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From the Experimental Station of the Veterinary Institute, Skara, and the Department of Pathology, College of Veterinary Medicine, Swedish University of Agricultural Sciences, Uppsala, Sweden.

PATHOLOGY OF BOVINE LAMINITIS ESPECIALLY AS REGARDS VASCULAR LESIONS*

By

Lennart Andersson and *Anders Bergman*

ANDERSSON, L. and A. BERGMAN: *Pathology of bovine laminitis especially as regards vascular lesions.* Acta vet. scand. 1980, *21*, 559—566. — Macro- and microscopical changes in the hooves of 14 cattle having a clinically established diagnosis of laminitis are described. Deviation of the pedal bone was found in 10 of the animals. In acute laminitis, the microscopical changes in the corium were hyperaemia, oedema, thrombosis and haemorrhages. Degenerative changes were found in the epidermis especially in the vicinity of thromboses of vessels in the corium. In chronic laminitis, arteriolosclerosis and arteriosclerosis were constant findings in the corium. There was also a high frequency of chronic thrombi and chronic granulation tissue. Prominent features in the lamellae epidermales were hyper- and parakeratosis. As judged from changes in arterioles and arteries, hypertension is suggested to be a pathogenetic factor in bovine laminitis.

cattle; laminitis; histology; arteriolosclerosis; arteriosclerosis.

The most comprehensive descriptions of the pathology of bovine laminitis have been given by *Nilsson* (1963) and *Maclean* (1971). In acute laminitis, blood congestion and haemorrhages were macroscopically observed in the corium. In a few cases haemorrhages were seen in the horn. Hyperaemia, oedema, thrombi, haemorrhages and accumulations of lymphocytes, histiocytes and fibroblasts were microscopically observed in the corium. Very few mast cells and no eosinophils were present. In the epidermis, the cells of the stratum germinativum and stratum

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spinosum were enlarged and disorientated, with a partial or complete disappearance of keratogenic substance. Acidophilic keratin bodies were found in the lamellae epidermales.

In chronic laminitis, *Nilsson* observed a high frequency of pedal bone deviation, hoof deformation and old haemorrhages in the horn of the sole. Microscopically, both authors observed old thrombi, accumulations of mononuclear cells, chronic granulation tissue with marked proliferation of capillaries, and heavy fibrosis in the corium. Fibrosis was also common around nerves. The lamellae coriales were thicker, and the lamellae epidermales thinner than normal. In the lamellae coriales, vessels appeared in increased numbers. *Maclean* observed dilation of capillaries and veins, as well as changes in arteries and arterioles including intimal proliferation, hypertrophy of the tunica media, and fibrosis of the tunica adventitia. *Nilsson* reported a marked increase in the number of mast cells in chronic laminitis compared with acute laminitis. No such difference was found by *Maclean*. Both authors noted branching of the papillary corium of the sole. *Nilsson* observed a reduction of keratogenic substance in the epidermis, and the presence of acidophilic keratin bodies in the lamellae epidermales.

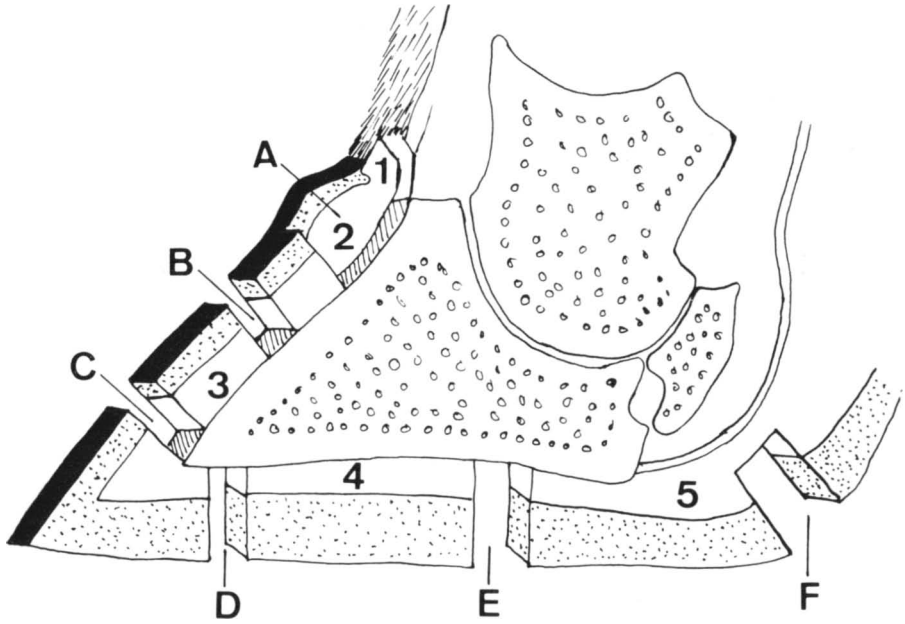
The aim of this investigation is to give an account of pathological changes in clinically diagnosed cases of laminitis.

