Erythrocyte dyscrasia, anemia, and hypothyroidism in chronically underweight llamas

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Summary: A syndrome characterized by anemia, erythrocyte dyscrasia, low body weight, and hypothyroidism was observed in 8 llamas (Lama glama). At initial examination (1 to 23 months of age; median, 7.5 months), llamas (3 males, 5 females) were markedly underweight (29 to 55 kg; median, 36 kg) and anemic (PCV, 12.9 to 25.5% [median, 19%]). Five of the llamas became progressively more anemic over time; in 2 of them, PCV decreased to <10%. Erythrocyte changes included severe poikilocytosis, anisocytosis, asymmetric distribution of hemoglobin within the cytoplasm, and cytoplasmic extensions from one or both poles. Six llamas had moderate to severe valgus deformities of the carpus. All llamas had low baseline serum thyroxine concentration and diminished response to thyrotropin administration. Baseline and post-thyrotropin triiodothyronine concentrations did not have consistent patterns. Five llamas were hypophosphatemic and 7 had low serum iron concentration (iron concentration was not determined in 1 llama). Orally administered iron supplementation did not induce clinical improvement. Because 3 of the affected llamas were full sisters, a genetic basis for the problem has to be considered. It was not possible to evaluate the familial relationship of the other 5 affected llamas. Although the underlying cause of the problem was not established, the prognosis for affected llamas is guarded to poor.

Between June 1986 and July 1989, 23 llamas (Lama glama) were examined because they were not growing at the expected rate, were unthrifty, and/or had small stature coupled with angular limb deformities (ADD) of the thoracic or pelvic limbs. A subset of 8 llamas had anemia, erythrocyte dyscrasia, and hypothyroidism. The other 15 llamas had a range of metabolic problems probably not directly related to abnormal erythrocytes or hypothyroidism. To the best of our knowledge, this combination of conditions has not been previously reported in llamas and represents a clinically important problem.

Materials and Methods

Llamas—Eight llamas (3 males, 5 females) belonging to 6 owners were examined. Initial clinical signs of disease included unthriftness, failure to grow at a normal rate, and/or thoracic or pelvic limb deformities. Each llama was examined, and samples were collected for CBC, serum biochemical analysis (serum urea nitrogen [SUN], creatinine, glucose, total protein, albumin, total bilirubin, alkaline phosphatase [ALP], creatine kinase [CK], y-glutamyltransferase [GGT], alanine transaminase [ALT]), electrolytes [sodium, potassium, chloride], calcium, phosphorous, magnesium, sodium, iron, copper, zinc, total iron binding capacity [TIBC], vitamin E), and fecal examination for parasites. Bone marrow biopsy was performed in 6 llamas. Bilateral survey radiography of the thoracic and/or pelvic limbs was performed for most llamas. Serum triiodothyronine (T3) and thyroxine (T4) concentrations were measured before and after thyrotropin administration. Serum protein concentration was measured by electrophoresis. Necropsy was done on llamas 1, 2, and 4 through 7.

Analysis of samples.—The CBC was evaluated, using an automated hematologic analyzer to compensate for the small mean size of llama erythrocytes. The RBC for transmission electron microscopy were prepared by resuspending the erythrocyte fraction in buffered 2.5% glutaraldehyde after centrifugation. After washing, cells were further fixed in 1% buffered osmium tetroxide, dehydrated, and infiltrated with then embedded in epon/araldite. Thin sections were prepared, using an ultramicrotome, stained with uranyl and lead salts, and examined by use of a transmission electron microscope.

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Figure 1—Two llamas of the study. The affected smaller sexually intact male (llama 5 foreground) was 33 months old and weighed 44 kg; the clinically normal, larger llama (background) was 18 months old and weighed 120 kg, normal body weight for a sexually intact male of that age. Notice also the angular limb deformity in the affected llama.

Figure 2—Body weight plotted as a function of age in affected llamas. Shaded region represents the normal range of body weight observed in llamas of similar age. Weight ranges were derived from unpublished morphometric studies conducted at Oregon State University evaluating the growth characteristics of 270 clinically normal llamas. Preliminary analysis indicates that the growth rates of males and females during the first year does not differ.

