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Bone spavin in Icelandic horses

Aspects of predisposition, pathogenesis and prognosis

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SWEDISH UNIVERSITY OF AGRICULTURAL SCIENCES

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Abstract

Bone spavin is an osteoarthrosis (OA) of the centrodistal tarsal joint (CD), the tarsometatarsal joint (TMT) and occasionally the proximal intertarsal joint (PIT). In order to detect and describe the earliest changes compatible with OA, specimens from the CD of young Icelandic horses were examined by high detail radiography (0-6 year, n = 111) and histology (0-4 year, n = 82). Histological chondronecrosis was seen in 33% of the joints, located both medially and laterally. Radiographic sclerosis of the subchondral bone was recorded in 60% of the specimens, most often medially. The medial subchondral bone sclerosis was not correlated with the chondronecrosis, but laterally the bone sclerosis was considered to be secondary to the cartilage lesions.

In a field survey, 614 Icelandic horses in the age range of 6-12 year (mean age 7.9 year), and in use for riding were examined radiographically and clinically for OA in the distal tarsal joints, to estimate the prevalence and clinical relevance of the disease in the riding horse population, to evaluate the effect of potential (environmental and intrinsic) risk factors and to estimate the heritability of the disease. Radiographic signs of OA in the distal tarsal joints (RS) were found in 30.3% of the horses and hindlimb lameness after flexion test of the tarsus was found in 32.4%. There was a significant correlation between the two diagnostic methods and 16.4% of the horses had both of RS and lameness after flexion test. The survival culling rate of the horses in the five following years was significantly affected by RS and horses with the combination of RS and a positive flexion test had the poorest prognosis.

The prevalence of RS was strongly correlated to age and tarsal angle (increased as the tarsal angle decreased). The birthplace was also significantly associated with RS, and considered to be an indirect genetic effect. The prevalence of lameness after flexion test was not influenced by age but a significant effect of sire was established. The prevalence was higher for horses that were broken to saddle late (6 year or older) and for horses that had not participated in a stud show. The heritability of age-at-onset of RS, reflecting the predisposition for OA, was estimated to be 0.33 and a similar figure was found for the heritability of lameness after flexion test.

It was concluded that bone spavin is a common disease in Icelandic horses affecting their durability, although often subclinically manifested. The high prevalence of histological findings in the young horses (1-4 year) and radiographical findings in the 6-12 year old horses demonstrated a progressive nature of the disease although the progression may be slow. The initiation of the disease was unrelated to the use of the horses for riding and workload was not found to effect the development of the disease negatively. The medium-high heritability together with the association to the tarsal angle and the radiographic pattern of uneven distribution of load in the CD joint, strongly indicate that poor tarsal

conformation or architecture of the distal tarsal joints is the main etiological factor of the disease.

Key words: Bone spavin, osteoarthrosis, tarsus, diagnosis, prevalence, predisposing factors, heritability, Icelandic horse.

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Key words: Bone spavin, osteoarthrosis, tarsus, diagnosis, prevalence, predisposing factors, heritability, Icelandic horse,

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Contents

Appendix

Papers I – VI

The present thesis is based on the following papers, which will be referred to by their Roman numerals:

I. Björnsdóttir, S., Ekman, S., Eksell, P. and Lord, P. High detail radiography and histology of the central intertarsal joint of young Icelandic horses. Manuscript.

II. Björnsdóttir, S., Axelsson, M., Eksell, P., Sigurdsson, H., Carlsten, J. (2000) A radiographic and clinical survey of degenerative joint disease in the distal tarsal joints in Icelandic Horses . Equine vet. J. 32: 268-272

III. Björnsdóttir, S., Árnason, Th. and Lord, P. The rate of culling due to bone spavin in Icelandic horses: Survival analysis. Submitted.

IV. Axelsson, M., Björnsdóttir, S., Eksell, P., Häggström, J., Sigurdsson, H. and Carlsten, J. (2001) Risk factors associated with hind limb lameness and degenerative joint disease in the distal tarsus of Icelandic horses. Equine vet. J. 33 (1) 84-90.

V. Björnsdóttir, S., Árnason, T., Axelsson, M., Eksell, P., Sigurdsson, H., Carlsten, J. (2000). The heritability of degenerative joint disease in the distal tarsal joints in Icelandic horses. Livest. Prod. Sci. 63, 77-83.