MATERIAL AND METHODS

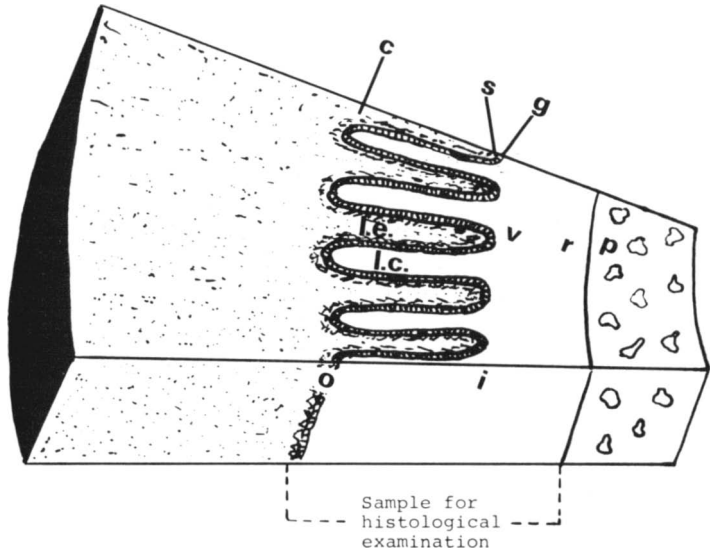
The clinical material comprised 13 heifers and cows and one bull, 1½—8 years old, with a clinically established diagnosis of laminitis. The animals were part of a larger clinical investigation (*Andersson* 1980). Eight animals were of the Swedish Red and White (SRB) breed and six were Swedish Friesians (SLB). Most of them were slaughtered because of persistent lameness. The period between the first observed clinical symptoms and slaughter varied from 1 to 160 days.

The reference material consisted of five bulls about 1 year old, three non-pregnant heifers 1—2 years old, and three cows 3—7 years old. At the time of slaughter these animals were healthy and had not previously been affected by any observable hoof disease.

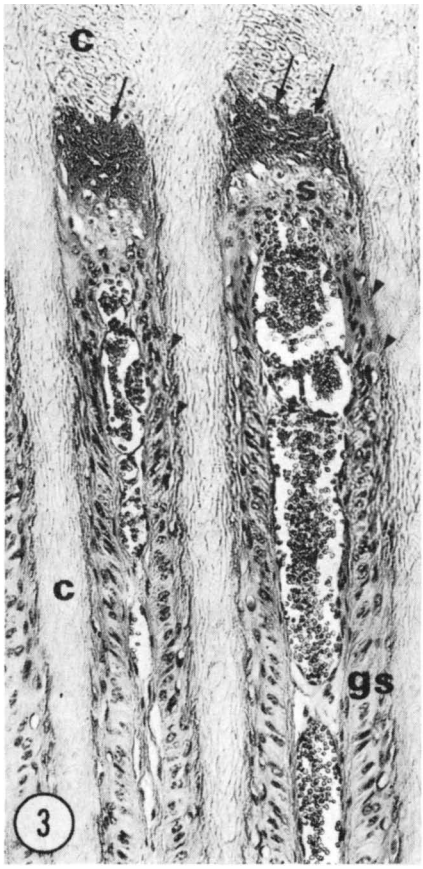
At slaughter medial and lateral hooves of one forefoot and one hind foot were preserved for pathological-anatomical ex-