The symbols O, △, ▲, □, ◊, and ▽ are used to represent llamas 1–5 and 7 and 8, respectively. Llama 6 was not included in the figure for purposes of scaling because it was considerably older (67 months) and heavier (80 to 86 kg) at the time of initial evaluation.

kg at birth. Most owners first noticed that the crias appeared smaller than those of similar age (between 4 and 9 months). Several owners also observed that affected llamas were unusually docile and did not play actively with other llamas in the herd. Llama age at initial examination either at the Oregon State University Veterinary Teaching Hospital (VTTH) or by the referring veterinarian was between 1 and 23 months, with median age of 7.5 months. Because some of the initial examinations were conducted on the owner's farm, some of the initial body weight values were estimates. Llamas were born in California and Oregon and raised in California, Oregon, and Idaho.

All llamas were extremely thin, with prominent ribs, spine, and ilia. Several llamas had an arched appearance to the back, particularly when walking. Larger and older llamas 6, 7, and 8 were more nearly normal in appearance and gait. Although the coat on llamas 1–3 and 6–8 was moderately dense, the coat on llamas 1–3 and 7 was dull, and the coat on llamas 4 and 5 was thin and dull. Llamas 1–3, 5 (Fig 1), 7, and 8 had moderate to severe valgus of the thoracic and/or pelvic limbs (Table 1).

Llamas 1–5, 7, and 8 were considerably underweight (Fig 2). Although llama 6 was underweight for its age, it reached a peak weight of 86 kg at 69 months of age and was more active and alert than the older llamas of this study.

Erythrocyte morphologic findings—Erythrocyte morphology was abnormal, with marked anisocytosis and poikilocytosis in all llamas. Cytoplasmic extensions from one or both poles of the erythrocytes were observed in > 5% of the RBC from all llamas. A high percentage of cells had uneven distribution of hemoglobin within the cytoplasm, with
Table 1.—Characteristics of llamas with failure to thrive

<table>
<thead>
<tr>
<th>Llama No.</th>
<th>Gender</th>
<th>Age* (mo)</th>
<th>Weight† (kg)</th>
<th>Limbs‡</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>F♀</td>
<td>8</td>
<td>32½</td>
<td>Ald-thoracic</td>
<td>Vaginal discharge, unthriftiness</td>
</tr>
<tr>
<td>2</td>
<td>F♀</td>
<td>6</td>
<td>29</td>
<td>Ald-thoracic</td>
<td>Pronounced humping of back</td>
</tr>
<tr>
<td>3</td>
<td>F♀</td>
<td>1</td>
<td>45½</td>
<td>Ald-thoracic</td>
<td>Normal CBC, serum chemical profile, and thyroid function at 1 month of age</td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>7</td>
<td>44</td>
<td>Normal</td>
<td>Low birth weight, chronic unilateral ear infection starting at 3 months of age</td>
</tr>
<tr>
<td>5</td>
<td>M</td>
<td>11</td>
<td>44#</td>
<td>Ald-thoracic</td>
<td>Premature (8 kg birth weight), chronic coccidiosis when young</td>
</tr>
<tr>
<td>6</td>
<td>F</td>
<td>23</td>
<td>82</td>
<td>Normal</td>
<td>Born at approximately 3 years of age, aborted at unknown stage of gestation</td>
</tr>
<tr>
<td>7</td>
<td>F</td>
<td>5</td>
<td>65**</td>
<td>Ald-thoracic and pelvic</td>
<td>Thin, good coat</td>
</tr>
<tr>
<td>8</td>
<td>M</td>
<td>13</td>
<td>55</td>
<td>Slight Ald-thoracic</td>
<td></td>
</tr>
</tbody>
</table>

*Age at which llamas were examined at the veterinary teaching hospital or by the referring veterinarian; †Body weight when examined at teaching hospital; ‡Nonradiographic evaluation of thoracic and pelvic limbs; #Llamas 1–3 were full sisters; ½weight at 5 months; *weight at 5 months; #weight at 32 months; **weight at 13 months.

M — male; F — female; Ald — angular limb deformity.

Figure 3.—Photomicrograph of clinically normal (a) and abnormal (b) llama erythrocytes. Blood samples were smeared, air-dried, and stained with Wright-Giesma stain. In the erythrocyte preparations from abnormal llamas, notice the asymmetric hemoglobin distribution, the cytoplasmic extensions from one or both poles of the RBC, the cell folding, and extreme shape variability. Slight anisocytosis and poikilocytosis are sometimes observed in blood samples from clinically normal llamas. Bar = 8 μm.