VI. Árnason, Th. and Björnsdóttir, S. Heritability of age-at-onset of bone spavin in Icelandic horses estimated by survival analysis. Submitted.

The following abbrevations are used in the text:

BLUP	Best Linear Unbiased Prediction
CD	centrodistal joint
OR	Odds-Ratio
PIT	proximal intertarsal joint
RS	radiographic signs of osteoarthosis in the distal tarsal joints
SD	standard deviation
Tc	os tarsi centrale
T3	os tarsale tertium
T4	os tarsale quartum

Introduction

The Icelandic horse

The Icelandic horse has developed as an isolated breed since the settlement of the country in the 8th and 9th centuries (Adalsteinsson 1981). The breed originates mainly from Norway and a close relationship to the Norwegian breeds, (the Nordland horse, the Fjord horse and the Coldblooded Trotter) and to the Shetland pony has been confirmed by phylogenetic analysis of microsatellite markers (Bjørnstad and Røed 2001). It is not known how many horses founded the breed, but it has been suggested that the difficulty of transporting horses to the island may have limited the quantity but probably increased the quality of the horses selected for the transport (Arnbjörnsson 1975). Horses were of great importance in the Viking age both for travelling and pleasure, especially stallion fights. Horse breeding for this purpose is described in the Icelandic Sagas. A period of decline in the horse breeding began in the twelfth century and lasted for almost seven hundred years. Cold climate and poor feeding in this period put a pressure on natural selection for robust horses that survived in hard conditions.

At the end of the 18th century the first law concerning horse breeding was passed in Iceland and the studbook of the Icelandic horse was initiated in 1923 (Hugason 1994). Since 1950, the breeding stock has been evaluated in field performance tests (Arnason 1984, Hugason 1994), usually at the age of 4 - 8 years. The official breeding standard consists now of eight conformation traits and seven riding performance traits, scored in the tests (Sigurdsson 2002). For details in English see www.feif.org . Since 1986 the estimated breeding values have been obtained by a multiple-trait animal model (Best Linear Unbiased Prediction, BLUP) (Arnason and van Vleck 2000).

The population size has varied considerably since the first official census of horses in 1703 (Figure 1). Only 8,600 horses (3000 mares) survived the great plague in 1784, and this is estimated to be the lowest number since the establishment of the breed (Bjarnason 1966). The native population was in the year 2000 approximately 74,000 horses. Approximately 10,000 foals were borne that year, but 50% were slaughtered for meat production (Statistics from the Icelandic Farmers Association 2001). The registration of horses in Iceland is voluntary and has traditionally included mostly breeding horses. The registration has improved successively from 1991 when a central database was established. The horse industry is of significant importance to the country, both economically and culturally. Export of riding horses has increased successively from the middle of the 19th century and in the last decade, 2-3,000 horses were exported per year. The value of the horses has also increased in this period. The Icelandic horse is now bred in almost all countries in Western Europe and North America and the population abroad has exceeded 100,000 horses (Statistics from the Icelandic Farmers Association 2001).

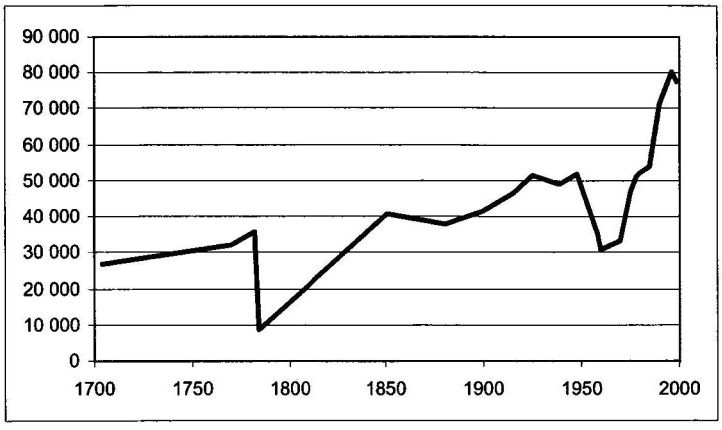

Figure 1. The Icelandic horse population in the period 1700 - 2000

As the history of intense artificial selection of Icelandic horses is short, a great phenotypic variation can be seen in many traits such as colour, gait and conformation. A typical Icelandic horse is compact in shape and the mean height at the withers, measured with a rod, was 136,9 cm (SD 2.8) for mares and 138.6 cm (SD 3.9) for stallions, judged for breeding in 2001 (Sigurdsson *et al.* 2002). The best qualities of the horses are lively temperament, strong but supple character and the ability to perform the gait *toelt* in addition to walk, trot, pace and gallop (Hugason 1994). *Toelt* (Figure 2) is a symmetric 4-beat gait without suspension (Feldmann and Rostock 1986) and is appreciated for both pleasure riding and sport. The sequence of footfalls is demonstrated at the web site (www.eidfaxi.is/fraedsla/)