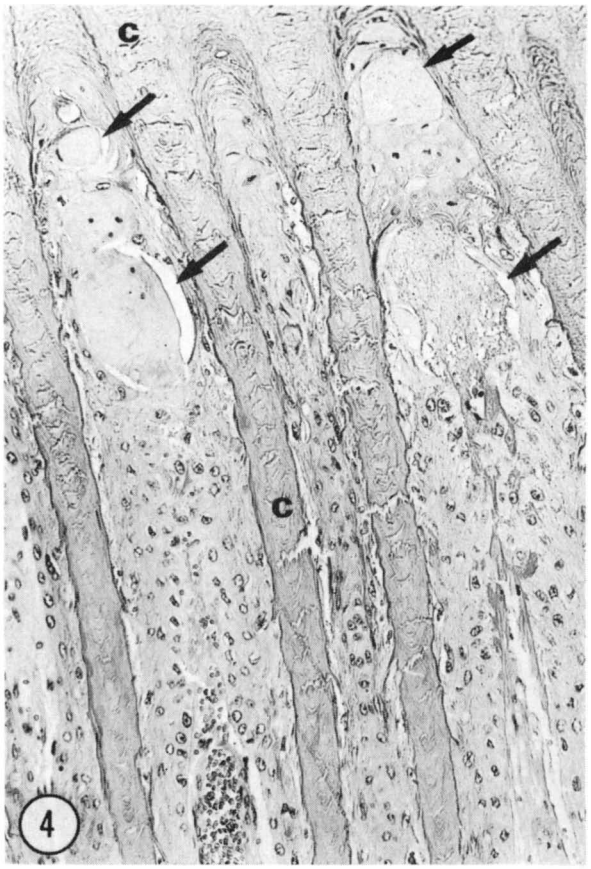


F i g u r e 1. Sagittal slice in the centre of the bovine digit. Specimens for histological examination were taken in A (sagittal section) and B-F (cross section).
1, perioplic corium; 2, coronary corium; 3, lamellar corium; 4, solar corium; 5, bulbar corium.



F i g u r e 2. Cross section in the wall (Fig. 1 B or C).
p, pedal bone; r, stratum reticulare; v, stratum vasculosum; l.c., lamella corialis; l.e., lamella epidermalis; g, stratum germinativum; s, stratum spinosum; c, stratum corneum; i, inner, and o, outer border of stratum lamellatum.