Hemoglobin clumping in either one half of the cell or in the tips of the erythrocytes. Condensation of hemoglobin in the pole regions of the cells resulted in a thin, semitranslucent region in the center of the cells. Other cells were folded in the regions where hemoglobin had been displaced toward the poles (Fig 3). Electron microscopy of affected cells revealed a characteristic condensation of hemoglobin within the ends of the erythrocytes (Fig 4). The mean, SD, and range for the mean corpuscular volume (MCV), mean corpuscular hemoglobin concentration (MCHC), and mean corpuscular hemoglobin (MCH) erythrocyte indices for 36 samples collected from 8 llamas were 27.5, 4.3, 16.3 to 39.5 fl; 44.5, 5.4, 33.0 to 54.3 g/dl; and 14.0, 5.0, 9.5 to 27.7 pg, respectively. Normal ranges for MCV and MCHC in llamas are 21.0 to 28.0 fl and 43.2 to 46.6 g/dl, respectively.a

Although percentages varied somewhat between llamas, most had > 80% affected RBC in samples collected over periods ≤ 5 years. Some severely affected llamas had nearly 100% abnormal cells. Only llama 6 had appreciable reduction in the percentage of affected cells during the course of the study. In samples obtained from llama 6 at 23 months of age, severe anisocytosis and poikilocytosis were evident. When initially examined at the VTH at 63 months of age, llama 6 had PCV of 20% and high percentage of abnormal erythrocytes. Shortly before death attributable to undetermined cause(s) at 76 months of age, the PCV had increased to 29.4%, and the percentage of abnormal erythrocytes had decreased to < 20%. Slight erythrocyte anisocytosis and poikilocytosis are common observations in samples obtained from clinically normal llamas.

Anemia—One of the most consistent hematologic abnormalities was moderate to severe anemia

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aWeiser G, Colorado State University, Medicine, Fort Collins, Colo: Personal communication, 1988.
Figure 4—Transmission electron micrographs of erythrocytes from affected llamas. 

a—Abnormal hemoglobin distribution gives the erythrocytes their characteristic appearance. Bar = 1.0 μm. 
b—Granular material is probably crystallized hemoglobin (arrowhead; a). Bar = 0.7 μm.

Figure 5—Packed cell volume plotted as a function of age in affected llamas. The shaded region represents the lower range of PCV in clinically normal males and females (26 to 42%). Blood samples from llama 6 were collected for longer than 42 months. Only samples collected prior to 42 months of age in llama 6 have been presented for reasons of clarity. The symbols O, ●, ▲, □, ▲, F, and ▼ are used to represent llamas 1–8, respectively.

Although the llamas were moderately to severely anemic, appreciable (> 1%) reticuloocyte response was observed in only llama 1 at 8 months of age (10.1%). By 11 months of age, the PCV in the same llama had decreased to 15% and no reticuloocytes were subsequently observed. Nucleated erythrocytes were observed in blood smears obtained from 6 llamas (8 of 36 samples; mean, 10.4 nucleated RBC/100 WBC; range, 1 to 37 nucleated RBC/100 WBC). The regenerative leukogram has not been adequately described in clinically normal llamas, precluding accurate characterization of the hematopoietic response.

Thyroid function evaluation—Baseline T₃ concentration and response to thyrotropin administration was not consistent; initial concentration ranged from low to normal (Fig 6 top). In contrast, baseline T₄ concentration was low and a markedly diminished response to thyrotropin was evident (Fig 6 bottom). Orally administered thyroid supplementation was attempted in 4 llamas, using various compounds and dosage regimens. Although T₃ and T₄ values in some of the llamas increased to normal, clinical improvement was not observed.

Vitamin and trace mineral analysis—Most selenium, vitamin E, zinc, and copper concentrations were within normal ranges reported for ruminants or llamas (Table 2). Serum iron concentration in llamas 1–6 and 8 was lower than normal, whereas serum TIBC concentration was within the normal range for llamas. Orally administered iron supplementation was attempted in llamas 1–3, 5, 6, and 8, using a variety of products. Owner compliance was variable, and consistent increase in PCV

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Soaxine, Daniele Pharmaceuticals, St Petersburg, Fla.


Synthroid, Boots-Flint, Inc, Lincolnshire, Ill.

Lixitonic, Beecham Laboratories, Bristol, Tenn.

Red Cell, Omaha Vaccine, Inc, Omaha, Neb.
was not observed. Erythrocyte morphology was unchanged.