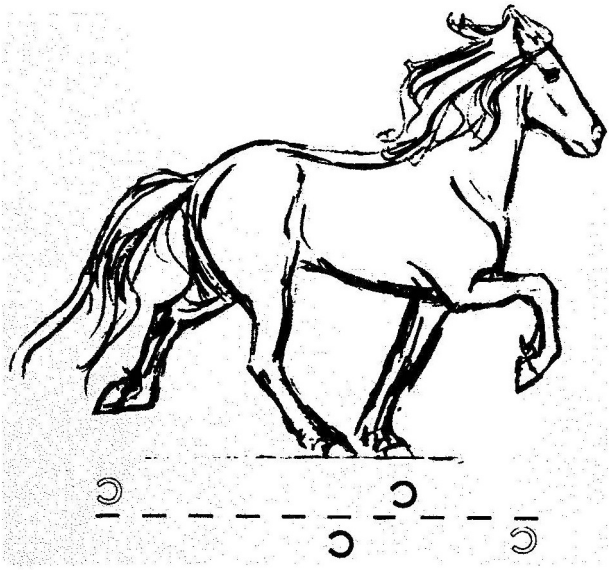

Figure 2. Icelandic horse showing the gait *toelt*. (Courtesy of Petur Behrens)

Icelandic horses are used for pleasure riding and for special gait competitions. They are usually broken to saddle at the age of 4 or 5, but until then they are free roaming (ranging), usually on large areas and fed outside during the winter. The most active period for riding is between 6 and 12 years, which is also a common age for export of horses. The horses are however often in use for riding up to the age of 20 years.

Spavin has been known as a cause of lameness ever since horses were first used by man (Schebitz 1965). The disease was first described and distinguished from other conditions of the tarsus by Busch in 1788, and characterised by periostal new bone formation medial to the distal hock. In 1822, Havemann related the disease to the joint surfaces and ankylosis of the distal tarsal joints (Wamberg 1955).

Bone spavin has existed in the Icelandic horse since the origin of the breed. Evidences of this can be found on tarsal and metatarsal bones preserved from graves (Figure 3) documented to originate from the heathen times, i.e. before year 1000 (Eldjárn 2000). Based on clinical signs, bone spavin was described to be a common disease in Icelandic horses a century ago (Einarsson 1931).

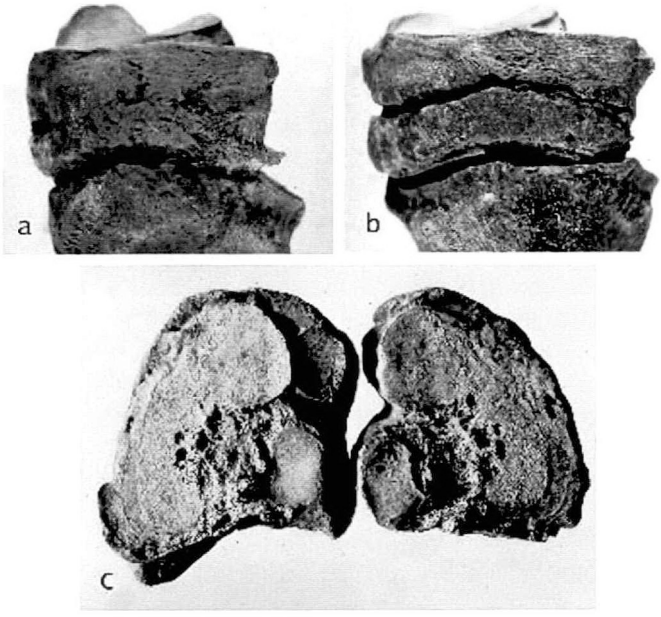

Figure 3. Bones from the graves from the pre-Christian period in Iceland (894-1000 ad.).
a) Tarsus with fused Tc and T3. b) Tarsus with periarticular osteophytes on the CD joint.
c) The joint surfaces of the CD joint of the tarsus in b. The irregular defects on the joint surfaces are pathological. Other joints had smooth surfaces.

