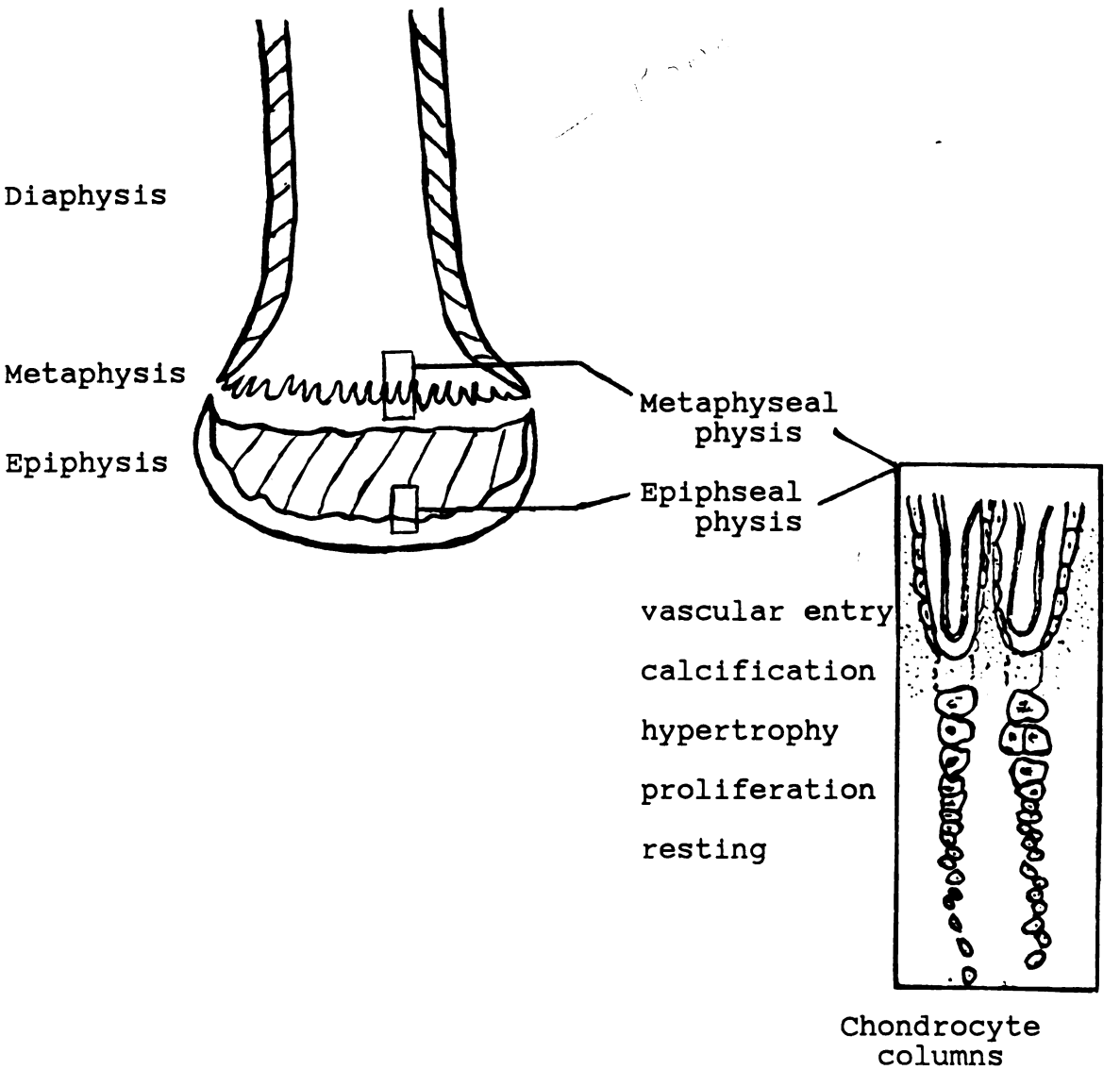


Figure 1. Diagramatic representation of the parts of a long bone and an expanded inset of the physes indicting zones of chrondrocyte maturation.

The transition of cartilage to bone is highly organized. Rapid orderly proliferation of new cartilage cells is followed by hypertrophy, calcification, invasion of blood vessels, and new bone formation. Within this region of complex events is the primary lesion of osteochondrosis.

In osteochondrosis, there is a disturbance of the normal differentiation of the cells. Both the metaphyseal physis and epiphyseal physis are affected. Abnormal cartilage differentiation means "calcification of the matrix does not take place and vessels from the bone marrow do not penetrate the cartilage."[2] Endochondral ossification ceases and often areas of cartilage are retained.[2]

Retained cartilage can occur at any site of endochondral ossification. In the horses, the site of predilection is the epiphysis of long bones and subchondral area of short bones.[4] Retention of articular cartilage may be associated with "thickening, degeneration, and subsequent cartilage flap formation."[6] Retention of articular cartilage results in the formation of structurally inferior bone. A fracture may develop in association with the abnormal bone formation. Usually this "breakdown" occurs following physical activity.[6]

Osteochondrosis, in summary, is a failure of endochondral ossification resulting in retained cartilage

and inferior bone production. Osteochondritic lesions may be small incidental findings at necropsy, or serious defects capable of producing lameness, arthritis, and/or pathological fractures.

Subchondral Cyst

Undifferentiated cartilage can persist beyond maturity of a horse and is subject to cyst formation and/or necrosis.[4] Central lesions of the articular cartilage can result from thickened and retained cartilage at a weight bearing site with infolding of the cartilage and cyst formation.[2] The medial condyle of the distal femur is the most commonly reported site.[7] Other sites include the carpus, fetlock, pastern and tibial condyles. Joint effusion and gait abnormalities are common with cystic lesions, though some are asymptomatic.

Osteochondritis Dissecans

An alternative outcome to thickened retained cartilage is osteochondritis dissecans. Cracks and fissures form in the thickened articular cartilage and eventually extend into the synovial joint.[2] Joint pressure can lead to avulsion of a cartilage flap which may or may not stay attached. If cartilage flaps or loose bodies can maintain a blood supply (usually from the periphery of the joint), ossification occurs.

The femoropatellar and tibiotarsal joints are the principal sites of osteochondritis dissecans in the horse.[7] Other sites include the scapulohumeral and humeroradial joints Fluid distention of the joint capsule is generally marked. Radiographic changes may be incidental findings without clinical signs.

Osteochondritis dissecans may also be manifested by lameness which may occur before or after training begins. Lesions are commonly found bilaterally, even when lameness is unilateral.[8]

Physitis

The physis is the area of a bone involved with growth. Histologically, it is divided into a resting zone, zone of proliferation, zone of hypertrophy, and zone of calcification. In physitis, the transition of cartilage into bone loses its orderly longitudinal process. Focal areas of thickness result in bending of the cartilage columns in the zone of proliferation and zone of hypertrophy. The addition of physical stress to distorted cartilage columns results in microfractures of new bone trabeculae and hemorrhage in the zone of calcification.[9] This disturbance in growth results in bone being laid down transversely. Transverse trabeculation is a pathological event and indicates an "intermittent, stop-and-go activity."[4] Severe

abnormalities within the physis may lead to necrosis of the resting and/or proliferating zones, and premature physeal closure.[9]

Abnormal physeal widening can be seen radiographically in physitis. Increased density and sclerosis in the metaphysis give the growth area a flared appearance. Additional enlargement may occur from periosteal proliferation on either side of the physis. Large islands of cartilage may be retained within the metaphysis and appear as radiolucent areas.[9]

Clinically, physitis is manifested as physeal enlargement with or without lameness, and can occur during a rapid growth phase of a physis.[9] The most common sites include the distal radius, distal metacarpal and metatarsal bones, proximal first phalanx, and distal tibia. More often, the visible swelling at the physis is not associated with any lameness. Since the physis is a temporary structure and subject to bone remodeling, physeal enlargement may diminish. Based on extensive histological studies,[5] physitis should be viewed as a "warning sign" that osteochondrosis may be affecting articular sites or that secondary physeal complications (such as angular limb or flexure deformities) may ensue. However, the degree to which such histological defects are within normal morphological variation is not known. In a study of ninety clinically normal foals, thirteen

were observed to have abnormalities related to retained cartilage and trabecular discontinuity.[10] Whether or not the observed lesions were the earliest stages of clinical disease (physitis) was undetermined.

Angular Limb Deformities

Angular limb deformities can be congenital or acquired.[11,12] Congenital factors contributing to angular limb deformities include intrauterine malposition, joint laxity, and prematurity.[5,11] This review, however, will be concerned with only acquired angular limb deformities attributed to delayed endochondral ossification.

Angular limb deformities are described radiographically by metaphyseal flaring, asymmetry and "overlapping" of the epiphysis. Radiographically, the physis generally appears "blurred and indistinct" and usually irregular in width as well as wedge-shaped.[13] In the most common angular limb deformity of foals, valgus deformity of the carpus, stress across the lateral part of the growth plate, has been hypothesized as an etiological factor.[12] Lesions have been found predominantly in the lateral distal radial physis and resemble the growth plate lesions produced in compression experiments.[14]

Limb angulation in foals may be due to defects in the physeal region and generally occurs at the sites common to physitis.[10] Disturbed bone formation of the physis can be manifested as a localized lesion with retention of cartilage. Cartilage retention in the physis can result in loss of structural integrity, collapse of bone trabecula and limb angulation.[6] Uneven growth may perpetuate the angular or rotational deformities of the limb. If premature or asymetrical physeal closure occurs, the limb may be shortened and angulated.[6,9]

Horse owners often mistake angular limb deformity for rickets which has a similar gross appearance. Cartilage retention is not a feature of vitamin D deficiency rickets nor simple calcium deficiency. Histological appearance of vitamin D and calcium deficiency includes increased osteoid production and lack of bone mineralization.

Acquired Flexure Deformities

Acquired flexure deformities in foals are commonly associated with pain. Conditions such as painful physitis and osteochondrosis dissecans of the scapulohumeral and femoropatellar joints have been implicated.[15] Because of this association, flexure deformities are considered a manifestation of DOD. Pain

in the limb may reduce weight bearing and initiate reflex withdrawal. The result is flexor muscle contraction, shortened tendons, and altered joint position. Other theories suggest the flexure deformity develops due to a rapid bone growth and failure in lengthening of tendons and ligaments.[17,18] One author suggests these theories are "not entirely compatible with our knowledge of bone growth of the distal limb."[15] Limited bone growth occurs from the midcannon distally after two months of age. Most cases of flexure deformities develop following this period.[15] Experimental work suggests that adult horse tendons may be able to elongate at least 15%.[19] Such orders of elongation suggest that, even if tendons ceased growing, the growth of bone would not result in contracture.

In the theory of pain-induced contracture, as with physitis or osteochondrosis, some percentage of the body weight is shifted off the affected limbs thus decreasing the ground force.[20] Shortening of the suspensory ligament and flexor tendons occurs as ground force decreases. It is suggested that, if such a situation persists, the tendons crosslink in the shortened position.[20]

Acquired flexure deformities can be unilateral or bilateral and usually occur as flexure deformities of the metacarpophalangeal or distal interphalangeal joint.

Cervical Vertebral Malformations

Cervical vertebral malformation of horses is characterized by spinal cord compression and neurologic dysfunction.[21] Stenosis of the cervical vertebral canal is due to abnormal bone development of the vertebrae. The dorsal facets, articular processes, and often surrounding soft tissue are usually involved. Clinical symptoms in young horses appear between six months to five years of age.[22] In a recent study, cervical vertebral lesions were observed in foals as early as ninety days after birth.[23] One author suggested that the neck may represent an "exquisitely sensitive site for development of cartilage defects."[23] It is interesting to note that malformation and malarticulation may occur in some horses without neurologic signs.

Most investigators agree that osteochondrosis is an important part of the disease process of cervical vertebral malformation.[21,22,23,24] In young horses with cervical vertebral malformation, one often observes concurrent physitis of the long bones, especially the distal radius.[22,25] In a recent survey of 390 yearling Thoroughbreds and Standardbreds from twenty horse farms, physitis and joint effusion were observed in many of these individuals.[3] In addition, two yearlings showed evidence of spinal ataxia which was attributed to

cervical vertebral malformation. A report of histomorphometric studies of vertebral lesions suggested a substantial reduction in bone turnover and decreased mineralization of the bone matrix.[25] Previously reported histologic changes described osteosclerosis, osteochondrosis, or degenerative joint disease.[24]

B. Proposed Etiologies

Genetic, traumatic/exertional, endocrine and nutritional factors appear to influence the incidence of DOD. The nutritional factors implicated are: overfeeding (energy and/or protein); calcium and phosphorus imbalances; copper; zinc; and vitamin A and D.

Genetic Factors

A relationship between rapid growth and occurrence of osteochondrosis has been described and may be genetically coupled.[26,27,28,29,30] Studies in various species show significant differences in frequency of osteochondrotic lesions among certain breeds and strains. Individuals with a higher frequency of osteochondrosis e.g., Landrace and Yorkshire breeds of pigs[26] and broiler strains of poultry,[31] have a rapid growth rate and a body constitution characterized by a large muscle mass and comparatively little fat. Genetic selection has been based on production qualities of economic importance. It was shown that pigs with lower growth rates and a less

muscular body constitution do not develop osteochondrosis.[26] Such pigs were obtained by breeding commercial pigs to wild hogs. It was also shown that differences in the frequency of osteochondrosis existed between offspring of certain boars within the Landrace and Yorkshire breeds and between offspring of certain broiler strains of poultry.[31,32] In looking at these studies, however, it is difficult to separate genetics from nutrition because a capacity for large food intake is a prerequisite for rapid growth; breeds with higher incidence of osteochondrosis ate the most food and had the fastest growth rate.

The literature on osteochondrosis in man is contradictory and confusing. Opinions regarding etiology, pathogenesis, diagnosis and treatment of osteochondrosis vary. The majority of authors considered osteochondrosis in man to be primarily a lesion of subchondral bone.[33,34,35] Investigations in animals demonstrated that osteochondrosis is a cartilage disease which only secondarily affects bone.[4,26,28,29,30,31] In man, diseases with obscure etiologies such as Legg-Perthes disease, and Osgood-Schlatter's disease, are considered to be forms of osteochondrosis.[35] The lesions associated with these diseases, however, are not consistent with the term osteochondrosis as it is defined in animals. Because of conflicting terminology, genetic

associations of osteochondrosis in man are difficult to interpret. However, many familial cases of osteochondrosis in man have been reported.[36,37,38,39,40]

Heritability in horses of one clinical manifestation of osteochondrosis (cervical vertebral malformation) was addressed in three different investigations.[22,41,42] In one report of 121 cases of cervical vertebral malformation, 31% were attributed to one foundation sire.[41] This study, however, was performed prior to the availability of radiography and myelography capable of demonstrating spinal cord compression.

An investigation in Great Britain[42] ruled out autosomal dominant and sex-linked recessive inheritance, but could not rule out autosomal recessive inheritance pattern in cervical vertebral malformations. The lack of increased numbers of "wobblers" produced in closely bred populations, however, suggested an autosomal recessive mode of inheritance was highly unlikely.

Investigators at Washington State University[22] reported on their prospective breeding program to produce foals with cervical vertebral malformations. Both mares and stallions used demonstrated compressive cord lesions at the third and fourth cervical vertebra. Of the twenty-two foals born from these matings, none developed this same lesion. Of interest, however, is the high

incidence of other clinical manifestations of osteochondrosis. The incidence of physitis was nine out of twenty-two foals (40%) and of flexure deformities was seven out of twenty-two foals (30%).

A genetic study of osteochondritis dissecans in Swedish horses reported that certain sires produced offspring with a significantly higher frequency of osteochondritis dissecans when compared with the progeny of other stallions.[43] The authors concluded that "the whole complex of osteochondritis dissecans probably has a multifactorial background, of which genetic factors constitute one part."[43] Danish studies also indicate that osteochondrosis has a strong genetic predisposition and the Danish Warmblood Registry will not allow registration of stallions with osteochondrotic lesions.

Genetic involvement could be of several modes.[44] Already suggested is the genetic predisposition caused by inherited growth rates or type of conformation.[26] The study of Danish Warmbloods suggests that genetic factors, other than those regulating size, seem to be involved. Genetics could also be involved in utilization or requirements of nutrients. Examples of genetic-nutrient interaction have been presented in the literature for requirements of copper[45,46] and Vitamin E.[47]

Trauma/Exertional Factors

Many authors suggest that trauma is a factor which influences DOD in calves,[48] horses[10,12,44,49,50,51] and man.[52] Trauma has been interpreted to include many things. Compression of the growth plate by unbalanced weight distribution (such as conformational abnormalities or unilateral lameness) is known to cause growth retardation.[10,51] The result of this compression may be an inhibition of endochondral ossification and an acceleration of fusion of the growth plate.[51]

Another interpretation suggests trauma plays a triggering role in avulsion of chondral or osteochondral fragments.[49] In an extensive study of fractures occurring in Thoroughbreds at racetracks, histopathological procedures were performed to determine whether the fractures were pathological or primarily traumatic in origin.[4] Of the fifty-three fractures examined, twenty-four were associated with histopathological lesions of osteochondrosis.