**Serum biochemical findings**—In all llamas, SUN, creatinine, total bilirubin, GGT, ALP, and glucose values were within normal ranges. Serum protein concentration had no consistent changes. Serum CK and ALT activities were high in llama 3 during a period of inappetence and increased lethargy. Serum CK activity was also high in llama 4 in samples obtained shortly before its death. Of 23 llamas, 15 had normal phosphorus concentration, 1 was hyperphosphatemic, and 7 were hypophosphatemic.9

**Parasites**—All llamas had zero or low (<100 eggs/g of feces) fecal egg count.

**Radiographic findings**—Llamas 1 and 4–8 were evaluated radiographically. Valgus deformities of the thoracic limbs were detected in llamas 1, 4, and 5. Sites of deviation included the distal portion of the radius and ulna in llamas 1 and 5, radial diaphysis in llama 4, and distal portion of the metacarpus in llama 1. Bone age and architecture were considered normal in llamas 4 and 8. Distal radial, ulnar, and metacarpal flaring was visible in llamas 1 and 7. Flaring was severe, with nonsymmetric bulbous enlargements evident in llama 1. Focal osteopenia in the metaphyses was observed in llamas 1, 5, 6, and 7. The zones were markedly discrete in llama 6, set off from more-normal tra-

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**Table 2**—Vitamin and mineral concentrations* in llamas with failure to thrive

<table>
<thead>
<tr>
<th>Llama No.</th>
<th>Selenium (µg/dl)</th>
<th>Vitamin E (µg/dl)</th>
<th>Copper (µg/dl)</th>
<th>Zinc (µg/dl)</th>
<th>Iron (µg/dl)</th>
<th>TIBC (µg/dl)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.210 to 0.226</td>
<td>2.10</td>
<td>40</td>
<td>30</td>
<td>18 to 20</td>
<td>300 to 463</td>
</tr>
<tr>
<td>2</td>
<td>0.099</td>
<td>1.19</td>
<td>40</td>
<td>39</td>
<td>16</td>
<td>351</td>
</tr>
<tr>
<td>3</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>68</td>
<td>411</td>
</tr>
<tr>
<td>4</td>
<td>0.118</td>
<td>2.07</td>
<td>39</td>
<td>112</td>
<td>11</td>
<td>264</td>
</tr>
<tr>
<td>5</td>
<td>0.095</td>
<td>0.82</td>
<td>55</td>
<td>33</td>
<td>64</td>
<td>261</td>
</tr>
<tr>
<td>6</td>
<td>0.213</td>
<td>0.90</td>
<td>50</td>
<td>32</td>
<td>58</td>
<td>348</td>
</tr>
<tr>
<td>7</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>8</td>
<td>0.191</td>
<td>1.27</td>
<td>31</td>
<td>172</td>
<td>7</td>
<td>333</td>
</tr>
</tbody>
</table>

*Normal concentration ranges for vitamin and mineral concentrations in llamas and other species: Selenium—0.08 to 0.50 µg/ml (sheep), 0.07 to 0.30 µg/ml (cows); Vitamin E—0.65 to 1.50 µg/ml (sheep), 2.0 to 4.0 µg/ml (cows); Copper—58 to 100, 80 to 200 µg/dl (sheep), 33 to 35, 80 to 150 µg/dl (cows); Zinc—80 to 150 µg/dl (sheep), 70 to 140 µg/dl (cows); Iron—70 to 148 µg/dl (llamas), 230 to 370 µg/dl (llama). NA = not available; TIBC = total iron-binding capacity.

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* was not observed. Erythrocyte morphology was unchanged.

**Serum biochemical findings**—In all llamas, SUN, creatinine, total bilirubin, GGT, ALP, and glucose values were within normal ranges. Serum protein concentration had no consistent changes. Serum CK and ALT activities were high in llama 3 during a period of inappetence and increased lethargy. Serum CK activity was also high in llama 4 in samples obtained shortly before its death. Of 23 llamas, 15 had normal phosphorus concentration, 1 was hyperphosphatemic, and 7 were hypophosphatemic.9

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**Figure 6**—Changes in serum triiodothyronine (T₃) and thyroxine (T₄) concentrations before and at 2, 4, 6, 8, and 24 hours after administration of 3 IU of thyrotropin/44 kg of body weight. The shaded regions represent the 80% confidence intervals for the predicted response to thyrotropin.4

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beculation by metaphyseal growth lines. Growth lines were also seen in llama 1.