The synovial joint

The gross anatomy of the equine synovial joint consists of apposing osseous structures covered by articular cartilage, joint space with a synovial fluid, all surrounded by a joint capsule and ligaments. The function of the joint is to enable movement and transfer load.

The following description is a summary of the reviews of Todhunter (1996), Pool (1996), Palmer and co-workers (1994) and McIlwraith (2002). The articular cartilage is avascular and aneural and consists of chondrocytes embedded with a matrix substance of water, collagen, proteoglycans, glycoaminoglycans and non-collagenous proteins. The articular cartilage is morphological divided into noncalcified and calcified cartilage by the tidemark. In the noncalcified cartilage, the chondrocytes obtain nutrients and remove metabolic waste products by diffusion of the synovial fluid. Chemical and hormonal stimuli from the vascular system of the synovium reach chondrocytes by the same way. In the calcified cartilage, blood vessels in the subchondral bone provide nutrition to the chondrocytes. The chondrocytes synthesise, organise and regulate the composition of a complex extracellular matrix, which determines the mechanical function of the articular cartilage. Collagen fibrils, type II, are concentrated in the superficial, tangential layer to resist tensile strain during weight bearing. Another important component, proteoglycan, made of glycosaminoglycan chains covalently attached to a protein core, is responsible for the elastic properties of the cartilage. The concentration of proteoglycan increases in the deeper cartilage layer. The proteoglycans provide an osmotic pressure, attracting water into the cartilage. During load, compression of the cartilage causes exudation and redistribution of fluid within different regions of the cartilage. The movement of water, nutrients and wastes within the cartilage matrix is facilitated when the articular cartilage is cyclically loaded during locomotion. The subchondral bone provides structural support to the overlying articular cartilage. It is divided into the subchondral bone plate and the trabecular bone, which absorbs a considerable part of the impact under load. Subchondral bone becomes denser in response to exercise (Pool and Meagher 1990, Norrdin *et al.* 1998). The joint capsule, which also is an important shock absorber of the joint, consists of a thick fibrous outer layer containing the capsular ligament and is lined by an inner synovial membrane with synoviocytes. A small volume of synovial fluid occupies the intraarticular space in healthy joints, providing lubrication of the articular surfaces. The synoviocytes secrete hyaluronan (non-sulfated glycosaminoglycan), into the synovial fluid (ultrafiltrate of plasma) contributing to increased viscosity of the lubricant and reduced friction. Nerve fibers are distributed to the fibrous joint capsule and associated ligaments. An extensive nerve supply has been demonstrated in the periosteum, compacta, spongiosa and marrow of bone tissue.

Osteoarthrosis (OA)

OA or degenerative joint disease is a chronic disorder of synovial joints characterised by progressive deterioration of articular cartilage, accompanied by changes in the bone and soft tissue of the joint, including subchondral bone sclerosis and marginal osteophyte formation (McIlwraith and Vachon 1988). Osteoarthrosis has been defined as a primary mechanically induced degenerative lesion of articular cartilage and bone with a secondary inflammation, whereas osteoarthritis has been defined as a primary inflammation of the joint, with a secondary degeneration of the joint tissue. As the diseases progress, a distinction between the two will be impossible as the morphology will be very similar (Radin 1995). In humans OA is often cited as noninflammatory because the synovial fluid typically contains few neutrophils and the synovium does not exhibit significant cellular proliferation or infiltration by inflammatory leukocytes, except in advanced disease. The "activated chondrocytes" have however been found to produce inflammatory mediators *in vitro* and *ex vivo* (Attur *et al.* 2002). Therefore, it is probable not possible to distinguish between the terms osteoarthosis and osteoarthritis.

In the horse, the degenerative process which results in OA may be associated with poor conformation and / or hard use (Butler 2000 a). The pattern of joint injury in the different breeds of athletic horses reflects different biomechanical forces sustained by the joint structures (Pool 1996). Overload arthrosis occurs commonly in racehorses and is characterised by subchondral bone sclerosis accompanied by necrosis of bone beneath viable cartilage (Norrdin *et al.* 1998). OA can also be induced by desmotomy of ligaments causing instability (Simmons *et al.* 1999). The term secondary joint disease is used when the primary cause is known, such as osteochondrosis and intraarticular fracture (Butler 2000 a).