Trauma is also interpreted as excessive exercise in young horses. There are anecdotal reports of exercise-related increases in the incidence of physitis[44] and angular limb deformities.[12] Stress, such as working young horses on treadmills, might predispose to DOD.[44]

On the other hand, confinement to a box stall and lack of exercise might be contributing factors to DOD.

In an investigation with dairy calves housed in confinement from birth until five months of age, the effects of hard flooring were studied.[48] Microscopic morphological variations, consistent with osteochondrosis, were found in both groups of calves. However, the frequency and severity were greater in the group on hard flooring.

Another study observed the effects of weight overloading on the canine humeral head.[53] These dogs were prevented from bearing weight on one forelimb, therefore increasing the stress on the opposite limb, for a period of ten to eighteen weeks. No significant lesions were produced radiographically or histologically. However, the same procedure, in combination with exogenously administered growth hormone, produced pronounced changes of the articular cartilage and subchondral bone (more so than hormone treatment alone). These lesions resembled changes in the early stage of spontaneous osteochondritis dissecans. This indicated an internal factor within the tissue was necessary before an external factor, such as trauma, could influence DOD.

Several investigations in horses have evaluated the effect of exercise on bone development and growth.[54,55,56] Results of these studies using photometric density scans,[57] indicated a trend toward increased bone mineral deposition and an incrase in third

metacarpal bone circumference with exercise. No incidence of lameness or radiographic bone abnormalities was detected during these studies. Investigators concluded that exercise-training of young growing horses may result in horses with greater athletic potential and durability. However, these studies were relatively brief (approximately ninety days) and no histological examinations were performed.

Endocrine Factors

Many endocrine factors control metabolic regulation of growing cartilage.[58] Growth hormone, insulin, and insulin-like growth factor I stimulate the production of new cartilage cells.[59] A direct effect of growth hormone (from the anterior pituitary) occurs on the differentiation and replication of cells at the proliferative zone of the growth plate. An indirect effect of growth hormone on the liver stimulates secretion of insulin-like growth factor I (also called somatomedin C).[58] A local effect on proliferating cartilage cells takes place in the presence of insulin or hepatic insulin-like growth factor I, stimulating the cells themselves to secrete insulin-like growth factor.[59] Direct, indirect, and local hormone effects are important in the regulation of normal cartilage growth and

maintaining synchrony in the growth of muscle, fat, and skeletal tissue.

Maturation of cartilage appears to be dependent on the thyroid hormones.[58] Hypothyroidism produces delayed appearance of ossification centers and delayed development of bone in cartilage models. The histologic appearance of hypothyroidism includes reduction in metaphyseal capillary invasion of both growth plate and articular cartilages and failure of chondrocyte maturation.[60,61] Thyroid hormones are also required for synthesis of insulin-like growth factor I by the liver.[58]

Vitamin D facilitates the mineralization of bone and stimulates growing cartilage.[58] Vitamin D metabolites have been reported[59] to maintain growth plate architecture and stimulate matrix vesicle secretion, but more work is needed to explain fully their exact role.

A series of studies has indicated that endocrine regulation of cartilage growth is mediated by the nutrient intake of young horses.[62,63] In one study, circulating concentrations of insulin, triiodothyronine (T_3) and thyroxine (T_4) were measured in Thoroughbred weanlings following meal ingestion.[62] Concentrations of each hormone increased and the magnitude of the increase was dependent on carbohydrate content of the meal given. It was hypothesized that "carbohydrate-driven changes in T_3 and T_4 metabolism may have important consequences for

growth regulation."[62] An investigation followed where Thoroughbred weanlings were fed high and low carbohydrate diets for nine months.[63] Biochemical studies on biopsy specimens of growth-plate tissue exhibited significantly decreased collagen and proteoglycan contents and increased cellularity in the foals on high carbohydrate, compared to low carbohydrate, diets. Histological studies on biopsy specimens from growth plates showed changes consistent with retarded cartilage maturation. It was concluded that alterations in the timing of postprandial hormone secretion might desynchronize the metabolic effects on growing skeletal tissue.

The inhibitory effect of calcitonin on bone resorption is well documented, but little is known of its effect on cartilage.[58] Serum calcitonin levels are highest at birth and remain elevated during the first year of life.[64] A recent study demonstrated, both in vivo and in vitro, evidence that calcitonin promotes cartilage maturation by accelerating chondrocyte hypertrophy and matrix formation.[65] The significance of this observation is uncertain but provides an interesting basis for further studies.

There are many other hormones (e.g., glucocorticoids), growth factors (e.g., platelet-derived growth factor) and local factors (e.g., cartilage-derived factor) that may, influence cartilage growth.[58] However,

our present knowledge on the role of these endocrine factors regarding DOD is minimal.

Nutritional Factors

Nutritional factors implicated in the etiology of DOD are overfeeding (energy and/or protein), calcium and phosphorus imbalances, copper, zinc, and vitamins A and D.

Overfeeding (energy and/or protein). The question of how fast a horse should grow for maximum performance and soundness remains unresolved. The rate of growth in young horses is dependent on the level of energy and protein, as well as adequate amounts of minerals and vitamins. Daily levels of digestible energy (MCal/day) and crude protein (kg/day) recommended by the National Research Council (NRC)[66] are intended to be used as guidelines for growing horses. However, weanlings and yearlings given free access to high quality rations generally consume quantities greater than these recommendations. Such overfeeding of energy and/or protein is frequently suggested to cause skeletal disorders in young horses.

Overfeeding has been linked to osteochondrosis in dogs,[29], pigs,[27], broilers,[31] and horses.[28] Some of these authors postulated a genetic predisposition associated with rapid growth and excessively high energy

feeding.[27,28,31] Overfeeding appears to be involved in the etiology of certain types of cervical vertebral malformations.[24]

Overfeeding of balanced rations has also been associated with physitis[67] and flexure deformities.[18] One report suggested overfeeding caused above-average weight gains and, therefore, greater stress on the skeleton resulting in the onset of physitis.[68] Another study presented evidence that, underfeeding of foals, followed by a period of overfeeding resulted in a condition similar to flexure deformities.[69] Control foals on the same high energy ration, but without growth restrictions, did not develop the condition.

The clinical association of overfeeding and DOD has been made without mention of the predominant association between overfeeding and apparent normalcy.[28] Apparently normal growing horses receiving rations containing excess energy, protein, calcium and phosphorus, relative to NRC recommendations,[66] have been reported by several authors.[3,70,71] Thus, overfeeding and rapid growth alone are not sufficient causes for DOD. Whether or not they are necessary causative factors remains undetermined.

Extensive studies have been conducted on the relationship of excessive carbohydrate intake, hormone levels, and bone formation.[59] The influence of dietary

starch and sugar is mediated by insulin, insulin-like growth factor I, T_4 and T_3. The diet-induced serum concentrations of these hormones may exacerbate certain abnormalities in growing cartilage.[63]

If one assumes that an increase in skeletal growth rate causes an increase in other nutrient requirements, then overfeeding might also induce deficiencies of essential minerals.[67] It has been suggested that, as the demands of growth and performance become higher, the optimal ranges of nutrients become narrower.[72] If so, a more nourishing diet, capable of meeting the extra demand of rapid growth, should be designed.

Calcium and phosphorus imbalances. Calcium and phosphorus are essential macrominerals for proper bone growth and development in horses. As discussed previously in the endocrine section, calcium homeostasis is controlled intrinsically by parathyroid hormone, calcitonin, and vitamin D.[73] Parathyroid hormone is produced by the chief cells of the parathyroid gland, and acts to prevent hypocalcemia. Calcitonin, produced by the thyroid C cells, antagonizes the effect of parathyroid hormone on bone and accounts for the fine minute to minute regulation of serum calcium levels. Vitamin D, ingested or produced endogenously, is

converted to 25(OH) vitamin D in the liver and further hydroxylated to 1-25$(OH)_2$ vitamin D in the kidney. While vitamin D aids in intestinal calcium absorption, the equine kidney also plays a critical role in calcium homeostasis. Horses have been shown to excrete a much larger proportion of absorbed calcium in the urine than other species.[74]

The main effect of calcium deficiency is on the skeleton. In young, growing animals, a simple calcium deficiency results in rickets and in adults the disease is called osteomalacia. In each case, bones become soft and often deformed due to failure of calcification of the cartilage matrix. Vitamin D deficiency results in poor utilization of dietary calcium. Vitamin D deficiency may also produce the same abnormal bone development as simple calcium deficiency even when calcium concentration of the diet is adequate.[75] The histological picture of rickets is one of reduced calcification.

A deficiency of calcium (or even normal amounts) in the presence of excess phosphorus also causes abnormal bone, but in this instance, excess bone resorption by osteocytic osteolysis (resorption deep within bone) results in osteodystrophy fibrosa. This condition is characterized, histologically, by replacement of osseous tissue with fibrous connective tissue.[76] The parathyroid gland is hyperactive in an attempt to maintain normal

blood serum calcium. There is a generalized effect on the entire skeleton. In horses, this disease is often called "Big Head" or "Bran Disease" and results from feeding excess dietary phosphorus, especially phosphorus concentrations that are two or more times greater than dietary calcium concentrations. High phosphorus diets depress intestinal absorption of calcium in horses.[77]

In DOD, there is no absence of bone calcification, a characteristic which distinguishes it from the previously mentioned mineral imbalances. Instead, DOD is characterized by failure of epiphyseal and metaphyseal capillaries to penetrate the articular and physeal cartilages. This results in thickening of the cartilage, the appearance of abnormal subchondral bone and metaphyseal radiolucency due to cartilage retention.[2]

It has been suggested by one study that the primary metabolic disturbance of DOD is "nutritional hypercalcitoninism."[4] This theory implies that excessive dietary calcium causes hypercalcemia and hypergastrinism, both of which cause hypercalcitoninism. The targets for elevated calcitonin activity are bone (wherein retardation of bone resorption leads to osteopetrosis) and cartilage (wherein retardation of cell differentiation leads to osteochondrosis). Calcitonin activity on bone would eventually reverse the

hypercalcemia but hypergastrinism would remain due to high calcium in the diet.[4]

This theory of nutritional hypercalcitoninism is supported by another study in which Great Dane puppies were fed a ration high in energy, protein, and calcium for up to sixty weeks.[29] Hypertrophic osteodystrophy was diagnosed within two weeks and osteochondrosis, with cervical vertebral malformation, was diagnosed after twenty-four weeks. Electron microscopy showed that the thyroid cells were hyperactive in these overfed dogs. This study indicated that twice the recommended level of calcium induced hypercalcitoninism.

Hypercalcitoninism was described in young heifers[78] which were fed calcium at 70% above that recommended by NRC.[66] Enlargement of the distal metatarsus and lateral deviation of the metatarsophalangeal axis were clinical signs observed after a few months. Histologic and microradiographic analyses confirmed the presence of osteochondrosis with transverse trabeculation and also osteopetrosis. Following reversal from high to normal dietary calcium, plasma gastrin decreased significantly. Plasma calcitonin, however, underwent no significant changes.

Other investigators performed experiments to determine the role of calcitonin in the maturation of mammalian growth plate cartilage.[65] Cartilage maturation

was assessed by measurement of alkaline phosphatase activity (a biochemical marker of hypertrophied chondrocytes) and by histological examination. Subcutaneous administration of calcitonin in normal rats caused widening of the physeal plates due to an increased area of the zone of maturation. Alkaline phosphatase activity increased as well. In vitro, incubated growth plate cartilage responded to increased calcitonin again by enlargement of the zone of hypertrophied chondrocytes and increased alkaline phosphatase activity.

DOD may also be related to excess calcium in the diet through reduced absorption and utilization of other minerals. The classic example of a nutritional disease precipitated by high dietary calcium is the zinc deficiency, parakeratosis, in pigs.[79] This disease may not appear in animals fed a normal level of calcium, but can become a serious problem when dietary calcium is increased without changing the zinc intake. Similar, but less dramatic, reductions in mineral utilization induced by excess calcium have been reported for magnesium, iron, iodine, manganese, and copper.[79]

There are at least two published reports of field surveys regarding feeding practices of growing horses. Data from the University of Pennsylvania were based on nutritional consultations involving twelve horse farms.[70] Results indicated concentrates were improperly formulated

with calcium and phosphorus for the type of forage being fed. The outcome was either excess protein and calcium, or not enough phosphorus in the ration. These imbalances, however, were not associated with concurrent bone problems.

A second survey by workers at The Ohio State University involved 384 yearlings on nineteen horse breeding farms in Ohio and Kentucky.[3] Scores were derived for each farm based on clinical manifestation of DOD. These scores were correlated with various nutrient concentrations in the farm rations. Only two of the nineteen farm rations were below NRC recommendation[66] for percent calcium (.55%), and only one farm ration was slightly under NRC recommendation[66] for percent phosphorus (.40%) in the ration. However, when farm scores were regressed on calcium and phosphorus concentration, a significant relationship was observed between farms with more skeletal problems and rations lower in calcium and phosphorus.

Copper. The most commonly reported trace mineral deficiency to cause naturally occurring skeletal disease in young horses is copper.[3,80,81,82,83,84,85,86,87] Since copper was recognized as an essential trace element for the higher animal species,[88] its role in ruminant nutrition and physiology has been extensively studied and

described.[89] In contrast, the role of copper in equine nutrition and physiology for years received little attention.

Copper is an essential cofactor in the enzyme lysyl oxidase (a diamine oxidase). Lysyl oxidase is required for the proper maturation of connective tissue, including elastic tissue and bone.[90] The prominent clinical signs of lysyl oxidase deficiency differ among animal species. Young dogs, which were made severely deficient in copper, developed a bone disorder characterized by abnormally thin cortices, deficient trabeculae and wide epiphyses.[91] Fractures and deformities of the bones occurred in many of the animals of this study. Histologically the disorder consisted of a diffuse osteoporosis with no primary disturbance in the calcification mechanism.

Skeletal changes associated with copper deficiency have also been reported in swine.[92] Microscopic examination of this disorder indicated a marked reduction in osteoblastic activity as evidenced by a failure of bone to be deposited on the calcified cartilage matrix plus failure in removal of the matrix. In contrast, the growth of cartilage did not appear to be affected. Several other species are reported to exhibit deformities of the skeleton and joints due to copper deficiency.[93,94,95]

In the 1940's, eroded lesions were observed involving the articular cartilage in the joints of calves[96] and foals,[97] and were prevented by feeding supplemental copper in the ration.[80] Prior to these early reports, a bone disorder was described in foals grazing pastures near a zinc smelter.[98] Similar erosions of the articular cartilage were noted in these foals and abnormally high concentrations of zinc were found in the bones, liver, and urine as well as in the dams' milk.

Some thirty years later, a case report of a Thoroughbred yearling described exostosis involving all four lower limbs plus lameness with reluctance to move.[81] Although copper concentrations in the ration were found to be adequate (15.5 ppm), high dietary levels of molybdenum were blamed for inducing a copper deficiency. Clinical improvements resulted following copper supplementation. A similar case of osteodysgenesis in a foal associated with copper deficiency was reported from New Zealand.[82]

The paucity of information concerning dietary copper in horses prompted an investigation by researchers at The Ohio State University to study correlations of dietary minerals with the severity and incidence of DOD.[3] The results of this correlational study indicated a strong inverse relationship between dietary levels of calcium, phosphorus, zinc, and copper and the development

of physitis, contracted tendons and osteochondritis dissecans lesions in yearlings. Following this survey, a trial was conducted to study the effects of supplemental copper on the incidence of cartilage lesions in foals at 90 and 180 days of age.[22] Either a copper-supplemented ration (copper levels more than three times higher than NRC recommends[66]) or a control ration (adequate in copper) was fed to mares in their last trimester of pregnancy, throughout lactation, and to their foals as well. Overall there were greater than three times the number of cartilage lesions in foals on the control diet compared to foals on the copper-supplemented diet. The presence of articular lesions at 90 days of age implied that the development of the cartilage defects began prior to weaning.

Zinc. Several suspect cases of chronic zinc and cadmium toxicosis in horses near a zinc smelter were investigated following observations of lameness, swollen joints, and unthriftiness, particularly in foals.[83] Clinical symptoms in these foals were attributable to severe generalized osteochondrosis. Zinc and cadmium concentrations were markedly increased in the pancreas, liver, and kidney. The joint cartilage lesions were similar to those induced experimentally in animals fed high zinc diets and may have been the result of a zinc-

induced abnormality of copper metabolism. A similar case of zinc toxicosis and induced copper deficiency was reported by workers in Australia.[85] They found lesions consistent with generalized osteochondrosis in eight Thoroughbred foals from two horse farms. All foals studied had low serum copper concentrations, and elevated or high-normal serum zinc concentrations. No evidence of environmental contamination was found to explain the data in this study.

Vitamin A and D. Bone development in growing animals is modulated by both vitamin A and D. The vitamin most likely found inadequate in horse rations is vitamin A. Green forages contain ample concentrations of vitamin A precursors, however, this concentration decreases with maturity and storage.[79] Naturally occurring cases of vitamin D deficiency in horses are rare.[66] Adequate amounts of vitamin D are generally acquired through ultraviolet light conversion of 7-dehydrocholesterol in the skin as well as from diets containing sun-cured feeds in which the ergosterol has been converted to vitamin D_2 (ergocalciferol).