**Bone marrow biopsy findings**—Bone marrow biopsy was performed on llamas 1, 2, 4–6, and 8. Cellular density was normal in llamas 1 and 6, slightly decreased in llamas 2, 4, and 5, and markedly decreased in llama 8. Megakaryocyte numbers were low in llamas 4 and 6. The mean myeloid-to-erythroid ratio (M/E) was 1.2 (range, 0.6 to 2.6). In comparison with normal M/E established for domestic ruminants, only llama 5 had abnormal M/E (2.6). Relative percentages of various cell stages were similar to those observed in ruminants. In all llamas, the erythropoietic precursors had small amounts of cytoplasm. On the basis of relative paucity of hemosiderin, iron content appeared to be low in all marrow samples.

**Necropsy findings**—Necropsy was performed on llamas 1, 2, and 4–7. All llamas were emaciated; llamas 1, 2, 5, and 7 had AFD of the thoracic limbs, and bone marrow from the femur of all llamas was markedly pale. Other gross anatomic changes were not consistently observed. Other specific changes included large peribronchial lymph nodes and cystic structures at the apex of the heart in llama 4, and a dilated esophagus in llama 6.

**Histopathologic findings**—In all llamas, the thyroid gland had marked variation of follicular size and in tinctorial properties of the colloid. In most llamas, the colloid stained weakly, with little recognizable scalloping of colloid to indicate phagocytosis by the follicular epithelial cells. Within each gland were large regions of small follicles with tall epithelium and no discernible colloid. A few corpora amylaceae-like spherical densities were observed within the colloid. In these areas, groups of degenerate follicles with pyknotic nuclei frequently had migrated to lie within the colloid. Lipofuscin was evident in follicular epithelial cells in all hypothyroid llamas. The accumulation of this pigment was variable, from very dense to a light dust-
ing of lipofuscin granules in the apical cytoplasm. In 1 llama, the thyroid gland was replaced by adipose tissue. Thyroid glands did not have inflammatory cell infiltrate. Other relevant histopathologic changes were not observed in other tissues.

**Discussion**

Failure to thrive has, in all probability, multiple causes in llamas. Of 23 llamas examined because of initial problems of unthriveness or failure to grow at a normal rate or for evaluation of ALD, 8 had abnormal erythrocyte morphology and low PCV and were hypothyroid. Of the remaining 15 llamas, 2 were euthyroid and had transitory erythrocyte changes that resolved within 2 months after initial evaluation. An additional 8 llamas were not anemic and were euthyroid, but had small body size. Most of the llamas in this latter group also had moderate to severe ALD. One other diminutive llama, for which thyroid function was not evaluated, had normal PCV and normal erythrocyte morphology. Finally, 4 other llamas were classified as not anemic and marginally hypothyroid. Some of these llamas had other concurrent metabolic problems. Parasitism was not identified as a primary problem in any llama.

Obvious correlation between geographic location and incidence of similarly affected llamas was not evident. Llamas studied were raised in Idaho, Oregon, and California, and 2 additional llamas have been evaluated in Michigan. Brief clinical descriptions have been published concerning 4 llamas examined in Colorado that have some of the same characteristics described in this report. Llamas of the Colorado group were anemic and of small stature. Changes in serum iron concentration and erythrocyte morphology were not reported. This widespread but sporadic geographic distribution suggests that toxic plants or other environmental agents probably are not a factor in the pathogenesis of this problem.

The genetic component of this problem is more difficult to evaluate. Because 3 of the affected llamas were full sisters (llamas 1-3), there is a strong suggestion of a genetic component to the condition. The dam’s fourth cria, a male from a different sire, has been evaluated at approximately 2-month interval since birth and appears to be growing at a normal rate. The llama is currently > 12 months old, has not had signs of anemia or erythrocyte dyscrasia, and has baseline T₃ and T₄ concentrations within normal limits. In contrast to the familial aspects of the problem suggested by findings in llamas 1-3, llama 8 has a full brother, approximately 1 year older and of normal stature, weighing > 150 kg. The genealogy of the other 5 affected llamas is incomplete. Interestingly, a small number of males were repeatedly found to be the sire, grandsire, or great-grandsire of all affected animals. Because the condition has been observed in 3 males and 5 females, it does not appear to be a sex-linked recessive trait, assuming a common genetic cause for all cases.