The radiographic abnormalities associated with OA include: periarticular osteophyte formation, subchondral bone sclerosis and loss of trabecular pattern, ill-defined small lucent zones in the subchondral bone, small well-defined osseous cyst-like lesions and narrowing of the joint space (Butler *et al.* 2000 a). Periarticular enthesiophytes (bone proliferation at the site of the attachment of the joint capsule, tendon or ligament to the bone surface) are a major feature of joints with chronic OA (Pool 1996).

OA of the distal tarsal joints, bone spavin

The tarsus consists of three rows of tarsal bones (Figure 4). The proximal row with the talus on the medial side and the calcaneus on the lateral side, the intertarsal row with os tarsi centrale (Tc) and the metatarsal row consisting of (from medially), the fused os tarsale primum and os tarsale secundum, the os tarsale tertium (T3) and the os tarsale quartum (T4) (Nickel *et al.* 1986). Together with the distal tibia and proximal metatarsal bones, they form a composite joint, articulatio tarsi comprising the tarsocrural, the proximal intertarsal (PIT), the distal intertarsal (also named centrodistal interatarsal, CD) and the tarsometatarsal (TMT) joint. The tarsocrural joint is responsible for most of the movement of the tarsus, as the distal tarsal joints have flat surfaces limiting the motion (Nickel *et al.* 1986).

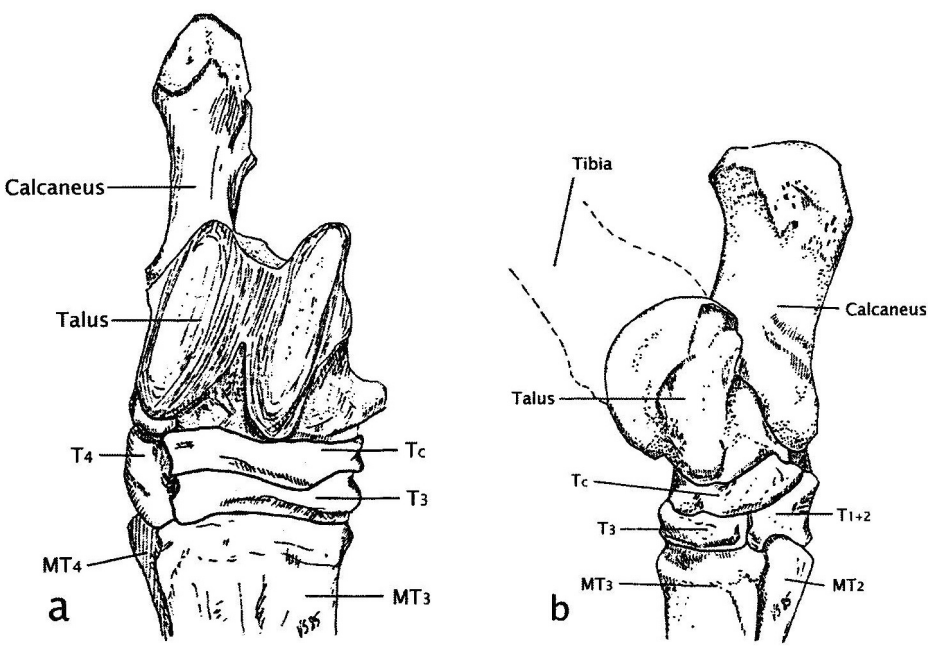

Figure 4. Schematic drawing of the tarsus, a) dorsal view, b) medial view.

The joints are surrounded by a common joint capsule which encloses separate synovial sacs. Communication between the CD and the TMT was demonstrated in 31% of cases studied by arthography (Kraus-Hansen *et al.* 1992). The joints are stabilised by collateral ligaments on either side of the tarsus, proximal and distal tarsal ligaments (e.g. the dorsal tarsal ligament), and tarsometatarsal ligaments (Nickel *et al.* 1986). The tendon (the medial terminal branch) of m. tibialis cranialis runs obliquely over the medial aspect of the tarsus, over the cunean bursa, and is sometimes referred to as the "tendon of spavin" (Nickel *et al.* 1986, Kainer 2002).