Bone changes occurring in vitamin A deficiency are associated with remodeling and increased osteoblastic activity.[79] Constriction of the spinal column and optic

foramen, due to abnormal bone development, can result in nervous disorders and blindness.

The general function of vitamin D is to maintain normal calcium and phosphorus plasma concentrations necessary for bone mineralization. As mentioned previously, vitamin D promotes intestinal calcium and phosphorus absorption and works in conjunction with parathyroid hormone to mobilize calcium for the bone.[79] Deficiency of vitamin D results in lack of bone mineralization.

Excess intake of vitamin D is characterized by soft tissue calcification and bone abnormalities.[66] Extremely high doses of vitamin D are lethal. Clinical symptoms include limb stiffness, reluctance to move and recumbency. Toxic levels of vitamin D can occur from excessive supplementation of diets or ingestion of certain plants.

Potential danger from inappropriate use of vitamin A and D supplements has been suggested.[67] One group of investigators conducted a feeding trial to observe the response of growing fillies to four levels of vitamin A.[71,99] Enlargement of "knees" and "hocks," and microscopic lesions of physitis developed in two of three fillies fed diets containing 100 times and 1000 times the NRC-recommended level of vitamin A.[71] One filly at the higher dose (1000 times recommended level) developed

"contracted flexor tendons."[72] Periosteal lysis was found on one metatarsus and on cranial bones of all fillies given high doses. Microscopic bone lesions were also found in fillies fed low vitamin A diets. Thus, skeletal abnormalities developed in fillies fed too little or too much vitamin A. In the same survey that correlated dietary minerals to incidence of DOD,[3] high dietary concentrations of supplemental vitamin A and D (estimated from feed labels) demonstrated a positive relationship to DOD.

To extend the current knowledge regarding DOD in horses, a field investigation was designed. The objective of this survey was to create a base of information from which to evaluate relationships between this disease and the environmental factors, nutrition, and management.

CHAPTER III

MATERIALS AND METHODS

A. Experimental Subjects

The project was designed to utilize weanlings of one breed in order to limit genetic variability. The American Quarter Horse is used for many types of work (pleasure, halter, racing, and stockwork). Therefore, this versatile breed offered an opportunity to compare various management practices within the same genetic pool.

The American Quarter Horse Association had registered approximately 1,500 Michigan-bred foals per year in 1983 and 1984. Owners of these foals are typically members of the Michigan Quarter Horse Association (MQHA). A MQHA membership list was obtained, and a letter and questionnaire (see the Appendix) were sent to all members (more than 1,100) to solicit participation in the project. The letter provided information on the intent of the project and significance and clinical manifestations of DOD. The questionnaire material sought information from the Quarter Horse owners about their years of experience in raising foals, about

the number of foals expected per farm in 1986, and whether or not the owners had perceived problems with DOD in their foals in past years.

More than 100 MQHA members responded. Of these respondents, those raising only one foal that year were eliminated. On the basis of the questionnaire, farms of sixty members were accepted as participant farms. The farm owners averaged twelve years of experience (range 2 to 30) in raising foals. An average of three foals per farm (range 2 to 17) were anticipated to be born in 1986.

Twenty-four (40%) of the selected farms reported previous problems with DOD (Table 1). Frequent manifestations of DOD reported were flexure deformities and epiphysitis (physitis), followed by angular limb deformities, joint fluid distention, and osteochondrosis. Only one farm reported a previous problem with cervical vertebral malformation. The problems reported by owners were based on their own formulated perceptions.

B. Farm Visitation

Arrangements were made to visit the selected farms for data collection when the average weanling age was approximately eight months. Farm visitations were made by the author and two assistants over a four-month period commencing in November, 1986. Data on the following variables were obtained from each weanling:

Table 1. Questionnaire results for frequency distribution of clinical manifestations of DOD perceived to be encountered by sixty Michigan Quarter Horse owners prior to survey

	Number	Percentage
Total Farms	60	100
With DOD History	24	40
Without DOD History	36	60
Manifestations		
Epiphysitis (physitis)	20	33.3
Flexure deformity	24	40.0
Angular limb deformity	14	23.3
Joint fluid distention	9	15.0
Osteochondrosis	3	5.0
Cervical vertebral malformation	1	1.6

1. Age (months);

2. Sex;

3. Weight (kg), estimated using a tape;

4. Height (cm), measured with a sliding stick scale from the ground to the highest point of the withers;

5. Body condition, using a score system (Table 2) based on a system previously reported;[100]

6. Radiographic scores, ranging from 0 to 5, derived from a radiograhic score point system (Table 3). Radiographs were taken of the left distal radius (cranial to caudal view) and of other sites if clinical abnormalities were observed (Figures 2-5). All radiographs were viewed and interpreted by a board-certified radiologist** who had no prior knowledge of the farms or rations being fed, but knew only the weanlings' ages;

7. Physical score, ranging from 0 to 5 derived from a physical score point system (Table 4). Physical score was based on close observation, palpation of all

---

*Portable Bowie unit, 20 mA, 80 kVp, 0.1 second, with cronex 4L film, using Dupont cassettes and Quanta III rare earth screen, Kodac automatic developer, 90 second processor (M6A-N)

**Dr. R. L. Stickle, Department of Large Animal Clinical Sciences, Veterinary Clinical Center, College of Veterinary Medicine, Michigan State University, East Lansing, Michigan.

Table 2. Body Condition Scoring System*

Grade	Description
1	Emaciated: Ribs easily visible; spinous processes sharp; skin sunken either side of backbone; rump sunken; pelvis and croup well defined; deep depression under tail.
2	Below Average: Ribs slightly visible; slight peak to backbone; croup well defined; slight cavity under tail.
3	Average: Ribs barely visible but readily palpated; backbone moderately covered and back flat but spinous processes palpable; pelvis covered by slight layer of fat; pelvis easily felt, no crease along top of pelvis.
4	Above Average: Ribs well covered; not visible but easily palpated; slight crease along backbone; pelvis covered by fat and rounded; slight crease along pelvis to root of tail; pelvis palpable with moderate pressure.
5	Obese: Ribs buried; difficult to feel; deep crease down spine; back broad; pelvis buried; difficult to feel.

*Adapted form Leighton-Hardman.[100]

Table 3. Radiographic Score Point System*

Points	Description
0	Normal.
1	Slight abnormalities, widening of the epiphysis/metaphysis with abnormal lucency.
2	Mild abnormalities, same as in grade 1, but to a greater degree as well as periosteal spur production.
3	Moderate abnormalities, same as in grade 2, but more advanced, and including irregular sclerotic physeal margin, soft tissue thickening, and joint distention.
4	Severe abnormalities, same as in grade 3 in addition to either abnormal physeal closure or angular limb deformity with misshapen epiphysis or collapsed cuboidal bones.
5	Articular abnormalities consistent with osteochondrosis in addition to physeal abnormalities associated with grade 3 or 4.

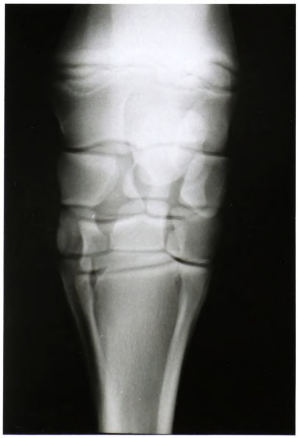


Figure 2. Example radiograph, cranial to caudal view, of distal radius, interpreted as normal (0 points).

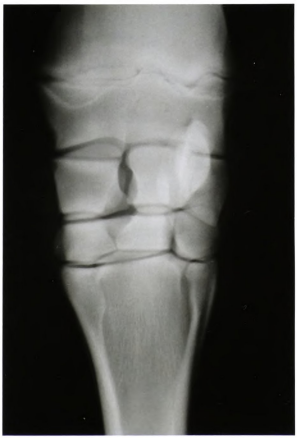


Figure 3. Example radiograph, cranial to caudal view, of distal radius, interpreted as slightly abnormal (1 point)

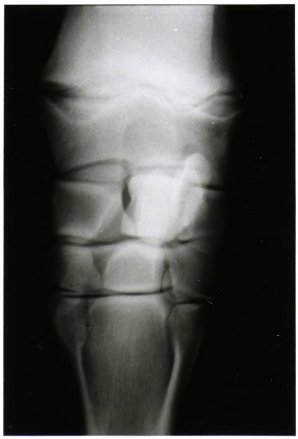


Figure 4. Example radiograph, cranial to caudal view, of distal radius, interpreted as mildly abnormal (2 points)

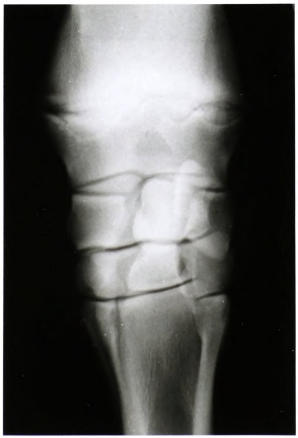


Figure 5. Example radiograph, cranial to caudal view, of distal radius, interpreted as moderately abnormal (3 points)

Table 4. Physical score point system[a]

Farm I.D. _____

Individual I.D. _____

Sex _____ Weight _____ Height _____

Condition: Obese(5) Above Avg(4) Average(3) Below Avg(2) Emaciated(1)

I. Visual Observation[b]	None (o pt)	Slight (½ pt)	Mild (1 pt)	Moderate (2 pt)	Severe (3 pt)
Epiphysitis					
Distal Radius	____	_____	____	_____	____
Distal Cannon	____	_____	____	_____	____
Distal Tibia	____	_____	____	_____	____
Joint Distension					
Stifle	____	_____	____	_____	____
Hock	____	_____	_____	_____	____
Feltlock	____	_____	_____	_____	____
Flexure deformities	____	_____	_____	_____	____
Angular Limb Deformities	____	_____	_____	_____	____
Ataxia or Paresis	____	_____	_____	_____	____

II. Concurrent Lameness (grade II or worse)#	Not Present (0 pt)	Present (5 pt)
Right Fore	_____	_____
Left Fore	_____	_____
Right Hind	_____	_____
Left HInd	_____	_____

[a]Source: Adopted from Knight et al.[3]

[b]Points were combined to give a single physical score. Sums were rounded off to the lower whole number and were not allowed to exceed a total of 5 points per weanling.

[c]The pressence of a concurrent lameness due to DOD was regarded as an automatic 5 point score.

four limbs, and gait analysis (jogging, backing, and circling) conducted by the author (Figures 6-9).

8. Total Weanling Score (TWS), calculated for each weanling by combining the physical score and the radiographic score. This score (range from 0 to 10) represented the degree of DOD clinically manifested in each weanling;

9. Blood serum analyses:

   a. Multi-element analysis (Ca, P, Mg, Fe, Zn, Cu, Mn) by inductively coupled argon plasma emission spectroscopy (ICP);[101]

   b. Selenium analyses by the fluorometric method of Whetter and Ullrey (1978);[102]

   c. Vitamin A (retinol, retinyl palmitate, retinyl acetate) by high performance liquid chromatography (HPLC) with a microporosil column and 60:40 hexane to chloroform solvent mixture in an isocratic system and using fluorometric detection at 330 and 470 nm for the excitation and emission wavelengths, respectively;[103]

   d. Vitamin E (αtocopheryl acetate and αtocopherol) by HPLC using a microporosil column and 85:15 hexane to chloroform solvent mixture in an isocratic system

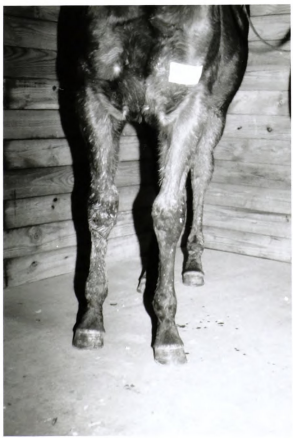


Figure 6. Photographic example, anterior view, of a weanling receiving a physical score of 1 based on visual evidence of slight physitis of distal radius (1/2 point) and slight angular limb deformity (1/2 point)

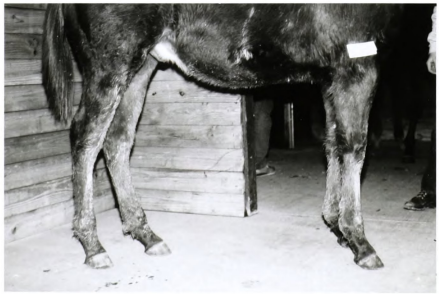


Figure 7. Photographic example, lateral view, of a weanling receiving a physical score of 1 based on visual evidence of slight physitis of distal radius (1/2 point) and slight angular limb deformity (1/2 point)

Figure 8. Photographic example, anterior view, of a weanling receiving a physical score of 5 based on moderate physitis of distal radius (2 points), slight physitis of distal metatarsal (1/2 point) moderate flexure deformity (2 points) and slight angular limb deformity (1/2 point)

Figure 9. Photographic example, lateral view, of a weanling receiving a physical score of 5 based on moderate physitis of distal radius (2 points), slight physitis of distal metatarsal (1/2 point) moderate flexure deformity (2 points) and slight angular limb deformity (1/2 point)

with detection by ultra-violet spectroscopy at 280 nm;[104]

10. Management information, recorded on a farm ration sheet (Table 5)
    a. Scale-weighed amounts of all feed stuffs fed each weanling daily
    b. Availability of pasture
    c. Age at weaning
    d. Access to creep feed
    e. Use and type of forced exercise
    f. Previous conditions that may have affected growth (illness, injuries, etc.); and
    g. Daily rate of gain was determined for each weanling, based on age, weight, and expected mature weight as compared to growth standards for the American Quarter Horse[105] (Table 7).

11. Nutrient density of feed stuffs. Samples of forage (core-drilled from six randomly selected bales), grain and supplements were submitted for laboratory analysis* of nutrient concentrations (Table 6). Calculated estimates of vitamins A, D, and E in the ration

---

*Holmes Laboratory, Inc., Millersburg, OH 44654.

Table 5. Farm Ration Sheet

Farm ration ID _____

Type of forage _____

Type of concentrate _____

Type of supplement _____

Amount fed daily:

forage _____

concentrate _____

supplement _____

Number of weanlings at present _____

Approximate age at weaning _____

At what age was grain started? _____

Were weanlings creep fed? _____

If yes, with what? _____

Have weanlings been on pasture? _____

If yes, for what period of time? _____

Have weanlings received any forced exercise? _____

If yes, what type? _____

Has present grain ration changed since the time of weaning? _____

If yes, how? _____

Additional comments:

_____

Table 6. Diet Analyses

Moisture %
Dry matter %
Crude protein %
Digestible protein %
Acid detergent fiber %
Crude fiber %
T.D.N. %
Estimated net energy MCal/Kg
Net energy lactation MCal/Kg
Net energy maintenance MCal/Kg
Net energy gain MCal/Kg
Calcium %
Phosphorus %
Magnesium %
Potassium %
Sulfur %
Sodium %
Molybdenum ppm
Iron ppm
Zinc ppm
Copper ppm
Manganese ppm

Table 7. Daily Rate of Gain Chart for weanling

Age	Growth Rate (kg/day)[a]				
	.45	.50	.55	.61	.67
	Body Weight (kg)				
6 months	<164	165-186	187-208	208-229	230-253
7 months	<186	1870212	213-237	238-262	263-287
8 months	<201	202-229	230-256	257-283	284-310
9 months	<220	221-250	251-280	281-309	310-339
10 months	<231	232-263	264-294	295-325	326-356
11 months	<243	244-275	276-308	309-340	341-373
12 months	<246	247-280	281-313	314-346	347-379

*Weanling age and measured body weight (kilograms) were used to determine the average daily rate of gain (kilogram) expected for the time interval of 6 months to 12 months of age.

were obtained by using information from feed and supplement labels;

12. Ration evaluation, using the Spartan Equine Ration Evaluation Program,[106] and based on individual data of age, weight, and rate of gain, and performed for each weanling. Nutrient concentrations of the ration were calculated on a dry matter basis. Amounts of nutrients being fed were expressed by the ration evaluation program as total daily weights (kilograms, grams, milligrams). These weights were converted to percentage either above or below the current 1978 recommendations by the National Research Council (NRC).[66]

13. Photographic documentation. Still photographs of each foal were taken, from anterior and lateral views, to document conformation and disease.

C. Analysis of Data

Data were analyzed using a general linear model (Statistical Analysis Systems)[107]. The level of confidence was set at $p < 0.05$. Total weanling scores (TWS) were regressed on sex, age, height, weight, body condition; ration concentrations of crude protein, digestible energy, calcium, phosphorus, magnesium, iron, zinc, copper, and manganese; serum concentrations of vitamin A, vitamin E, selenium, sodium, calcium, phosphorus, magnesium, iron, zinc, and copper; rate of

gain; daily weights of grain and forage consumed; age weaned; and management factors, such as pasture availability, creep feeding, and forced exercise. Correlation coefficients were determined for age and height, age and weight, and height and weight.