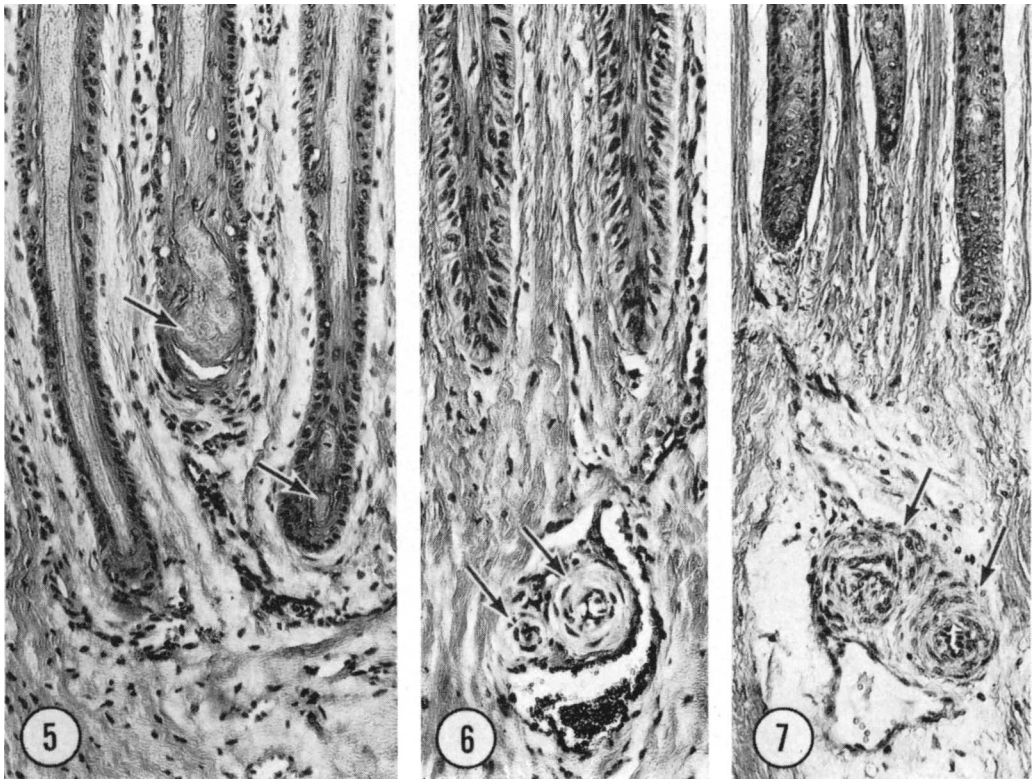




Figures 3 and 4. Cross sections distally in the wall (Fig. 1 C), outer part of the stratum lamellatum.

Figure 3. Reference material. Bull, 1 year old. Normal histology. g, stratum germinativum; s, stratum spinosum; c, stratum corneum. Keratogenic substance is seen as dark areas (arrows) and as thin dark rims (arrow heads). Haematoxylin & Eosin, × 160.

Figure 4. Acute laminitis. Dairy cow, 3 years old.
Fibrinous thrombi (arrows) are seen in peripheral capillaries. The cells in the stratum germinativum and spinosum are enlarged, weakly stained and locally pycnotic and vacuolized. There is a decrease in keratogenic substance. The stratum corneum (c) is fragile and easily ruptured at sectioning. There is compression of the capillary bed in one lamella.
Haematoxylin & Eosin, × 160.



Figures 5, 6 and 7. Cross sections distally in the wall (Fig. 1 C), stratum vasculosum and inner part of the stratum lamellatum.

Figure 5. Chronic laminitis. Dairy cow, 8 years old.
Note the retracted epidermal lamella, presence of keratin bodies (arrows) and the accumulation of inflammatory cells (lymphocytes and macrophages) around capillaries in the corium.
Haematoxylin & Eosin, × 160.

Figure 6. Reference material. Bull, 1 year old. Normal histology.
Arrows indicate arterioles in the stratum vasculosum.
Haematoxylin & Eosin, × 160.

Figure 7. Chronic laminitis. Bull, 4 years old.
The figure illustrates thickening of arterioles (arrows), with proliferation of smooth muscle cells in the vessel walls.
Verhoeff's elastin, × 160.