The role of the thyroid gland in the pathogenesis of the problem is unclear. Although severe hypothyroidism has been associated with mild normochromic normocytic anemia, it was not established in this group of llamas that a similar correlation exists between thyroid function and development of anemia and erythrocyte dyscrasia. It has also been clearly shown in other species that basal thyroid function may decrease in response to some chronic disease conditions, the “euthyroid sick syndrome.” Low baseline T₄ concentration may represent a similar condition in llamas, although the hyporesponsiveness of the thyroid gland to thyrotropin administration may indicate primary hypothyroidism.

Although the thyroid gland of hypothyroid llamas had histopathologic changes consistent with degeneration and follicular atrophy, similar changes were also seen in a few llamas with normal thyroid function. Thus, distinguishing affected llamas solely by histopathologic changes in the thyroid gland cannot be readily accomplished. The thyroid gland in some apparently normal llamas had considerable lipofuscin deposits and, in a few llamas, had scattered groups of small follicles. The differentiating features in affected llamas were in the tinctorial properties of the colloid and the clusters of degenerate, disorganized follicles. The cause of the thyroid dysfunction is unknown.

Thyroid hormone replacement did not consistently result in clinical improvement. Problems with hormone replacement included lack of owner compliance, palatability of the thyroid supplements, and adjustment of dosages. Although some llamas had minimal or transitory clinical improvement after initiation of thyroid supplementation, all became lethargic when supplementation was discontinued or when dosage was decreased. This suggests that exogenous hormones were being absorbed and suppressing endogenous thyroxine production. Within 4 weeks after discontinuation of treatment, 3 of the treated llamas died or were euthanatized because of weakening physical condition. If primary hypothyroidism was a relevant factor in the pathogenesis, hormone replacement (> 2 months’ duration) would have been anticipated to stimulate erythropoietic activity.

Angular limb deformities are commonly encountered in domestic animals including horses, and dogs. Causes include in utero malposition, vascular anomalies, hereditary achondroplasia, osteochondrodysplasias (including mucopolysaccharidoses and other storage diseases), rickets, trauma to open growth plates, and nutritional and endocrine disturbances. The ALD in llamas 1, 2, 4, and 5 were not apparent at birth and developed parallel with the observation of impaired growth. Lack of relevant osseous radiographic abnormalities other than osteopenia ex-
cluded most hereditary and congenital causes. The normal appearance at birth and apparently normal physes and epiphyses excluded congenital hypothyroidism. Osteopenia may result from malnutrition, disuse, or chronic hypoxia. These conditions all may have contributed to the low growth rate, weak bone, and subsequent limb deformities. Llama RBC previously have been characterized as having an elliptic shape, with a central zone of pallor, a thin, flat profile; and uniform dispersal of hemoglobin throughout the cytoplasm. Llama RBC also are characterized by an unusually low degree of deformability, compared with other mammalian RBC. The combination of elliptic shape and relative rigidity of the erythrocyte membrane results in an RBC with relatively high surface area to volume ratio, which facilitates rapid oxygen diffusion. Adaptations of llama RBC to high altitude and low oxygen availability include an unusually high hemoglobin oxygen-binding affinity displacing the oxygen hemoglobin dissociation curve to the left; high absolute intracellular hemoglobin concentration; and differences in 2,3 diphosphoglycerate-binding affinity. These erythrocyte characteristics may partially explain these llamas' ability to tolerate severe, chronic anemia.

It is not clear whether the erythrocyte dyscrasia observed in these llamas was a primary problem or a normal RBC response to anemia. Unlike non-camelid species, some degree of anisocytosis and poikilocytosis can be seen in blood samples obtained from nonanemic healthy llamas. Similarly, slight cytoplasmic extensions are sometimes seen in a small percentage of RBC. In comparison with clinically normal llamas, however, changes in RBC from affected llamas were far more extensive and involved a large percentage of RBC (> 80%).