Data on individual weanlings were combined for each farm to produce farm mean TWS, farm dietary mineral means (calcium, phosphorus, magnesium, iron, zinc, copper, and manganese), farm dietary vitamin means (vitamin A, D, and E), and farm means for weanling serum vitamin and mineral concentrations (vitamin A, vitamin E, selenium, sodium, calcium, phosphorus, magnesium, iron, zinc, and copper). Values for farm mean TWS were regressed on farm dietary mineral means, farm dietary vitamin means, and farm mean weanling serum vitamin and mineral concentrations. Values for farm dietary mineral mean and farm dietary vitamin mean were regressed on farm mean weanling serum vitamin and mineral concentration.

CHAPTER IV

RESULTS

A. Physical Characteristics, Physical Score, Radiographic Score and Total Weanling Score

Calculated mean values for physical characteristics, physical scores, radiographic scores, and total weanling scores (TWS) are summarized in Table 8. Due to missing values on eleven foals, calculations were made on 189 weanlings.

The weanlings surveyed included 89 females (47%) and 100 males (53%). The mean weanling age was 8.4 months. Though the range of age was three to twelve months, 87% of the sampled population was between seven and ten months of age. Mean weanling height and weight were 132.2 cm and 261.7 kg, respectively. Given the mean age of 8.4 months, the values for height and weight agree with the projected growth rate expected for a foal obtaining a mature weight of 500 kg,[66] and also agree with height and weight values for the Quarter Horse Breed.[105] Using Pearson correlation coefficients, strong

Table 8. Summary of physical characteristics, (sex, age, weight, height, body condition, rate of gain), physical score, radiographic score, and TWS, for 189 Quarter Horse weanlings examined for evidence of DOD.

Variable	Mean	Minimum	Maximum	Std. Dev.
Sex				
Female 89				
Male 100				
Weanling age (Months)	8.4	3.0	12.0	1.3
Weanling height at withers (cm)	132.3	114.3	147.3	5.6
Weanling weight (kg)	261.7	151.4	349.5	37.2
Body condition score (1 to 5)	3.75	2.00	5	0.50
Rate of gain (kg/day)	0.56	0.45	0.67	0.05
Physical score (0 to 5)	1.4	0	5	1.2
Radiographic score (0 to 5)	1.3	0	5	.7
TWS (0 to 10)	2.7	0	10	1.5

relationships were observed between age and height (r=.62), age and weight (r=.67), and weight and height (r=.80).

Overall, body condition was found to be above average with a mean weanling body condition score of 3.75. No foal received the lowest score of 1 (emaciated) and only two foals received the highest score of 5 (obese).

The mean value for weanling rate of gain was 0.56 kg per day estimated for the growth period between six and twelve months. This value compares similarly to the projected rate of gain of 0.53 kg per day for weanlings with expected mature weight of 500 kg.[66] Using the NRC weight values for such a weanling, the following is an example of the calculations used:

6 month old weanling estimated weight	230 kg
12 month old yearling estimated weight	325 kg
Weight gain over 180 days	+95 kg

Rate of daily gain 95kg/180 days = 0.53 kg/day

Frequency distribution of daily rate of gain for weanlings sampled (Table 9) appears to be normally distributed.

The mean weanling value for physical score (1.4) based on subjective visual assessment, was remarkably close to the mean radiographic score (1.3). A physical score of 2 or greater was observed in 42.3% of weanlings.

Table 9. Frequency distribution of rate of gain (kg/day) for 189 Quarter Horse weanlings examined for evidence of DOD.

Rate of gain (kg/d)	No. of Weanlings	Percent
.45	12	6.3
.50	28	14.8
.55	68	36.0
.61	56	29.6
.67	25	13.2

Table 10. Frequency distribution of TWS (sum of physical score and radiographic score) for 189 Quarter Horse weanlings examined for evidence of DOD

TWS (0-10)	No. of Weanlings	Percent
0	2	1.1
1	32	16.9
2	65	34.4
3	42	22.2
4	27	14.3
5	10	5.3
6	5	2.6
7	3	1.6
8	1	0.5
9	0	0
10	2	1.1

Similarly, a radiographic score of 2 or greater was given to 35.5% of the weanlings.

The mean value of TWS was 2.7 reflecting the fact that most weanlings were observed to have some evidence of DOD. The frequency distribution of TWS is summarized in Table 10. A TWS of 5 or greater was observed in twenty-one weanlings (11.1%). No significant relationships were observed between TWS and any of the variables for physical characteristics.

The frequency distribution of clinical manifestations observed is summarized in Table 11. Physitis was the most prevalent condition observed (74.6%), however, in most foals the degree of physitis was considered slight.

B. Management Factors

Data regarding management factors are summarized in Table 12. Mean age at weaning time for the sample population was 4.25 months. With a mean weanling age of 8.4 months, the average individual sampled had been weaned for approximately 4.15 months when examined.

Mean values for forage intake and grain intake were 3.6 kg/day and 3.8 kg/day, respectively. These values are in agreement with current NRC recommendations[66] of a forage to grain ratio, by weight, of 1:1. Thirty-three weanlings (17.5%), however, were

Table 11. Frequency distribution of observed clinical manifestations of DOD in 189 Quarter Horse weanlings examined for evidence of DOD

Clinical Manifestation	Observations	Percent Weanling
Physitis	141	74.6
Angular limb deformity	92	48.7
Flexure deformity	50	26.5
Joint distention	39	20.6
Osteochondritis	2	1.1
Cervical vertebral malformation	0	0

Table 12. Summary of management factors (weaning age, hay type, pasture availability, access to creep feed, forage intake, grain intake, and use of forced exercise) in 189 Quarter Horse weanlings examined for DOD.

	Frequency Distribution	Percent	Mean	Minimum	Maximum	Standard Deviation
Age at weaning (mo.)			4.25	2	6	1.0
Hay type-Ratio Alfalfa: Grass						
4:0	97	51.3				
3:1	68	35.9				
1:3	13	6.9				
0:4	11	5.9				
Access to unlimited pasture						
Yes	98	51.9				
No	91	48.1				
Access to unlimited creep feed						
Yes	78	41.3				
No	111	58.7				
Use of forced exercise						
Yes	54	28.6				
No	135	71.4				
Daily forage intake (kg/day)			3.6	0	7.3	1.4
Daily grain intake (kg/day)			3.8	1.4	10.0	1.5

fed rations that contained greater than 75% grain by weight.

Combining mean values for forage and grain intake, the mean total daily intake, as fed, was 7.4 kg/day. For the average weanling surveyed with a mean weight of 261.7 kg, this is approximately 2.8% of body weight. Assuming this ration was 90% dry matter, estimated daily dry matter intake was approximately 6.6 kg/day. This estimated value is nearly 1 kg/day more than the daily intake amount recommended by NRC[66] for a weanling with expected mature weight of 500 kg.

The types of forages fed were classified into four groups based on the ratio of alfalfa to grass mixture (Table 12). Forage that was primarily alfalfa (4:0) was observed in 50.3% of the weanling rations. Forage that was predominantly alfalfa, but contained some grass hay (3:1), was observed in 36.7% of the rations. Weanling rations containing primarily all grass hay (0:4) or predominantly grass hay with some alfalfa (1:3), comprised only 13% of the sampled population. Overall, the average quality of hay was good to excellent.

Approximately half (51.9%) of the weanlings surveyed received access to unlimited pasture forage during the previous growing season. Less than half (41.3%) of the weanlings were allowed access to unlimited creep fed grain prior to weaning age. Some form of

forced exercise (treadmill, lungeing, or ponying) was received by 54 weanlings (28.6%).

There was a significant ($p < 0.002$) relationship between weanlings with high TWS and forced exercise (Figure 10). During this survey, two severely lame weanlings were suspected, on the basis of gross examination, of having joint disease. Radiographic evaluation demonstrated changes consistent with osteochondritis dissecans. Although from different farms, both weanlings had received approximately 4 to 6 weeks of daily lungeing as a conditioning program for futurity shows.

Weanlings with high TWS showed near significant relationships ($p < 0.07$) to high daily grain intake (Figure 11). Weanlings with TWS of 6 or greater averaged grain intake of 4.9 kg/day (approximately 59% of ration fed).

C Ration Evaluations

Mean values for dietary nutrient concentrations are summarized in Table 13. Concentrations of nutrients fed were expressed as a percentage above (+%), below (-%), or equivalent (0%) to 1978 NRC recommendations[66] based on the age, measured weight, and estimated daily rate of gain (kg/day) for each weanling. Due to consideration of estimated rate of gain in each

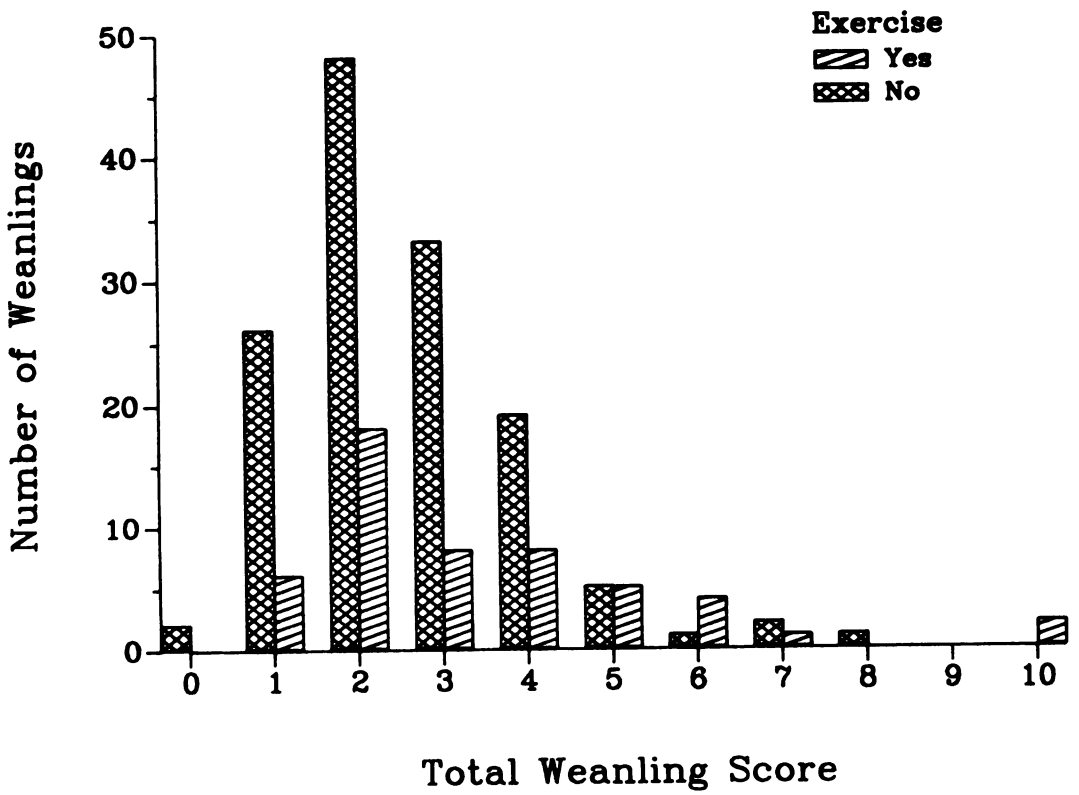


Figure 10. Relationship between total weanling score (0 to 10) and the number of weanlings undergoing forced exercise (single lined bars) and not undergoing forced exercise (cross lined bars)

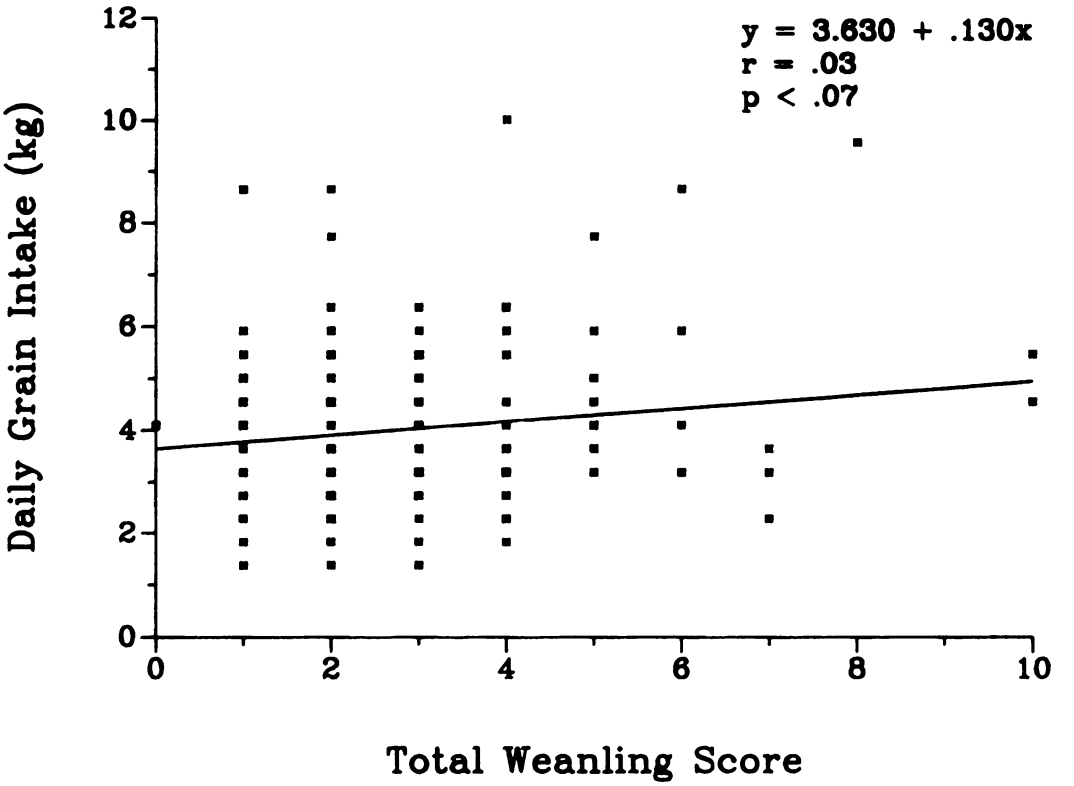


Figure 11. Scatter diagram illustrating the relationship between total weanling score (0 to 10) for 189 weanlings and daily grain intake (Kg)

Table 13. Summary of ration nutrient concentrations expressed as a percentage above (+ %) or below (- %) 1978 NRC recommended levels[66] for 189 Quarter Horse weanlings examined for DOD.

Ration Nutrient	Mean	Min	Max	SEM
Crude Protein	- 0.7	-42	- 41	12.3
Energy	+ 28.3	0	+ 65	12.8
Calcium	+ 13.5	-72	+111	39.3
Phosphorus	- 15.5	-49	+ 58	17.6
Magnesium	+120.3	+26	+241	46.8
Iron	+210.0	-42	+870	163.2
Zinc	+ 25.8	-70	+214	73.6
Copper	+101.6	-50	+650	203.9
Manganese	+ 47.5	-56	+280	66.3

individual weanling's ration evaluation, mean values for concentration of energy and protein were predictably close to NRC recommendations.[66] On the other hand, ration concentrations of macro and micro minerals were highly variable. Rations that depended on the natural mineral content of hay and grain (no supplementation) were markedly deficient in all minerals. Other rations were excessively supplemented, containing as much as six to eight times the recommended levels[66] for micro minerals.

A general trend was observed for low levels of all macro and micro minerals analyzed in relation to high TWS. Low ration concentrations of copper (Figure 12) were statistically significant ($p < 0.05$) and manganese concentrations were near significance ($p < 0.08$) (Figure 13). Of the 189 weanling rations evaluated, 29% were deficient in copper and 23.2% deficient in manganese.

D. Farm Dietary Mineral Means Determined for Sixty Farms

By averaging the ration concentrations of calcium, phosphorus, magnesium, iron, zinc, copper, and manganese for all weanlings on a farm, a farm dietary mineral mean was calculated (Table 14). Farm dietary mineral means were used to evaluate feeding practices for macro and micro minerals on the sixty farms surveyed.