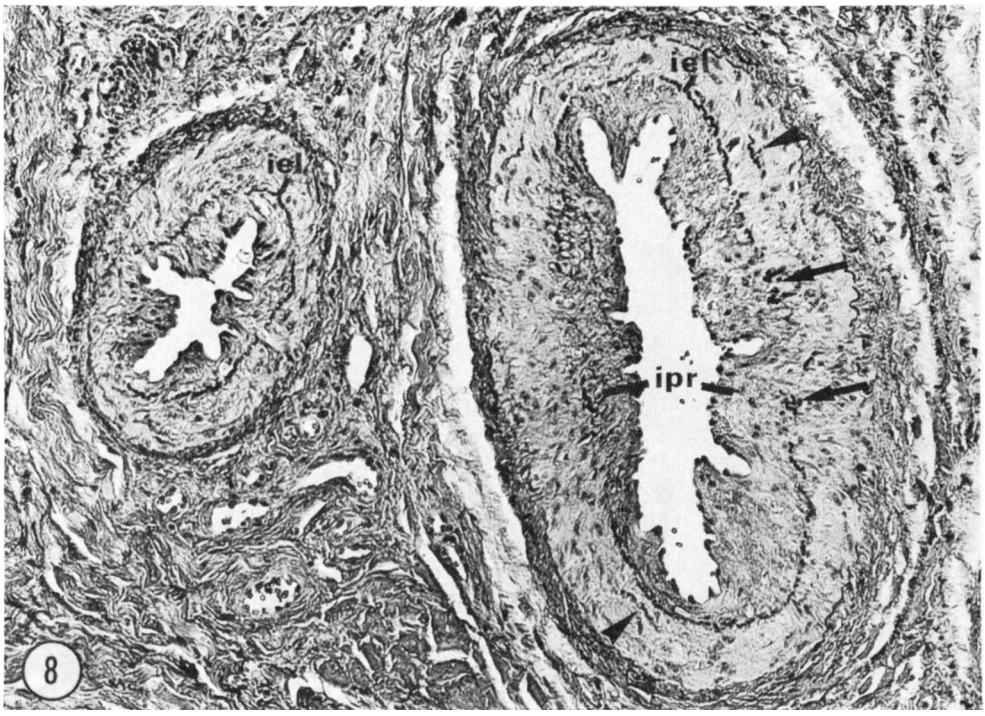


Figure 8. Arteriosclerosis in chronic laminitis. Dairy cow, 5 years old. Cross section in the solar corium (Fig. 1 D), illustrating fragmentation (arrows) of the internal elastic lamina (iel), presence of pseudoelastic fibres (arrow heads) and intimal proliferation (ipr) of smooth muscle cells.
Verhoeff's elastin, × 165.

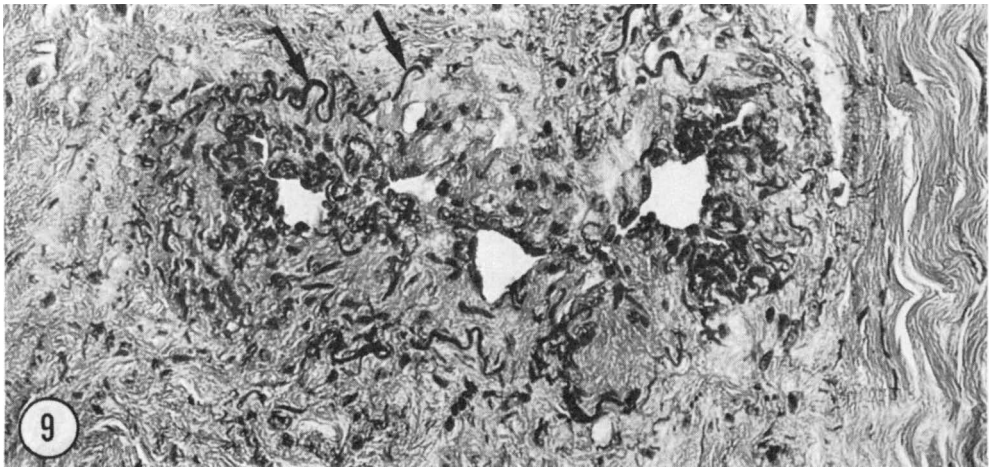


Figure 9. Advanced arterial damage in chronic laminitis. Dairy cow, 3 years old. Sagittal section in the coronary corium (Fig. 1 A). Arrows indicate fragments of the internal elastic lamina. Intimal proliferation and presence of pseudoelastic fibres as in Fig. 8.
Verhoeff's elastin, × 335.

amination. Each hoof was sawn so that a sagittal slice in the centre of the hoof was obtained. From the sagittal slice samples were cut from the perioplic, coronary, lamellar, solar and bulbar regions (Fig. 1 A-F), comprising the corium and part of the epidermis (Fig. 2). These samples were fixed in 10 % formalin and embedded in paraffin. Sections 5 μm thick were stained with haematoxylin and eosin, Verhoeff's elastin, Heidenhain's iron haematoxylin, Masson's trichrome, toluidine blue and periodic acid-Schiff. Sometimes selective staining techniques were used, such as Martius' scarlet blue for fibrin, Perls's reaction for iron pigments, von Kossa's method for calcium salts, and Scarlet red for fat.

The nomenclature of the anatomical features used is according to Nomina Anatomica Veterinaria (1973) as referred to by *Greenough* (1978).

RESULTS

Reference material. In the reference material, no macroscopical changes were observed. Microscopically the bulls showed slight perivascular accumulations of lymphocytes, plasma cells and macrophages in the corium. A few eosinophils and single mast cells were occasionally seen perivascularly in the perioplic and coronary corium. The stratum lamellatum formed a regular pattern (Figs. 3 and 6). In three females, a similar histological picture existed, with the addition of a cushion-like intimal proliferation locally in the arterioles. In the remaining three females, there were obvious pathological changes. In the lamellae coriales, at the innermost part of the stratum lamellatum, local moderate pericapillary accumulations of lymphocytes and macrophages were seen. In the adjacent lamellae epidermales hyper- and parakeratosis were present. Thus, the lamellae were often retracted and contained large, irregular, keratin bodies, some of which contained nucleated cells. The cells in the stratum germinativum and stratum spinosum were small and hyperchromatic. In some areas there was an apparent loss of these cells. The changes agreed with the histological picture in Fig. 5. Arteriosclerosis similar to the histological picture in Fig. 8 was found in one of the three females.