The clinical relevance of lack of reticulocytes in blood smears from the anemic llamas is uncertain. In dogs, cats, sheep, pigs, and cattle, an increase in reticulocyte numbers is considered a good indicator of a regenerative erythroid response whereas in horses, a similar response is not observed. Studies evaluating the normal response to blood loss in llamas have generated conflicting results. One group reported that nucleated RBC were a good indicator of a regenerative response to anemia. This is in contrast to our unpublished work in which a 40% loss of the llamas' blood volume over a 2-week period failed to elicit an appreciable release of either nucleated RBC or reticulocytes into the circulation. It is possible that a reticulocyte and/or nucleated RBC response may be observed in llamas only after more acute or chronic blood loss. Bone marrow biopsies did not indicate any consistent abnormalities to explain the erythrocyte dyscrasia. Although there was strong evidence of a decrease in erythrocyte production in llamas 5 (M.E., 2.6) and 8 (low bone marrow cellularity with normal M.E.), similar changes were not observed in the other llamas. The apparent decrease in cytoplasmic volumes of erythrocyte precursors in combination with low marrow iron content were consistent with a diagnosis of iron-deficiency anemia in these llamas.

Iron-deficiency anemia has been recognized in a range of species including people, pigs, cattle, horses, dogs, and cats. The low serum iron concentrations in the llamas indicate that chronic iron deficiency may be a factor in the development of the severe anemia seen in this species. Orally administered iron supplementation in 6 llamas did not, however, result in an increase in PCV or resolution of the dyscrasia. In llamas in which iron concentration was measured multiple times, consistent changes were not observed in either serum iron or TIBC concentration. This indicates inappropriate supplementation dosages and/or formulations or failure of intestinal iron absorption. Although most iron-deficiency anemias are usually associated with enteric blood loss, gross or histologic changes to suggest chronic enteric blood loss were not evident. It has not been determined which, if any, of these problems are applicable to llamas. To further address the possible role of defects in iron absorption, injectable iron supplementation was started in llamas 8. The dyscrasia resolved, and the PCV increased to > 40% after treatments at 2-week intervals for 6 months.

Because normal values for blood copper and zinc concentrations have not been published for llamas, it is not possible to adequately assess the mineral status of our llamas. Although copper deficiency has been documented to induce anemia in some species, the copper concentration measured in the llamas of this study was similar to that reported for sheep and cattle. Likewise, zinc deficiency has been shown to cause growth impairment and anemia in some domestic livestock species. The zinc concentration measured in the affected llamas was similar to that reported in cattle and sheep as well as in healthy llamas (data not shown).

The cause and clinical relevance of hypophosphatemia in 5 llamas was unclear. Hypophosphatemia has been reported as a problem in alpacas with stunted growth and ALD. Hypophosphatemia has also been associated with high phosphorus excretion rates in alpacas; however, severe anemia and erythrocyte dyscrasia have not been reported as concurrent problems. Supplemental dietary phosphorus has been reported to correct the problem. Phosphorus supplementation was not investigated in our llamas.

The prognosis for llamas diagnosed with this problem is guarded to poor. Of the 8 llamas evaluated in this study, only 2 are still alive. Llamas 4, 6 normal ranges established by Dr. A. Morrie Craig, Oregon State University, Corvallis, Ore.
6 Fowler M, University of California, Davis, Calif: Personal communication, 1990.
5, and 6 were evaluated at the VTH for periods that ranged between 4 and 13 months. Although the llamas were carefully monitored, given access to good forage, repeatedly dewormed, and given thyroid hormone replacement, none responded appreciably during this period. Llamas 1, 4, and 7 were euthanatized at 39, 16, and 33 months of age, respectively, because of severe weakness, general debilitation, and inability to maintain body weight and condition. Llama 2 died during sample collection, and llamas 5 and 6 died at 35 and 76 months of age in the field. Llama 3 (28 months) is still markedly underweight, growing poorly, and has rough coat and the humped appearance seen in most of the affected llamas. The llamas' response to injectable iron supplementation has been variable. Owner compliance with injectable iron administration to llama 3 has been inconsistent. Llama 8 (>24 months) is still underweight, but has good coat and normal PCV and erythrocyte morphology after prolonged injectable iron supplementation.

The cause, either single or multiple, of this clinical condition has not been resolved. Although hypothyroidism was a consistent finding, a correlation between the erythrocyte dyscrasia and thyroid dysfunction has not been established. Likewise, the question of whether the erythrocyte dyscrasia was a primary problem or normal response to severe chronic anemia in this species has not been resolved. Finally, low serum iron concentration was a consistent observation, but the underlying cause of the deficiency is unknown. Owing to the multitude of unresolved issues, the clinical importance of the problem to the llama industry, and the poor prognosis for affected llamas, research should focus on the dynamics of iron and thyroid metabolism, erythrocyte function and dynamics, and normal skeletal growth and development.

References