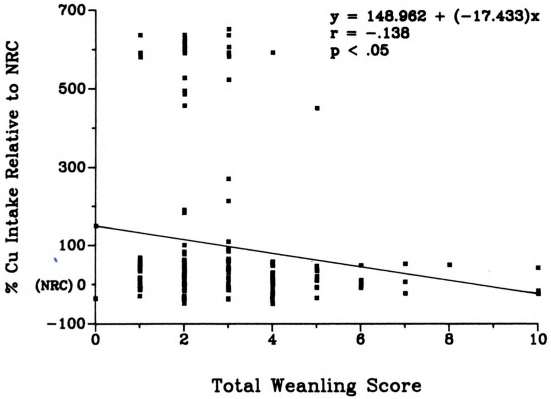


Figure 12. Scatter diagram illustrating the relationship between total weanling scores (0 to 10) for 189 weanlings and percent of dietary copper intake relative to NRC-recommended levels [66]

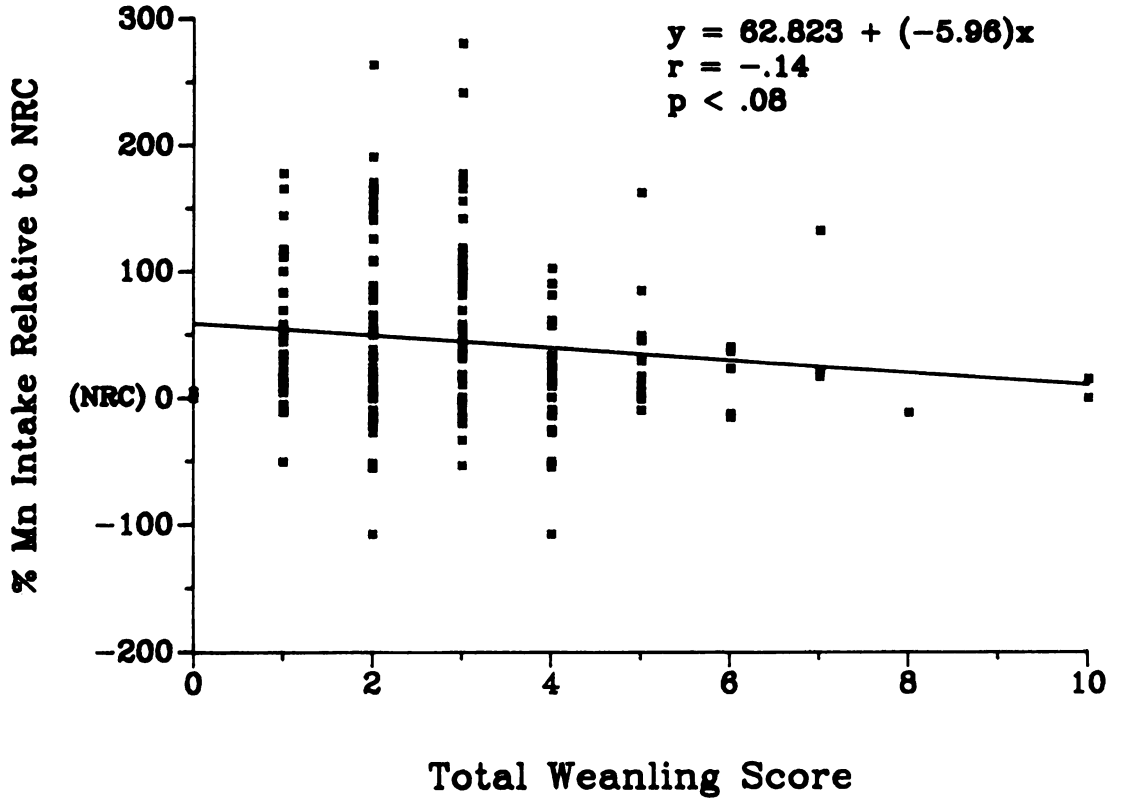


Figure 13. Scatter diagram illustrating the relationship between total weanling score (0 to 10) for 189 weanlings and percent of dietary manganese intake relative to NRC-ecommended levels[66]

Table 14. Farm dietary mineral means (expressed as percentage above or below 1978 NRC recommendations)[66] and relative mineral adequacy of rations fed weanlings on 60 Quarter Horse farms.

Nutrient	Farm Mean %	Number of Farms Deficient	% Farms Deficient
Calcium	+ 6.3	28	46.7
Phosphorus	- 19.1	50	83.3
Magnesium	+118.9	1	1.7
Iron	+196.6	1	1.7
Zinc	+ 12.1	32	53.3
Copper	+ 47.8	22	36.7
Manganese	+ 37.5	15	25.0

Many farms were feeding rations deficient in phosphorus (59/60) and calcium (20/60). Eleven of the sixty farms had a deficiency greater than 25% of the recommended levels[66] for calcium; whereas, twenty-six farms had a deficiency greater than 25% of the recommended levels of phosphorus. A calcium excess greater than 25% of recommended levels was observed on twelve farms, but a phosphorus excess at this level was found only on one farm.

Twenty-three farms (38.3%) were feeding rations with both calcium and phosphorus below recommended levels.[66] Despite these calculated deficiencies, the calcium to phosphorus ratios fell between 3:1 and 1:1 on fifty-six farms. Three farms had ratios greater than 3:1, and one farm had a ratio less than 1:1.

Of the farms surveyed, 53% were feeding weanling rations deficient in zinc, 36.7% were deficient in copper, and 25% were deficient in manganese. Trace mineral salt blocks were available to weanlings on all farms surveyed. Consumption of this supplement was not estimated in ration calculations unless directly added to the daily ration on an individual basis.

A farm mean TWS was calculated by averaging the individual TWS for all weanlings on a farm. No statistically significant correlation was observed between farm mean TWS and farm dietary mineral means.

E. Weanling Serum Analyses for Vitamin and Minerals

The mean values calculated for weanling serum vitamin A, vitamin E, and mineral (selenium, sodium, calcium, phosphorus, magnesium, iron, zinc, copper) analyses are presented in Table 15. High TWS (increased severity of DOD) was significantly ($p < .01$) correlated with high serum vitamin E concentrations (Figure 14).

F. Farm Means for Weanling Serum Vitamin and Mineral Concentrations

The farm means for weanling serum vitamin and mineral concentrations were calculated for the sixty farms surveyed are presented in Table 16. No significant ($p < 0.05$) correlations were observed between farm mean TWS and farm means for weanling serum vitamin and mineral concentrations. High farm mean TWS reflected near significant correlation to high farm mean serum concentration of vitamin E ($p < 0.07$). Farm mean serum concentration of magnesium was significantly correlated ($p < .03$) to farm mean dietary magnesium concentration and farm mean dietary serum copper concentration was significantly correlated to farm mean dietary copper concentrations ($p < 0.002$).

Table 15. Summary of serum vitamin and mineral concentrations for 189 Quarter Horse weanlings examined for DOD.

Nurtrient	Mean	Min	Max	SEM	Normal
Vitamin A (ng/ml)	243	95	706	79.4	150-300[a]
Vitamin E (ug/ml)	1.34	0.046	2.84	0.49	1.3-2.0[a]
Selenium (ng/ml)	96	16	196	32.7	90-110[b]
Sodium (ppm)	3031	2800	3900	130	3011+266[c]
Calcium (ppm)	127	100	170	13.4	116±19[c]
Phosphorus* (ppm)	133	88	196	19.0	112±31[c]
Magnesium (ppm)	18.9	13	28	2.5	18.0±3.0[c]
Iron (ppm)	2.4	0.7	8.6	0.88	3.2±2.8[c]
Zinc (ppm)	0.75	0.4	2.9	0.23	1.4±1.1[c]
Copper (ppm)	1.4	0.8	3.6	0.39	1.2±.3[c]

*Total phosphorus of which approximately 50% is inorganic phosphorus.

[a]From Stowe (1968b)[103]

[b]From Stowe (1967)[104]

[c]Mean ± SD, from Stowe et al. (1986)[106]

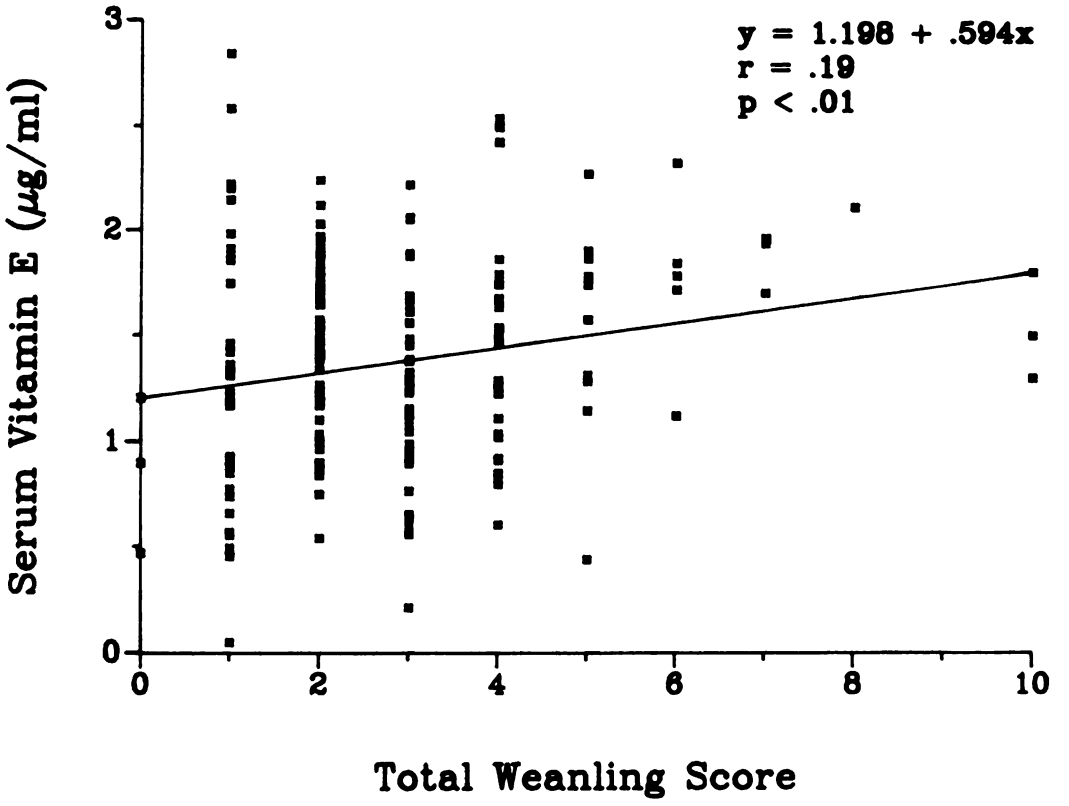


Figure 14. Scatter diagram illustrating the relationship between total weanling scores (0 to 10) for 189 weanlings and serum vitamin E concentrations (ug/ml)

Table 16. Farm means for weanling serum vitamin and mineral concentrations representing sixty Quarter Horse Farms.

Nutrient	Farm Mean	No. Farms Below Normal	% Farms Below Normal	Normal Values
Vitamin A (ng/ml)	233.7	6	10.0	150-300[a]
Vitamin E (ug/ml)	1.4	21	35.0	1.3-2.0[a]
Selenium (ng/ml)	90.9	31	51.7	90-110[b]
Sodium (ppm)	3043	0	0	3011±266[c]
Calcium (ppm)	126.5	0	0	117±19[c]
Phosphorus* (ppm)	133.1	0	0	112±31[c]
Magnesium (ppm)	19.2	0	0	18.0±3.0[c]
Iron (ppm)	2.4	0	0	3.2±2.8[c]
Zinc (ppm)	0.78	0	0	1.4±1.1[c]
Copper (ppm)	1.38	0	0	1.2±0.3[c]

*Total phosphorus of which approximately 50% is inorganic phosphorus.

[a]From Stowe (1968b).[103]

[b]From Stowe (1967).[104]

[c]Mean ± SD, from Stowe et al. (1986).[101]

G. Calculated Farm Mean Dietary Vitamin A, D, and E Concentrations

Calculated estimates of vitamins A, D, and E in the farm rations are summarized in Table 17. Laboratory analyses of the ration were not performed for these nutrients. Of the sixty farms surveyed, seventeen were feeding rations with calculated high concentrations of vitamin A (>75,000 IU/day), and fourteen farms were feeding rations with calculated high levels of vitamin D (>24,000 IU/day) (Table 17). Calculated levels of vitamin E in the ration were high (>800 IU/day) on only three farms. Although farm mean TWS tended to be higher on farms with high levels of calculated vitamins A, D, and E, these correlations were not statistically significant. In general, these excessively high vitamin levels were due to daily feeding of commercially prepared vitamin supplements in addition to concentrates fortified with vitamins. Occasionally, these commercial supplements were fed at rates four times greater than labeled recommendations.

H. Population Grouping Based on Increasing TWS

The frequency distribution of TWS closely approximated a bell shaped curve. Using these data, the sampled weanling population was separated into four groups indicating increasing TWS (groups 1-4, with group

Table 17. Distribution of calculated ranges of supplemental dietary vitamin A, D, and E concentrations (IU/day) on sixty farms.

Vitamin A		Vitamin D		Vitamin E	
1000 IU/day	# Farms	1000 IU/day	# Farms	100 IU/day	# Farms
0 - 10	2	0 - 6	2	0 - 1	2
10 - 50	24	6 - 16	24	1 - 4	47
50 - 75	17	16 - 24	18	4 - 8	8
75 - 125	9	24 - 32	7	8 - 12	1
125 - 200	5	32 - 40	4	12 - 40	2
200 - 350	1	40 - 48	1		
350 - 500	2	48 - 96	2		
		96 - 160	1		

4 having the highest scores). The frequency distribution and group divisions are displayed in Figure 15.

Group means were calculated for physical score, radiographic score, TWS, and physical characteristics (Table 18), management factors (Table 19), serum vitamin A, vitamin E, and selenium values (Table 20), and ration nutrient concentrations (Table 21). Comparison data on forced exercise, daily grain intake, dietary copper intake, dietary manganese intake, and weanling serum vitamin E are presented in (Figures 16-20).

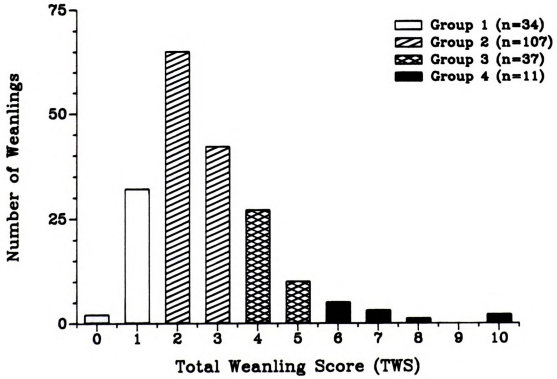


Figure 15. Frequency distribution of total weanling scores (0 to 10) from sampled weanling population separated into four groups (1 through 4) based on increasing severity of DOD.

Table 18. Group mean values for physical score, radiographic score, total weanling score, and physical characteristics for 189 weanling Quarter Horses.

Group	Physical Score (range 0-5)	Radiographic Score (range 0-5)	TWS (range 0-10)	Age (months)	Height at Withers (cm)	Estimated Weight (kg)	Sex Distribution	Estimated Rate of Gain (kg/day)
1	0	1	1	8	132.6	266	F 16 M 18	0.55
2	1	1	2	8	131.6	260	F 47 M 60	0.55
3	3	2	4	8	132.1	256	F 20 M 17	0.55
4	4	3	7	10	136.1	290	F 7 M 4	0.55

Table 19. Group frequency distribution of management factors evaluated on 189 weanling Quarter Horses

Group	Unlimited Creep Feeding		Availability of Pasture		Use of Forced Exercise		Daily Grain Intake		Daily Forage Intake	
	No.	%	No.	%	No.	%	kg/d	% of Ration	kg/day	% of Ration
1 (n=34)	12	35.3	18	53.0	6	17.6	4.0	52.6	3.6	47.4
2 (n=107)	44	41.4	56	52.3	23	21.9	3.9	50.6	3.8	49.4
3 (n-37)	17	45.9	15	40.5	13	35.1	4.1	53.9	3.5	46.1
4 (n=11)	6	54.5	5	45.5	7	63.6	4.9	59.0	3.4	41.0

Table 20. Group mean values for serum vitamin E, vitamin A, and selenium concentration for 189 weanling Quarter Horses

	Vitamin E (µg/ml)		Vitamin A (ng/ml)		Selenium (µg/ml)	
Group	Mean	Range	Mean	Range	Mean	Range
1	1.27	0.05-2.8	222	96-403	96	36-156
2	1.30	0.14-2.2	253	114-706	97	27-196
3	1.44	0.43-2.5	235	134-395	96	31.154
4	1.73	1.1-2.3	263	147-457	96	31-154
Normal Values	1.3-2.0[a]		150-300[a]		90-110[b]	

[a]From Stowe (1968b)[103]

[b]From Stowe (1967)[104]

Table 21. Group means of relative nutrient intakes (expressed as percentage above (+%), below (-%), or equivalent (0%) to 1978 NRC recommendations[66] and based on the age, weight, and estimated rate of daily gain (kg/day) for each weanling).

	Crude Protein	Digestable Energy	Calcium	Phosphorus	Magnesium	Iron	Zinc	Copper	Manganese
	% Mean (±SEM)	% Mean (±SEM)	% Mean (±SEM)	% Mean (±SEM)	% Mean (±SEM)	% Mean (±SEM)	% Mean (±SEM)	% Mean (±SEM)	% Mean (±SEM)
1	-4(2.2)	+30(2.0)	+ 8(6.0)	-17(2.8)	+127(2.8)	+183(19.5)	+27(11.3)	+112(36.5)	+52(9.8)
2	+2(10.0)	+28(1.2)	+18(3.7)	-13(1.5)	+120(1.5)	+233(16.2)	+32(7.7)	+120(21.0)	+51(7.2)
3	-3(2.4)	+27(2.0)	+13(7.6)	-17(3.9)	+115(3.9)	+192(34.8)	+ 8(9.0)	+ 43(24.0)	+21(7.2)
4	-5(3.5)	+33(5.0)	-10(8.5)	-24(3.5)	+107(3.5)	+133(60.7)	+13(21.0)	+ 24(11.3)	+22(13.0)

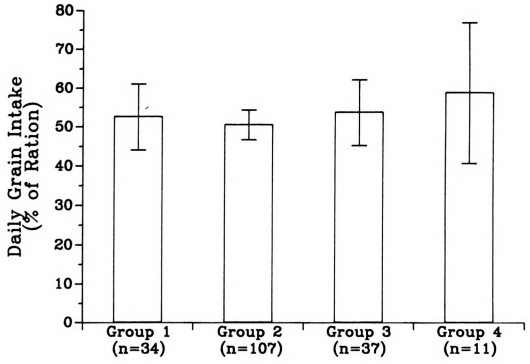


Figure 16. Bar graph comparing mean values of daily grain intake (percent of ration) for groups 1 through 4 described in Figure 15.