Clinical material. The clinical material could be histologically subdivided into one acute case and 13 chronic cases, eight of which showed signs of acute exacerbation. Macroscopically,

haemorrhages in the horn of the sole as well as deviation of the pedal bone in all hooves examined were seen in the acute case. Recent and/or old haemorrhages and deviation of the pedal bone, sometimes combined with a concave form of the hoof wall, were found in nine of the chronic cases. Pedal bone deviation was present in 35 %, or 18 of the 52 hooves examined (two lateral and four medial forehooves, seven lateral and five medial hind hooves).

Microscopically, the changes in the corium of the acute case comprised hyperaemia, oedema, focal infiltration of neutrophils, local fibrinous thrombi, local fibrinous exudation, and haemorrhages. The thrombi were present predominantly in the outermost part of the stratum lamellatum in sections from the distal part of the wall (Fig. 4). In the vessel walls, especially in small arteries and arterioles, there was a marked enlargement of the endothelial cells and of cells in the media. The latter cells also often showed nuclear hyperchromasia. Moderate pericapillary accumulations of cells, predominantly macrophages, were present. In the epidermis there were degenerative changes especially close to the sites of the thrombi (Fig. 4). Thus, the cells in the stratum germinativum and stratum spinosum were enlarged, locally vacuolized and pycnotic, and sometimes necrotic and calcified. A concomitant reduction in the staining properties of adjacent keratogenic substance was seen. The stratum corneum was fragile at sectioning. In the inner part of the stratum lamellatum the epidermal changes were restricted to a marked increased mitotic activity in the stratum germinativum and stratum spinosum.

In the chronic cases, the constant findings in the corium were local moderate to advanced arteriolosclerosis and arteriosclerosis, especially in the solar corium. These lesions sometimes resulted in the total occlusion of the vascular lumen. Thus a change often found in the arterioles was a thickening of the walls invariably associated with proliferation of smooth muscle cells (Fig. 7). The changes in the arteries were dominated by intimal prolifaration of smooth muscle cells with collagen deposits, splits and fragmentation of the internal elastic lamina, and formation of pseudoelastic fibres (Fig. 8). Occasionally the arterial walls were totally destroyed (Fig. 9). There were no signs of lipids in the arterial walls. In some cases there was locally a marked distention of arteries and veins. Other findings in the corium were chronic thrombi, chronic granulation tissue, and heavy periva-

ERRATUM

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scular accumulations of macrophages which locally contained haemosiderin. In most cases, the histological picture of the stratum lamellatum (Fig. 5) agreed with the picture found in the three females with pathological changes in the reference group. In some cases disconnected clusters of cells of the lamellae epidermales were seen at the inner part of the stratum lamellatum.

Chronic cases with acute exacerbation showed a combination of chronic and acute lesions as described above.

Mast cells and eosinophils were few in all diseased animals, and they were always localized to the perioplic and coronary corium.

DISCUSSION

Histologically, our findings in acute laminitis agree in general with those observed by *Nilsson* (1963) and *Maclean* (1971). In chronic laminitis, moderate to severe arteriosclerosis and arteriolosclerosis were constant features. Similar vascular changes were observed by *Maclean*. Another constant finding in chronic laminitis was hyperkeratosis with the formation of keratin bodies and parakeratosis. Similar "horn-like acidophilic bodies" were found also in acute laminitis by *Nilsson* and *Maclean* and in equine acute laminitis by *Obel* (1948). Mast cells were few both in acute and chronic cases in agreement with the observation by *Maclean*. *Nilsson*, on the other hand, reported an increase in the number of mast cells in chronic laminitis compared with acute laminitis.