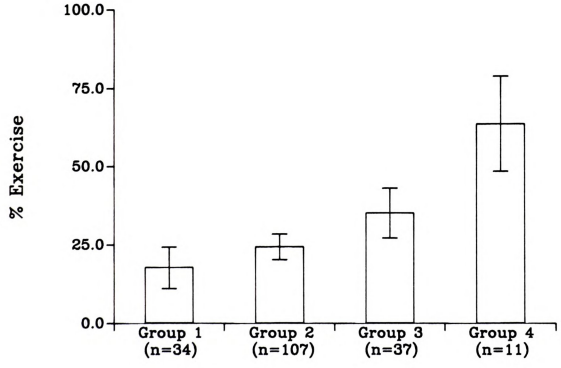


Figure 17. Bar graph comparison of mean values of percent weanlings undergoing forced exercise for groups 1 through 4 described in Figure 15.

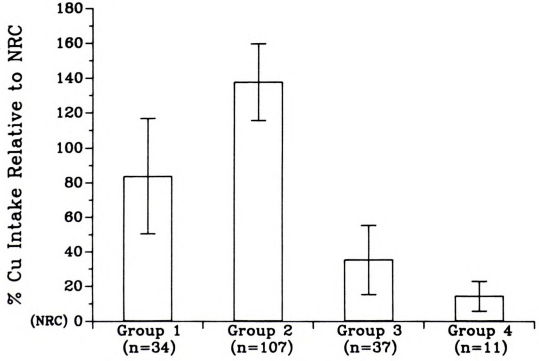


Figure 18. Bar graph comparison of mean values of percent dietary copper intake relative to NRC recommendations[66] for groups 1 through 4 described in Figure 15.

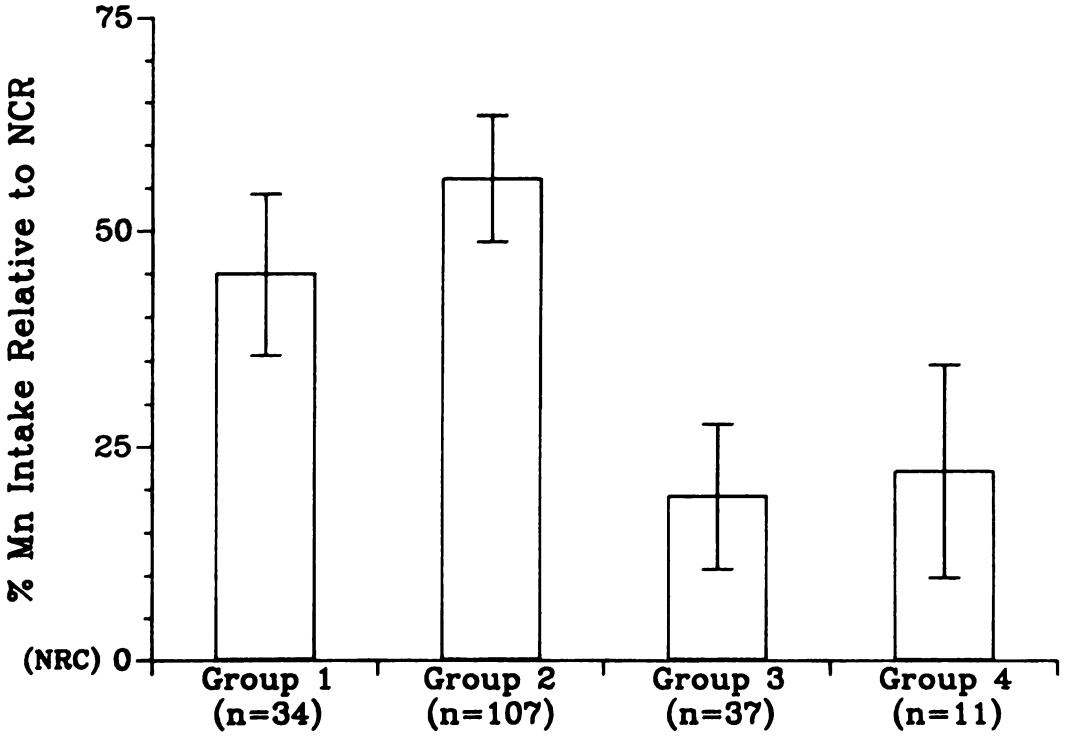


Figure 19. Bar graph comparison of mean values of percent dietary manganese intake relative to NRC recommendations[66] for groups 1 through 4 described in Figure 15.

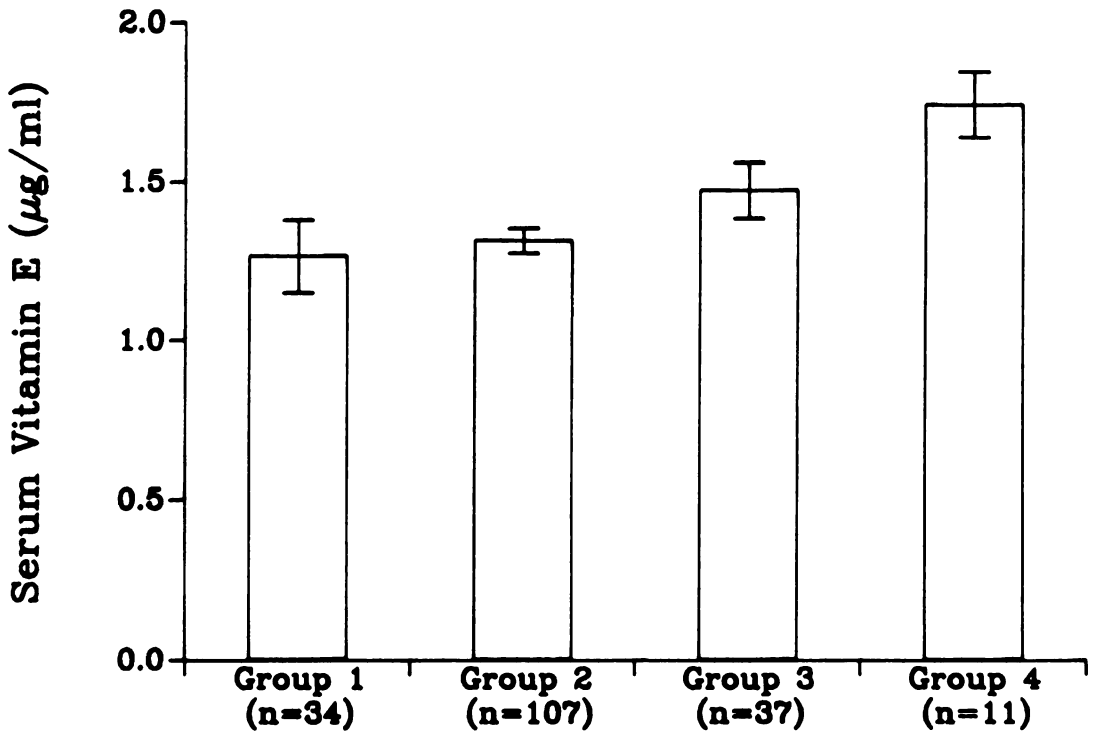


Figure 20. Bar graph comparison of mean values of serum vitamin E (ug/ml) for groups 1 through 4 described in Figure 15.

CHAPTER V

DISCUSSION

This study utilized a field survey method to evaluate relationships of various nutritional and management factors to DOD. The population of registered Quarter Horses in Michigan is estimated to be approximately 45,000.[108] Only a stratum of weanlings from this population was considered in the survey. From this stratum, a sample population of Michigan Quarter Horse weanling participants was acquired by a voluntary response survey (nonrandomized sampling). There is, presently, no available data base to determine whether or not the acquired sample population is a representative sample of Michigan Quarter Horse weanlings. The sample population can best be described as a quota sample. Data from the American Quarter Horse Association indicate that approximately 1,500 Quarter Horse foals were registered from Michigan in 1983 and 1984. The 189 weanlings evaluated in this survey most likely accounted for 10% or more of Michigan Quarter Horse weanling population at such point in time. For lack of a comparable data base, limitations may be placed on any statistical inferences.

A relationship has been described between animals genetically selected for rapid growth and osteochondrosis.[27,28] Parameters quantitating rapid growth (rate of daily gain, body weight, body height, and body condition) were evaluated in this study. A rate of gain of 0.53 kg/day is recommended (by NRC[66]) for weanlings between 6 and 12 months of age with expected mature weight of 500 kg. In this survey, 42.8% of weanlings had an estimated rate of gain of 0.61 kg/day or greater, and were considered above average in weight, height, and body condition. All of the above parameters failed to demonstrate any correlation to TWS. Many weanlings with high TWS were large for their age; however, a high number of weanlings with lower TWS were also large and rapidly growing. The possibility of genetic involvement, by tracing lineage, of foals was not evaluated. Data from this survey, however, suggest that factors other than genetic selection for rapid growth are necessary for DOD.

Trauma has been suggested as an etiological agent in DOD. Trauma has been interpreted to include excessive compressive forces on the developing growth plate. Some authors have suggested that above average body weight could result in such forces. No correlation was observed between DOD and body weight in this study.

Trauma could also be interpreted as excessive exercise on an immature physis. Previous studies[55]

indicated that exercise programs were beneficial to bone development. Exercise, in four to eight month old weanlings, was shown, on the basis of increased third metacarpal circumference and density, to stimulate bone mineralization and presumably the development of horses with greater athletic potential and durability. Such studies overlooked the effects of exercise on endochondral ossification. The relationship of DOD with the use of forced exercise (lungeing, treadmill, or ponying for > 4 weeks) for "fitting out" futurity prospects was the most statistically significant finding of this survey. To the author's knowledge, this study represents the first substantiated report demonstrating such a correlation. Whether or not the exercise directly inhibited endochondral ossification or indirectly triggered early breakdown of existing diseased bone was not determined.

Many weanlings in this study (41%) received high daily grain intakes, some in conjunction with exercise programs. Previous investigations[53] suggest high carbohydrate diets, in conjunction with mechanical stress on the growth plate, result in even greater risk of disease.

An endocrine etiology has been proposed for DOD. Consumption of meals, concentrated in energy and protein, induced changes in circulating hormones involved with the regulation of cartilage growth. Postprandial surges in blood glucose and amino acids stimulated insulin secretion which, in turn, interfered with thyroxine secretion. These endocrine changes were associated with microscopic bone lesions consistent with DOD. The results from these investigations suggested rations based on large amounts of grain, fed once or twice a day, increased the risk of DOD. Data from the present study support this theory. A trend ($p < 0.07$) for higher TWS was observed in association with high dietary grain intake.

Overfeeding (of energy and/or protein) has been linked to DOD.[28,29] Nutrient intakes of energy and protein greatly influence growth rate. Weanling rations in this survey were frequently deficient in protein and excessive in energy relative to 1978 NRC recommendations (Table 13) based on estimated rates of gain. Low dietary protein concentrations are reported to depress growth rate, however, most foals in this project were above average in rate of gain (Table 9). No correlation was observed for dietary energy or protein concentrations and TWS. The form of energy and protein may be more important than the amount. For example, a diet of high

quality alfalfa hay could have an energy and protein concentration equivalent to a diet of mixed grain. However, the alfalfa hay diet would be greater by weight due to its high fiber content and would take longer to consume. Most likely the forage diet would affect blood insulin and thyroxine levels differently than the rapidly consumed, readily available carbohydrate diet.

Mineral and vitamin status of weanlings in this survey were assessed by both ration evaluation and serum analyses. Statistical relationships of mineral and vitamin status to DOD were examined individually for 189 weanlings, as well as collectively for sixty farms. Statistically significant relationships were observed only for individual weanling data.

Diets deficient in calcium and phosphorus may not greatly influence weight gains even though bone development may be abnormal. Lack of dietary calcium and phosphorus results in failure of mineralization of osteoid tissue. Of the sixty farm rations evaluated, twelve were deficient in calcium and twenty-six were deficient in phosphorus to a degree of 25% or more below 1978 NRC recommended levels.[66] Deficiencies generally occurred by feeding grain without adequate calcium or phosphorus supplementation. Although low dietary calcium and phosphorus concentrations were associated with high

TWS, these correlations were not statistically significant.

Data from a recent field survey in Ohio and Kentucky[3] suggested a negative correlation between DOD and dietary calcium and phosphorus. Of the nineteen farm rations evaluated, only two were deficient in calcium and none was deficient in phosphorus. These results differ considerably from results of the present study.

Other investigations have reported horse diets containing low or marginal levels of calcium and excess phosphorus resulted in secondary nutritional hyperparathyroidism.[109,110] Only one of the sixty farm rations in the present study had a ratio of calcium to phosphorus less than 1:1, indicating a low potential for this type of problem.

Several farms in the present study (15%) were feeding calcium concentrations 50% greater than NRC recommendations.[66] Although high dietary calcium has been postulated to cause hypercalcitoninism, leading to DOD,[4] no significant relationships were observed in this study. Whether or not the higher calcium concentrations exaggerated a marginal trace mineral deficiency was not determined. One farm ration, in particular, had a calcium concentration 50% greater than NRC recommendations and a copper concentration 7% greater than NRC recommendations. Weanlings on this farm

received no exercise conditioning program, had an average rate of gain, and consumed diets with a forage to grain ratio of 1:07. All three foals on this farm had high TWS. Certainly, other factors (e.g., genetics) could be responsible. On the other hand, excess calcium in the diet has been shown to reduce absorption and utilization of other minerals.

Simple copper deficiencies can interfere with bone development.[91,92] Recent studies by Knight and coworkers[3,23] imply a detrimental effect of marginal dietary copper concentrations on endochondral ossification in the horse. In a field survey by Knight,[3] over half of farm rations evaluated were below the recommended level of 9 ppm copper. In the present survey, 36.7% of farm rations were below this level. Both studies indicated significant correlations between copper and DOD. Ration calculations, by both Knight and this author, excluded trace mineral salt in the block form, but included trace mineral salt fed individually or as part of the grain concentrate. Knight, however, adjusted copper levels for molybdenum (using a copper to molybdenum ratio of 1:4). Although dietary molybdenum has been shown to be a significant antagonist of copper in ruminants (probably due to rumen conversion of molybdate to thiomolybdates), the same induced copper deficiency has not been demonstrated for horses.[111]

Diets of 20 ppm molybdenum failed to show any significant depression in plasma copper levels. The highest dietary molybdenum concentration for farm rations in this project were 4.3 ppm. This author chose not to adjust copper levels for molybdenum. Such a variation between methods may account for the different incidence of copper-deficient rations in the two surveys.

Copper metabolism may also be influenced by high dietary zinc concentrations. Skeletal abnormalities in young horses were attributed to zinc toxicity and its induced secondary copper deficiency.[82,83,85,98] Dietary zinc concentrations of 612 ppm or greater were associated with skeletal disease. Highest dietary zinc concentration observed in this study was approximately 120 ppm. In general, high zinc concentrations were due to commercially prepared supplements and were unrelated to forage contamination. The same commercial supplements also provided the highest dietary copper concentrations observed (approximately 55 ppm) and perhaps offset any zinc interference with copper metabolism.

Ponies were reported to tolerate dietary copper concentrations of 791 ppm with no adverse effects.[112] In the present study, three farm rations with the greatest dietary copper concentrations (approximately 55 ppm) also had low mean TWS (ranging 2 to 3). A feed trial[22] comparing diets containing 15 and 55 ppm copper, found

the incidence of histologic cartilage lesions, in foals at postmortem, to be three times greater at the lower copper level. Researchers suggested these data indicated NRC recommendations[66] for copper may be too low. Data from the present study appear to support this suggestion. Mean values for dietary copper concentration in group 4 were 24% greater than NRC recommendations.[66] This percentage may be misleading due to two individuals in this group with copper concentrations six times greater than NRC recommendations.

Zinc deficiency in foals is accompanied by a variety of symptoms including reduced growth rate.[113] As opposed to other species[114] there is no direct evidence of abnormal bone development in zinc-deficient horses. Correlation of low dietary zinc concentrations to DOD was observed by Knight et al.[3] While only three farm rations evaluated by these investigators were below NRC recommended levels[66] (40 ppm), the lowest scores for DOD were observed on farms feeding 80 to 90 ppm copper. In the present study, thirty-two farms (53%) fed weanling rations deficient in zinc. Zinc-deficient rations were frequently observed to be deficient in copper as well. Low dietary zinc concentrations tended to be associated with high TWS, but this correlation was not statistically significant.

The survey by Knight and coworkers observed only one farm ration below the 40 ppm recommended level for dietary manganese. No association was observed by these investigators, between dietary manganese concentrations, and scores for DOD. In the present study, 25% of farm rations evaluated were deficient in manganese. Correlation between TWS and dietary manganese concentration was near significance ($p < 0.08$). Reasons for the variation in incidence of zinc and manganese-deficient rations between the two surveys are unknown.

Only one farm ration was observed to be below NRC recommended level[66] of 50 ppm for iron. Three farm rations contained iron concentrations in the range of 350 to 500 ppm. No relationship was observed between dietary iron concentration and TWS.

Vitamin A and D influence bone development in growing foals. Toxic levels can occur from excessive supplementation. In the survey by Knight et al.,[3] two of fifteen farm rations (13.3%) contained excessive levels of vitamin A and D (>125,000 IU/day and >25,000 IU/day, respectively). The present study observed similar results with eight farm rations (13.3%) containing vitamin A levels estimated to be 125,000 IU/day, and sixteen farm rations (26.6%) containing vitamin D levels estimated to be >25,000 IU/day.

Although vitamin E is required in the equine diet, more research is needed to determine optimal levels for growth. Dietary vitamin E concentrations of 100 IU/day of dry matter were necessary to prevent muscle soreness, and lameness in zebra and Przewalski horses.[115] Supplements of 400 mg vitamin E/day in the winter were necessary to prevent seasonal changes in serum -tocopherol.[116] Signs of vitamin E toxicity in horses have not been produced, but based on studies in other species,[117] a maximum tolerable level would be 1000 IU/kg of dry diet.[118] For a 260 kg weanling receiving 7.4 kg diet/day, as fed, maximum tolerable levels for vitamin E would be approximately 7,000 IU/day. Two farms in the present study fed rations containing calculated vitamin E concentrations of 4000 IU/day. All other farm rations were below 1000 IU vitamin E/day with 47 rations (78.3%) containing 100 to 400 IU vitamin E/day.

Mean serum vitamin and mineral values of weanlings sampled (Table 15) were consistent with normal expected values for foals of similar age.[103,104] A broad range of values was observed for vitamin A, vitamin E, selenium, magnesium, iron, zinc, and copper. In general, this variability reflected concentrations of these nutrients in the ration, with significant correlation observed for magnesium and copper.

Farm mean for weanling serum vitamin and mineral concentrations (Table 16) indicated many farms were below expected normal ranges for selenium and vitamin E. Thirty-one (51.6%) farm serum selenium means were <90 ng/ml and twenty (33.3%) farm serum vitamin E means were <1.3 ug/ml. Seventeen (28.3%) farm serum selenium means were >110 ng/ml and only three (5%) farm serum vitamin E means were >2.0 ug/ml.

As discussed above, the majority of farms fed rations calculated to contain moderate levels of vitamin E with only three farms feeding estimated levels >800 IU/day. However, none of these farms was included in the three farms with serum means >2.0 ug vitamin E/ml. The large number of farm serum means <1.13 ug vitamin E/ml might be attributed to seasonal variation.[119] However, all samples were obtained during winter months (November to January) supposedly eliminating any seasonal effect.

Weanling serum concentrations of vitamin E were significantly positively correlated with TWS ($p < 0.01$). This significance, as displayed by group means in Figure 12, translates to very small differences in terms of serum concentrations of vitamin E. It was not determined by this study what role serum concentrations of vitamin E might play in DOD. Of interest to this author is the possible genetic-nutrient interaction previously reported for vitamin E regarding equine degenerative

myeloencephalopathy.[47] Perhaps this vitamin lacks direct involvement in the mechanism of DOD, but serves as a genetic marker. Other studies have pointed to the possibility of a breed difference in blood selenium levels.[120,121] Such possibilities indicate the need for further research of genetic involvement in DOD.

Farm means for weanling serum vitamin A were close to expected normal range. Eight farm means (13.3%) were >300 ng/ml vitamin A and six farms means (10%) were < 150 ng/ml vitamin A.

Field surveys, such as the present study, offer an opportunity to observe weanlings in their natural setting. Many environmental factors and their influence can be studied simultaneously. The difficulty lies in the recognition of animals with DOD. Both radiographic and physical assessments were used in this study to determine clinical DOD. Other researchers have shown that histological evidence is often present without clinical evidence.[4,22,63] If such histological lesions are significant, one would expect, with time and training, the defect would become clinically apparent. Long-term epidemiological studies may, therefore, be more informative.

Lesions of DOD have been reported in very young foals as well as a fetus.[4,22] Nutrition of the mare during gestation and lactation was not evaluated in this

study. Further epidemiological studies are needed to determine relationships of mare nutrition to DOD in the foal.

CHAPTER VI

SUMMARY

Equine developmental orthopedic disease (DOD) probably involves the interaction of multiple genes and is influenced by multiple environmental factors. For these reasons, a survey was performed to evaluate the environmental components of DOD in a population of weanling Michigan Quarter Horses.

Sixty farms were visited between November 1986 and February 1987. Data were collected on 189 Quarter Horse weanlings for evaluation of growth characteristics and rate of daily gain.

A radiographic score and physical score were determined for each weanling. Both assessments were independently derived by a point system in which increasing numerical values corresponded to increasing severity of DOD. Total weanling score (TWS) was calculated for each weanling by combining the radiographic score and physical score.

Serum from each weanling was analyzed for vitamin A, vitamin E, selenium, sodium, calcium, phosphorus, magnesium, iron, zinc, and copper. Farm means for

weanling serum vitamin and mineral concentrations were determined for sixty farms.

Scale-weighed amounts of all feed stuffs fed daily were recorded. Grain and forage samples were collected and submitted for laboratory analysis of nutrient concentrations. Ration evaluation was performed for each weanling based on age, weight, rate of daily gain, and expected mature weight.

Information regarding management was recorded for age at weaning, availability of pasture, access to creep feed, and use of forced exercise.

Data were analyzed for relationships between TWS and variables for growth characteristics, dietary nutrient concentrations, serum vitamin and mineral concentrations, and management factors.

The majority of weanlings examined had some evidence of DOD. TWS tended to be associated with lower dietary mineral concentrations of calcium, phosphorus, magnesium, iron, zinc, and manganese. The TWS was statistically inversely related to dietary copper. The TWS did not correlate to ration concentrations of energy or protein. Serum vitamin E was positively correlated to TWS. No relationships were observed between any growth characteristics and TWS. The use of forced exercise (lungeing, treadmill, or ponying for > 4 weeks) correlated with high TWS.

Results of this survey suggest that lowered dietary copper, increased serum vitamin E, and increased forced exercise are associated with increased severity of DOD. Consideration of these three factors in farm programs might contribute to decreasing the incidence of DOD in weanling foals, however, further research is needed to confirm the influence of these environmental factors, as well as the role of genetics in DOD.

APPENDICES

APPENDIX A

INFORMATIVE LETTER ON PROPOSED PROJECT AND DOD

Michigan Quarter Horse Association Member:

This letter is to inform you of a research project being conducted through Michigan State University. A representative sample of the Quarter Horse weanlings in Michigan for 1986 will be needed for this investigation. The objective of this project is to perform a field survey of weanling rations and observe correlations to metabolic bone disease.

Metabolic bone disease is a serious problem of young, growing animals. The permanent structural damage that can occur with metabolic bone disease can lead to complete loss of performance and value of the animal. The incidence of clinical cases of metabolic bone disease appears to be on the increase. Currently, the cause of this disease remains unknown, but many people feel the two most important factors are nutrition imbalance and a genetic predisposition to rapid, early growth.

Metabolic bone disease can be defined as any condition that results from a disturbance in the change of the cartilage precursor of the skeleton into functional bone.

Clinically, this disease is manifested in horses by the following conditions:

1. Epiphysitis or physitis

   This condition is observed as an increased thickness or widening of the growth plate. The most common site for physitis is the distal radius, just above the carpus. This gives a flared appearance to the knee. Physitis is also observed in the distal cannon bone, pastern bones and distal tibia, just above the hock. Occasionally, mild to severe lameness will be associated with physitis.

2. Acquired contracted tendons

   The pain or lameness that can occur with physitis can lead to unequal weight bearing in the limb, resulting in contracted flexor tendons. The severity of this condition can range from upright pasterns to complete knuckling over of the fetlock or club foot.

3. Acquired angular limb deformity

   Physitis can result in structural defects of the cartilage, creating uneven growth and subsequent angular or rotational deformities of the limb.

4. Osteochondrosis

   This is a condition where cartilage is hindered in its normal conversion into bone. In general, physitis could be considered a form of osteochondrosis at the growth plate, but usually the term osteochondrosis is associated with peripheral lesions of the articular cartilage. This can occur in any joint, but most commonly in the hock, stifle and shoulder.

5. Osteochondritis Dissecans

   This is a stage of osteochondrosis where defective cartilage extends to the articular surface of the joint and can form flaps or loose pieces within the joint. This can lead to degenerative arthritis.

6. Subchondral Bone Cyst

   This is a stage of osteochondrosis where the defective cartilage stays central to the articular surface and creates an island of retained cartilage that is not converted to bone. This defect can structurally weaken the bone.

7. Cervical Vertebral Malformation

   Osteochondrosis can occur in the vertebral bones of the neck, resulting in bone deformities that put pressure on the spinal cord, causing tissue damage. This is observed as incoordination and weakness of the limbs commonly referred to as "Wobbler Syndrome."

The nutritional factors most often cited to be related to metabolic bone disease are protein, energy, calcium, phosphorus, zinc, and copper. Some workers claim overfeeding alone will cause disease, while others feel major and trace mineral imbalances to be the cause. Reports from the few clinical studies conducted have been contradictory. A need continues to investigate the role of nutrition in metabolic bone disease. Hopefully, the information gathered through this project will help in prevention and management of this problem.

APPENDIX B

REQUEST TO QUARTER HORSE BREEDERS TO COMPLETE QUESTIONNAIRE

MICHIGAN STATE UNIVERSITY

COLLEGE OF VETERINARY MEDICINE
LARGE ANIMAL CLINICAL SCIENCES

EAST LANSING • MICHIGAN • 48824-1314

Metabolic Bone Disease Research Project

Please fill out the following questionnaire if you will be raising Quarter Horse weanlings during 1986 and are interested in participating in this research project. If you are selected to be a participant, there will be no cost to you, and you will be informed of the results of your evaluation. There will be no published information that states your name, nor your farm or animal's name. Please return this form to:

Dr. Amy Williams
Veterinary Clinical Center - LCS
Michigan State University
East Lansing, MI 48824

You will be notified by September 15, 1986 whether you were selected for participation. Thank you for your interest.

Very truly yours,

M. A. Williams, DVM

M. A. Williams, DVM

APPENDIX C

QUESTIONNAIRE TO IDENTIFY POTENTIAL PARTICIPANTS IN THE PROJECT

Name: _____

Street Address: _____

City & Zip Code: _____

Phone: (Home) AC _____/_____

(Work) AC _____/_____

How many live foals did you have born this year? (1986) ____

Please indicate the number of foals born in each of the following months:

January _____

February _____

March _____

April _____

May _____

June _____

At what age do you generally wean your foals? _____

How many of these foals do you expect to own through
February 1987? _____
February 1988: _____

How many years have you raised Quarter Horses? _____

In previous years that you raised foals, did you ever have problems with:

		Yes	No
1.	epiphysitis	___	_____
2.	contracted tendons	___	_____
3.	angular limb deformities	___	_____
4.	osteochondrosis	___	_____
5.	fluid swelling of hock or stifle joints	___	_____
6.	cervical vertebral malformation	___	_____

If selected to participate in this project, would you be willing to:

		Yes	No
1.	Arrange a time with the investigator to allow a visitation to your farm for examination of your foals?	___	___
2.	Provide 2 or 3 workers to assist in holding the weanlings for measurements, photographs, radiographs, and samples to be taken	___	___
3.	Provide samples of the hay and grain rations being fed the weanlings and accurate information regarding amounts of each feed plus information on any supplements fed?	___	___
4.	Allow blood samples to be drawn on your weanlings for analysis of serum mineral levels?	___	___

LIST OF REFERENCES

LIST OF REFERENCES

1. McIlwraith CW. Bones of contention. The Blood-Horse 1986; 39: 6996.

2. Stromberg B. A review of the salient features of osteochondrosis in the horse. Eq Vet J 1979; 11: 211-214.

3. Knight DA, Gabel AA, Reed SM, et al. Correlation of dietary mineral to incidence and severity of metabolic bone disease in Ohio and Kentucky. Proc Am Assoc Eq Pract 1985; 31: 445-461.

4. Krook L., Maylin GA. Fractures in Thoroughbred race horses. Cornell Vet 1988; 78 (suppl. 11): 1-133.

5. Firth EC, Poulos PW. Development of the epiphysis, metaphysis and diaphysis in the foal. Proc Am Assoc Eq Pract 1987; 33: 787-794.

6. Bramlage LR. Clinical manifestations of disturbed bone formation in the horse. Proc Am Assoc Eq Pract 1987; 33: 135-142.

7. Trotter GW, McIlwraith CW. Osteochondritis dissecans and subchondral cyst lesions and their relationship to osteochondrosis in the horse. Eq Vet Sci 1981; 157-162.

8. Rejno S, Stromberg B. Osteochondrosis in the horse. II. Pathology. Acta Radiol 1978; 358: 153-178.

9. White SL. Clinical manifestations and pathophysiology of osteochondrosis. Proc Am Assoc Eq Pract 1980; 26: 69-80.

10. Firth EC, Poulos PW. Retained cartilage in the distal radial physis of foals. Vet Path 1984; 21: 10-17.

11. Campbell JR. Bone growth in foals and epiphyseal compression. Eq Vet J 1977; 9:116-121.

12. Auer JA. Angular limb deformities in foals. Part I Congenital factors. Comp Cont Ed 1982; 4: S330-339.

13. Auer JA. Angular limb deformities in foals. Part II Developmental factors. Comp Cont Ed 1983; 5: S27-S40.

14. Pharr JW. Radiographic findings in foals with angular limb deformities. J Am Vet Med Assoc 1981; 179: 811-817.

15. Trueta J, Trias A. The vascular contribution to osteogenesis. IV. The effect of pressure on the epiphyseal cartilage of the rabbit. J Bone Joint Surg 1961; 43: 800-813.

16. Stashak TS. Adam's lameness in horses. Philadelphia: Lea and Febiger, Philadelphia 1987; 454-463.

17. Fackelman GE. Flexure deformity of the metacarpophalangeal joints in growing horses. Comp Cont Ed 1979; 1: S1-S7.

18. Owen JM. Abnormal flexion of the corono-pedal joint of "contracted tendons" in unweaned foals. Eq Vet J 1975; 7: 40-45.

19. Lochner FK, Milne DW, Mills EJ, Groom JJ. In vivo and in vitro measurement of tendon strain in the horse. Am J Vet Res 1980; 41: 1929-1937.

20. Rooney JR. Postnatal contracture of young horses. Eq Vet Sci 19; 5: 204-208.

21. Reed SM, Knight DA, Weisbrode SE, et al. The relationship of cervical vertebral malformation to developmental orthopedic disease. Proc Am Assoc Eq Pract 1987; 33: 139-142.

22. Wagner PC, Grant BD, Watrous BJ, et al. A study of the heritability of cervical vertebral malformation in horses. Proc Am Assoc Eq Pract 1985; 31: 43-50.

23. Knight DA, Weisbrode SE, Schmall LM, et al. Copper supplementation and cartilage lesions in foals. Proc Am Assoc Eq Pract 1987; 33: 191-194.

24. Mayhew IG deLahunta A., Whitlock RH, et al. Spinal cord diseases in the horse. Cornell Vet 1978; 68 (Suppl 6): 71.

25. Reed SM, Newbrey J, Norton K, et al. Pathogenesis of cervical vertebral malformation. Proc Am Assoc Eq Pract 1985; 31: 37-42.

26. Reiland S, Ordell N, Lundeheim N, et al. Heredity of osteochondrosis, body constitution and leg weakness in the pig. Acta Radiol 1978; 358: 123-138.

27. Reiland S. The effect of decreased growth rate on frequency and severity of osteochondrosis in pigs. Acta Radiol 1978; 358: 107-122.

28. Stromberg B, Rejno S. Osteochondrosis in the horse. I. A clinical and radiological investigation of osteochondritis dissecans of the knee and hock joint. Acta Radiol 1978; 358: 139-152.

29. Hedhammar A, Wu FM, Krook L, et al. Overnutrition and skeletal disease. An experimental study in growing Great Dane dogs. Cornell Vet 1974; 64 (suppl 5): 1-160.

30. Poulos PW. Tibial dyschondroplasia (osteochondrosis) in the turkey. A morphologic investigation. Acta Radiol 1978; 197-228.

31. Poulos PW, Reiland S, Elwinger K, et al. Skeletal lesions in the broiler with special reference to dyschondroplasia (osteochondrosis): Pathology, frequency, and clinical significance in two strains of birds on high and low energy feed. Acta Radiol 1978; 358: 229-276.

32. Reiland S, Andersson K. Crossbreeding experiments with swine. Influence of different combinations of breeds on frequency and severity of osteochondrosis. A preliminary report. Acta Agric Scand 1978; suppl 21: 486-489.