Regarding the aetiology, *Nilsson* claimed bovine laminitis to be an expression of an allergic reaction and emphasized the role of histamine, thus supporting the theory of *Åkerblom* (1934) concerning equine laminitis. Likewise *Tizard* (1977) suggested a type I hypersensitivity reaction to be associated with the disease. Bovine laminitis is often noted in digestive disorders induced by giving high rations of concentrates, containing easily digestible carbohydrates, to non-accustomed animals (*Rosenberger* 1978). Carbohydrate overload in cattle is associated with lactic acidosis (*Dunlop & Hammond* 1965) and changes in the ruminal microflora with the appearance of bacterial endotoxins in the circulatory system (*Dougherty et al.* 1975). In agreement, lactic acidosis (*Garner et al.* 1977 a) and changes in the intestinal microflora (*Garner et al.* 1978) with the excessive release of bacterial endotoxins (*Moore et al.* 1979) are seen in equine

laminitis, induced by carbohydrate overload. The action of endotoxin in the presence of lactic acidosis may be at least partially responsible for the onset and establishment of equine laminitis (*Moore et al.*). The same hypothesis also seems adequate concerning bovine laminitis. The pathophysiological process in the hooves in acute laminitis may be summarized as a toxic influence on capillary walls, causing an unsufficient nutrient supply to the keratin producing cells with a synthesis of structurally incompetent keratin. Progressive circulatory changes may involve aggregation of erythrocytes and platelets with further loss of capillary integrity. According to another theory (*Obel*) the pathophysiological process in laminitic hooves primarily occurs in the epidermis, and the changes in the corium are secondary. Our findings in acute laminitis are dominated by circulatory disturbances, favouring the concept of a primary vascular defect.

In a clinical investigation, *Coffman et al.* (1972) observed hypertension both in acute and chronic equine laminitis. Serious progressive exacerbative cases were found to be more hypertensive than uncomplicated acute cases. Hypertension has also been demonstrated in experimentally induced equine laminitis (*Garner et al.* 1975 a, b, 1977 b). Hypertension is known to be one of the factors causing arteriolosclerosis and arteriosclerosis. Hyperplastic arteriolosclerosis is seen in human malignant hypertension (*Robbins* 1974). The lesion is characterized by a concentric laminated thickening of the arteriolar wall with progressive occlusion of the lumen. In our cases of chronic laminitis, similar hyperplastic or proliferative changes were found in the arterioles. The pathology and pathogenesis in arteriosclerosis have been described by *Cheville* (1976), among others. Microscopically, the lesions first seen in the arterial wall are breaks in the internal elastic lamina, followed by myocyte infiltration and subsequent proliferation within the intima. It is assumed that the myocytes alone are responsible for the reparatory processes seen in the artery, i.e. formation of pseudoelastic and collagen fibres. Experimental studies have shown that injury to the endothelium can be the principal cause leading to the onset of arteriosclerosis. It is also assumed that local lesions such as arteritis or systematic changes in blood pressure and flow can be influential. The deposition of thrombi has been proposed as a cause of some arteriosclerotic lesions.

The changes in arterioles and arteries, observed in our ma-

terial, indicate that hypertension, as found in equine laminitis, may also be one factor in the pathogenesis in bovine laminitis.

In an investigation of Dutch Friesian cows, *Peterse* (1980) observed a subclinical form of laminitis. Gait and standing position were normal, but changes in the hooves were found in almost all animals and comprised haemorrhages in the horn of the sole and a concave form of the hoof wall. In our reference material, changes similar to those found in chronic laminitis were present in some females, thus indicating the existence of subclinical cases of laminitis as observed by *Peterse*.

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REFERENCES

Andersson, L.: Frequency studies and clinical observations in bovine laminitis. Nord. Vet.-Med. 1980, *32*, 301—307.

Cheville, N. F.: Cell Pathology. The Iowa State University Press, Ames 1976, 454—457.

Coffman, J. R., H. E. Garner, A. W. Hahn & J. Hartley: Characterization of refractory laminitis. Proc. Amer. Ass. Equine Pract. 1972, 351—358.

Dougherty, R. W., K. S. Coburn, H. M. Cook & M. J. Allison: Preliminary study of appearance of endotoxin in circulatory system of sheep and cattle after induced grain engorgement. Amer. J. vet. Res. 1975, *36*, 831—832.