33. Campbell CJ, Ranawat CS. Osteochondritis dissecans: The question of etiology. J Trauma 1966; 6: 201.

34. Clanton TO, DeLee JC. Osteochondritis dissecans: History, pathophysiology and current treatment concepts. Clin Orth Rel Res 1982; 167: 50-62.

35. Siffert RS. Classification of the osteochondroses. Clin Orth Rel Res 1984; 158: 10-18.

36. Fraser WN. Familial osteochondritis dissecans. J Bone Joint Surg 1966; 48B: 598.

37. Gardiner TB. Osteochondritis dissecans in three members of one family. J Bone Joint Surg 1955; 37B: 139.

38. Petrie RW. Etiology of osteochondritis dissecans. J Bone Joint Surg 1977; 59B: 366.

39. Pick MP. Familial osteochondritis dissecans. J Bone Joint Surg 1955; 37B: 142.

40. Duthie RB, Houghton GR. Constitutional aspects of the osteochondroses. Clin Orth Rel Res 1984; 158: 19-27.

41. Dimock WW. "Wobbles"- An hereditary disease in horses. J Hered 1950; 41: 319.

42. Falco MJ, Whitwell K, Palmer AC. An investigation into the genetics of "Wobbler Disease" in Thoroughbred horses in Britain. Eq Vet J 1976; 8: 165.

43. Hoppe F, Philipsson J. A genetic study of osteochondrosis dissecans in Swedish horses. Eq Pract 1985; 7: 7.

44. Hintz HF. Factors which influence developmental orthopedic disease. Proc Am Assoc Eq Pract 1987; 33: 159-162.

45. Woolliams JA, Weiner G, Woolliams C, et al. Retention of copper in the liver of sheep genetically selected for high and low concentrations of copper in plasma. Anim Prod 1985; 41: 219.

46. Thornburg LP, Polley D, Dimmitt R. The diagnosis and treatment of copper toxicosis in dogs. Canine Prac 1984; 11: 36.

47. Mayhew IG, Brown CM, Stowe HD, et al. Equine degenerative myeloencephalopathy. A vitamin E deficiency that might be familial. J Vet Int Med 1987; 1: 45.

48. White SL, Rowland GN, Whitlock RH. Radiographic, macroscopic and microscopic changes in growth plates of calves raised on hard flooring. Am J Vet Res 1984; 45: 633-639.

49. Trotter GW, McIlwraith CW. Osteochondrosis in the horse: Pathogenesis and clinical syndromes. Proc Am Assoc Eq Pract 1980; 26: 141-160.

50. McIlwraith CW. Subchondral cystic lesions (osteochondrosis) in the horse. Comp Cont Ed 1982; 4: S394-S404.

51. Brown MP, MacCallum FJ. Observations on growth plates in limbs of foals. The Vet Rec 1976; 98: 443-446.

52. Singer KM, Roy SP. Osteochondrosis of the humeral capitellum. Amer J Sports Med 1984; 12: 351-360.

53. Paatsama S, Rokkanen P, Jussila J. Etiological factors in osteochondritis dissecans. Acta Orthop Scand 1975; 46: 906-918.

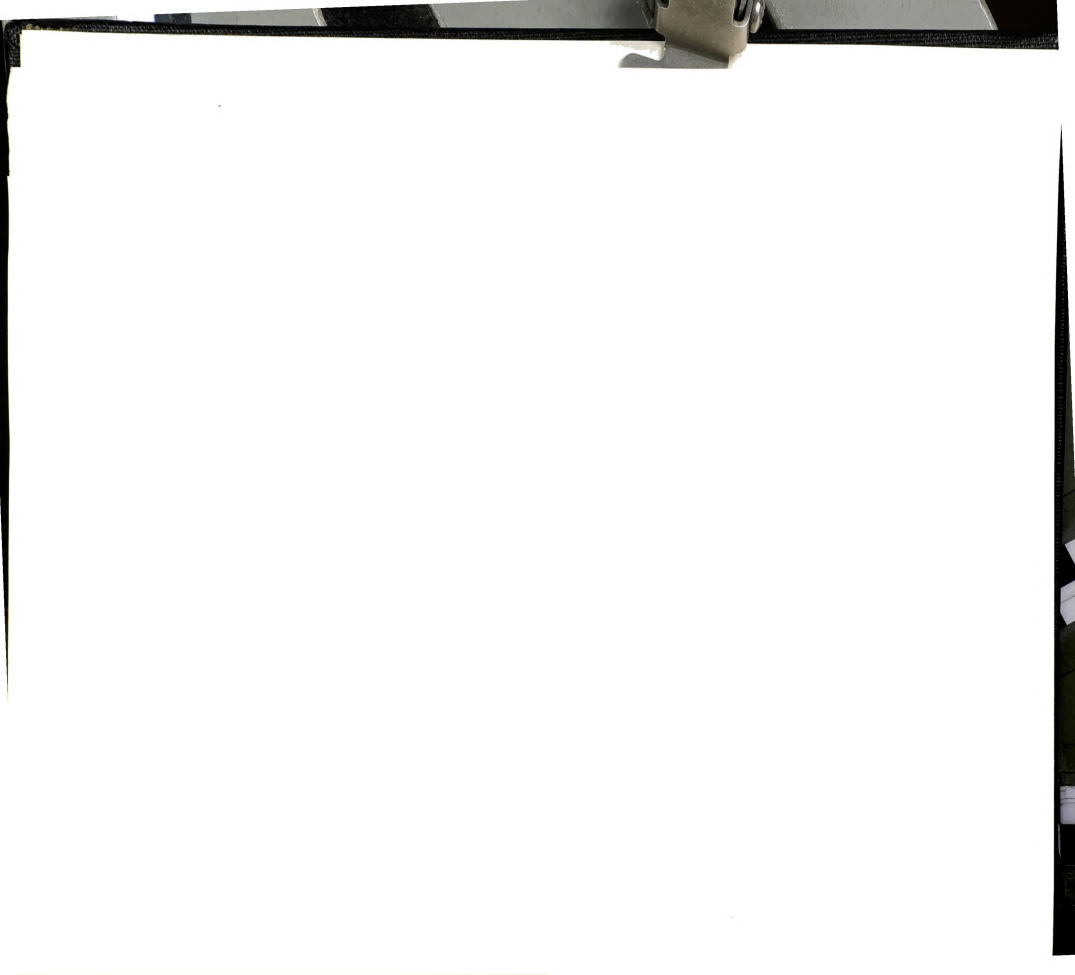
54. Millis DL, Lieb S, Ott EA. Influence of exercise and training on bone development in yearling horses. Proc Eq Nutr Phys 1983; 8: 50-54.

55. Raub RH, Jackson SG, Baker JP. The effect of exercise on bone development and growth and the circulating levels of cortisol, insulin and thyroxine in weanling horses. Proc Eq Nutr Phys 1987; 10: 409-414.

56. Schryver HF, Hintz HF, Lowe JE. Calcium metabolism, body composition and sweat losses of exercised horses. Amer J Vet Res 1978; 39: 245.

57. Meakim DW, Ott EA, Asquith RL, et al. Estimation of mineral content of the equine third metacarpal by radiographic photometry. J Anim Sci 1981; 53: 1019.

58. Canalis E. The hormonal and local regulation of bone formation. Endocrine Rev 1983; 4: 62-77.



59. Glade MJ. The role of endocrine factors in equine developmental orthopedic disease. Proc Am Assoc Eq Pract 1987; 33: 171-189.

60. Vivrette SL, Reimers TJ, Krook L. Skeletal disease in a hypothyroid foal. Cornell Vet 1984; 74: 373-386.

61. Shaver JR, Fretz PB, Doige CE, et al. Skeletal manifestations of suspected hypothyroidism in two foals. J Eq Med Surg 1979; 3: 269-275.

62. Glade MJ, Gupta S, Reimer TJ. Hormonal response to high and low planes of nutrition in weanling thoroughbreds. J Anim Sci 1984; 59: 658-665.

63. Glade MJ, Belling TH. Growth plate cartilage metabolism, morphology and biochemical composition in over and underfed horses. Growth 1984; 48: 473-482.

64. Klein GL, Wadlington EL, Collins ED, et al. Calcitonin levels in sera of infants and children: relations to age and periods of bone growth. Calcif Tissue Int 1984; 36: 63-638.

65. Burch WM, Corda G. Calcitonin stimulates maturation of mammalian growth plate cartilage. Endocrinolo 1985; 116: 1724-1728.

66. National Research Council. Nutrient requirements for horses. Washington, D.C.: National Academy of Sciences, 1978.

67. Hintz HF, Kallfelz FA. Some nutritional problems of the horse. Eq Vet J 1981; 13: 182-186.

68. Thompson KN, Jackson SG, Rooney JR. The effect of above average weight gains on the incidence of radiographic bone aberrations and epiphysitis in growing horses. Proc Eq Ntur Phys 1987; 10: 5-9.

69. Hintz HF, Schryver HF, Lowe JE. Delayed growth response and limb conformation in young horses. Proc Cornell Nutr Conf 1976; 94-96.

70. Kronfeld DS. Feeding on horse breeding farms. Proc Am Assoc Eq Pract 1978; 24: 461-464.

71. Donoghue S. Nutritionally related bone diseases. Proc Am Assoc Eq Pract 1980; 26: 65-67.

72. Kronfeld DS, Donoghue S. Metabolic convergence in developmental orthopedic disease. Am Assoc Eq Pract 1987; 33: 195-202.

73. Brewer BD. Disorders of equine calcium metabolism. Comp Cont Ed 1982; 4: S244-S252.

74. Schryver HF, Hintz HF, Lowe JE. Calcium and phosphorus in the nutrition of the horse. Cornell Vet 1984; 64: 493-514.

75. Georgievskii VI, Annenkov BN, Samokhin VT. The physiological role of macroelements. In: Mineral Nutrition of Animals. London: Butterworth and Co., 1982; 103-104.

76. Krook L, Lowe JE. Nutritional secondary hyper parathyroidism in the horse. Pathol Vet 1964; 1: suppl. 1.

77. Schryver HF, Hintz HF, Craig PH. Calcium metabolism in ponies fed a high phosphorus diet. J Nutrition 1971; 101: 259-264.

78. Rostkowski CM, Wilson TD, Allan GS, et al. Hypercalcitoninism without hypercalcitoninemia. Cornell Vet 1981; 71: 188-213.

79. Church DC, Pond W. Macrominerals. In: Basic Animal Nutrition and Feeding. 2nd ed. New York: John Wiley and Sons, 1982; 140.

80. Cupps PT, Howell CE. The effects of feeding supplemental copper to growing foals. J Anim Sci 1949; 8: 286.

81. Egan DA, Murrin MP. Copper-responsive osteodysgenesis in a Thoroughbred foal. Irish Vet J 1983; 27: 61-62.

82. Carbery JT. Osteodysgenesis in a foal associated with copper deficiency. New Zealand Vet J 1978; 26: 279-280.

83. Gunson DE, Kowalczyk DF, Shoop CR, et al. Environmental zinc and cadmium pollution associated with generalized osteochondrosis, osteoporosis and nephrocalcinosis in horses. J Am Vet Med Assoc 1982; 180: 295-299.

84. Bridges CH, Womack JE, Edward DH, et al. Considerations of copper metabolism in osteochondrosis of suckling foals. J Am Vet Med Assoc 1984; 185: 173-178.

85. Eamens GJ, Macadam JF, Laing EA. Skeletal abnormalities in young horses associated with zinc toxicity and hypocuprosis. Austr Vet J 1984; 61: 205-207.

86. Hildebran S, Hunt J. Copper-response epiphysitis and tendon contracture in a foal. Mod Vet Pract 1986; 67: 268-270.

87. Underwood EJ. Copper, molybdenum and sulfur. The mineral nutrition of livestock. 2nd ed. London: Commonwealth Agricultural Bureaux, 1981; 93.

88. Hart EB, Steenbock H, Waddell J, et al. Iron in nutrition. 7. Copper as a supplement to iron for hemoglobin building in the rat. J Biol Chem 1928; 77: 797-812.

89. Hidiroglou M. Zinc, copper and manganese deficiences and the ruminant skeleton: A review. Can J Anim Sci 1980; 60: 579-590.

90. Brewer NR. Comparative metabolism of copper. J Am Vet Med Assoc 1987; 190: 654-658.

91. Baxter JH, Van Wyk JJ. A bone disorder associated with copper deficiency. I. Gross morphological, roentgenological and chemical observations. Bull Johns Hopkins Hosp 1953; 93: 1-24.

92. Follis RH, Bush JA, Cartwright GE, et al. Studies on copper metabolism. VIII. Skeletal changes associated with copper deficiency in swine. Bull Johns Hopkins Hosp 1955; 97: 405-413.

93. Suttle NF, Field AC, Barlow RM. Experimental copper deficiency in sheep. J Comp Path 1970; 80: 151-162.

94. Flynn A, Franzmann AWA, Arneson P, et al. Indications of a copper deficiency in a subpopulation of Alaskan moose. J Nutr 1977; 107: 1182-1189.

95. Guggenheim K, Tal E, Zor V. The effect of copper on the mineralization of bones of mice fed on a meat diet. Br J Nutr 1964; 18: 529-535.

96. Washburn LE. Skeletal abnormality of probable nutritional-endocrine origin observed in cattle receiving antirachitogenic rations. J Anim Sci 1946; 5: 395.

97. Howell CE, Hart GH, Ittner NR. Vitamin A deficiency in horses. Amer J Vet Res 1941; 2: 60-67.

98. Graham R, Sampson J, Hester HR. Results of feeding zinc to pregnant mares and to mares nursing foals. J Am Vet Med Assoc 1940; 97: 41-47.

99. Donoghue S, Kronfeld DS, Berkowitz SJ, et al. Vitamin A nutrition in the equine: Growth, biochemistry, and hematology. J Nutr 1981; 111: 365.

100. Leighton-Hardman AC. Equine Nutrition. London: Pelham Books, 1980; 9-17.

101. Stowe HD, Braselton WE, Slanker M. Comparisons of equine and porcine multielement profiles of serum, liver and kidney samples obtained at postmortem. Proc Amer Assoc Lab Diag: Louisville, Ky, 1986;

102. Whetter PA, Ullrey DE. Improved fluorometric method for determining selenium. J Assoc of Anal Chem 1978; 61: 927-930.

103. Stowe HD. Experimental equine avitaminosis A and E. Proc Eq Nutr Res Soc: University of Ky. 1968b; 1:27.

104. Stowe HD. Serum selenium and related parameters of naturally and experimentally fed horses. J Nutr. 1967; 93:60-64.

105. Cunningham K., Fowler SH. A study of growth and development in the Quarter Horse. La Agri Exper Sta Bull 1961; 546: 1-26.

106. Van Saun R. Spartan equine ration evaluation program: Michigan State University, 1989.

107. SAS Institute Inc. SAS users guide: Statistics, version 5 ed. Cary, NC: SAS Institute Inc, 1985: 956 pp.

108. Michigan Agricultural Reporting Service. Michigan equine survey. Lansing, MI: Michigan Dept Agr; 1984: 35 pp.

109. Mason DK, Watkins KL, McNie JT. Diagnosis, treatment and prevention of nutritional secondary hyperparathyroidism in Thoroughbred race horses in Hong Kong. Eq Prac 1988; 3 (Suppl 10): 10-16.

110. Caple IW, Bourke JM, Ellis PG. An examination of the calcium and phosphorus nutrition of Thoroughbred race horses. Aust Vet J 1982; 58: 132-135.

111. Strickland K, Smith F, Woods M, Mason J. Dietary molybdenum as a putative copper antagonist in the horse. Eq Vet J 1987; 19: 50-54.

112. Smith JD, Jordan RM, Nelson ML. Tolerance of ponies to high levels of copper. J Anim Sci 1975; 41: 1645-1649.

113. Harrington DD, Walsh J., White V. Clinical and pathological findings in horses fed zinc deficient diets. Proc Eq Nutr Phys 1973; 3: 51-54.

114. Westmorland N, Hoekstra WG. Pathological defects in the epiphyseal cartilage of zinc deficient chicks. J Nutr 1969; 98: 76i-82.

115. Janssen, Ullrey (unpublished research, 1986).

116. Maenpaa PH, Pirhonen A, Koskinen E. Nutrition in mares and foals during the winter season: Effect of feeding two different vitamin-mineral concentrates. J Anim Sci 1988; 66: 1424-1429.

117. Nutritional Research Council. Vitamin Tolerance of Animals. Washington, DC: National Academy of Sciences, 1987.

118. Nutritional Research Council. Nutrient Requirements of Horses. Washington, DC: National Academy of Sciences, 1989.

119. Maenpaa PH, Koskinen T, Koskinen E. Serum profiles of vitamin A, E, and D in mares and foals during different seasons. J Anim Sci. 1988; 66: 1418-1423.

120. Langlands JP, Bowles D, Wilkins J, et al. Genotype as a source of variation in selenium concentration and glutathione peroxidase activity of whole blood from grazing sheep and cattle. Aust J Agric Res 1980; 31: 939-948.

121. Hayes JW, Stiner CG, Holmes MJ, Mackenzie SA. Comparison of selenium blood levels and dietary selenium in three breeds of horses. Eq Prac 1987; 9: 25-29