Dunlop, R. H. & P. B. Hammond: D-lactic acidosis of ruminants. Ann. N.Y. Acad. Sci. 1965, *119*, 1109—1131.

Garner, H. E., J. R. Coffman, A. W. Hahn, C. Salem & J. H. Johnson: Arterial pressure, cardiac output, plasma volume and L-lactate changes in equine laminitis. Physiologist 1975 a, *18*, 224.

Garner, H. E., J. R. Coffman, A. W. Hahn, D. P. Hutcheson & M. E. Tumbleson: Equine laminitis of alimentary origin: An experimental model. Amer. J. vet. Res. 1975 b, *36*, 441—444.

Garner, H. E., D. P. Hutcheson, J. R. Coffman, A. W. Hahn & C. Salem: Lactic acidosis: A factor associated with equine laminitis. J. Anim. Sci. 1977 a, *45*, 1037—1041.

Garner, H. E., A. W. Hahn, C. Salem, J. R. Coffman, D. P. Hutcheson & J. H. Johnson: Cardiac output, left ventricular ejection rate, plasma volume and heart rate changes in equine laminitis — hypertension. Amer. J. vet. Res. 1977 b, *38*, 725—729.

Garner, H. E., J. N. Moore, J. H. Johnson, L. Clark, J. F. Amend, L. G. Tritschler, J. R. Coffman, R. F. Sprouse, D. P. Hutcheson & C. A. Salem: Changes in the caecal flora associated with the onset of laminitis. Equine vet. J. 1978, *10*, 249—252.

Greenough, P. R.: The nomenclature of anatomical features of the bovine digits. Rep. 2nd Symp. Bovine Digital Diseases, Skara, Sweden 1978, 15—24.

Maclean, C. W.: The histology of laminitis in dairy cows. J. comp. Path. 1971, *18*, 563—570.

Moore, J. N., H. E. Garner, J. N. Berg & R. F. Sprouse: Intracecal endotoxin and lactate during the onset of equine laminitis: A preliminary report. Amer. J. vet. Res. 1979, *40*, 722—723.

Nilsson, S. A.: Clinical, Morphological, and Experimental Studies of Laminitis in Cattle. Acta vet. scand. 1963, *4*, Suppl. 1.

Obel, N.: Studies on the Histopathology of Acute Laminitis. Almquist & Wiksells Boktryckeri AB, Uppsala, Sweden 1948.

Peterse, D. J.: Judgement of Bovine Claws by the Occurrence of Sole Lesions. Thesis, Utrecht 1980.

Robbins, S. L.: Pathologic Basis of Disease. W. B. Saunders Book Company, Philadelphia, London, Toronto 1974, 602—604.

Rosenberger, G.: Krankheiten des Rindes. (Diseases of cattle). Verlag Paul Parey, Berlin und Hamburg 1978.

Tizard, J. R.: An Introduction to Veterinary Immunology. W. B. Saunders Book Company, Philadelphia, London, Toronto 1977, 297.

Åkerblom, E.: Über die Ätiologie und Pathogenese der Hufrehe beim Pferde. (On the aetiology and pathogenesis of equine alimentary laminitis). Skand. Arch. Physiol. 1934, *68*, Suppl. 1.

SAMMANFATTNING

Patologin vid fång, hos nötkreatur med särskild hänsyn till kärlförändringar.

Makro- och mikroskopiska förändringar i klövarna från 14 nötkreatur med den kliniska diagnosen fång beskrivs. Klövbensrotation påvisades hos 10 djur. Vid akut fång sågs histologiskt i läderhuden hyperemi, ödem, tromboser och blödningar. Degenerativa förändringar i epidermis iakttogs särskilt markant i anslutning till tromboser i corium. Vid kronisk fång var arteriolosclerос och arterioscleros ett genomgående fynd i corium. Kroniska tromber och kronisk granulationsvävnad var också vanligt förekommande. I lamellae epidermales var hyper- och parakeratosförändringar framträdande. På basis av förändringarna i arterioler och artärer bedöms hypertension vara en trolig faktor i patogenesen vid fång hos nötkreatur.

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Reprints may be requested from: Lennart Andersson, the Experimental Station of the Veterinary Institute, Box 234, S-532 00 Skara, Sweden.