The distal tarsal joints are low-motion joints, where the area of maximal weight bearing is nearly stationary during locomotion. They are therefore under a greater compression stress compared to the high-motion joints and hence more susceptible to non-physiologic loading and metabolic disturbance (Pool 1996).

Bone spavin is an OA of the distal tarsal joints, described as commonly occurring in all horse breeds including ponies (Barneveld 1983, Wyn-Jones 1988). Studies of German sport horses (Winter *et al.* 1996), young trotters (Hartung *et al.* 1983), young horses of different breeds (Laverty *et al.* 1991) and Dutch Warmblood foals (Barneveld and van Weeren 1999), have revealed high prevalences of radiographic and histological abnormalities compatible with bone spavin.

According to Sullins (2002), few adult performing horses have tarsal joints without radiographic changes. Most often the CD and the TMT joints are affected and the PIT joint is occasionally involved (Barneveld 1983, Butler *et al.* 2000 b, Sullins 2002).

Fibrosis of the joint capsule was stated to be the initial pathologic change in OA of the low-motion joint followed by full thickness necrosis of the articular cartilage, focal destruction of the bony support, an absence of synovitis and focal to complete bony ankylosis of the joint. (Pool 1996).

Radiography is considered essential for the diagnosis of bone spavin (Butler *et al.* 2000 b). The radiographic signs of OA in the distal tarsal joints (RS) include: periarticular osteophytes, subchondral bone lysis or rarifaction, and narrowing and collapse of joint spaces or ankylosis (Morgan 1972, Shelley and Dyson 1984, Park *et al.* 1996, Butler *et al.* 2000 b).

Clinical signs are most commonly found in mature horses in hard work (Gabel 1980) and include hindlimb lameness, positive flexion tests, reduced arc of the foot flight, reduced flexion of the hock, and wearing of the toe (Sullins 2002). The clinical manifestations are however variable and in many horses the relationship between pain associated with the distal joints of the hock and the radiographic abnormalities is poor (Butler *et al.* 2000b, Sullins 2002).

The aetiology of the disease is considered to be multifactorial (Wyn-Jones 1988). Inherited, poor tarsal conformation e.g. sickle hocks and cow hocks (Rooney 1969, Morgan 1972, Gabel 1980, Barneveld 1983, Wyn-Jones 1988), and special types of work (Rooney 1969, Gabel 1980) resulting in asynchronous movements of the tarsal bones (Rooney 1969) are examples of etiological factors which have been suggested. Specific injury (Sullins 2002) and periarticular trauma are also considered (Pool 1996). A genetic predisposition for OA in the distal tarsus was reported in Dutch warmbloods (Barneveld 1983), but the heritability was estimated to be low in German riding horses (Winter *et al.* 1996).

Bone spavin in Icelandic horses. Background of the thesis

Radiographic signs of OA in the distal tarsal joints are commonly found in Icelandic horses with clinical suspicion of bone spavin (Sigurdsson 1991). An important background for the study was, however, the frequent findings of RS in clinically sound horses on pre-purchase examinations, confusing the veterinarians as well as the owners. The clinical relevance of these radiographic changes needed to be clarified.

In a recent study, a high prevalence of radiographic signs of bone spavin (23%) and positive flexion test of the tarsus (25%) was found in Icelandic horses in Sweden (Eksell *et al.* 1998, Axelsson *et al.* 1998). The radiographic signs were strongly related to the variables age and sickle hock conformation (Eksell *et al.* 1998). These results gave rise to the question if the same prevalences would be found in the native population of Icelandic horses. Factors contributing to the aetiology of the disease needed also to be studied further to evaluate if it could be prevented by management or breeding. The following aetiological factors might be related to bone spavin in Icelandic horses: 1) High work load in young horses. 2) A concentration of mechanical stress in the tarsus when the horses *toelt.* 3) A concentration of mechanical stress in the tarsus due to a poor tarsal conformation. 4) Inheritance.

Aims of the investigation

1. To determine the age of onset and the nature of changes in the cartilage and subchondral bone of the centrodistal joint of young Icelandic horses by high detail radiography and histology.
2. To estimate the prevalence of radiographic signs of OA in the distal tarsal joints (RS) in a population of Icelandic horses being used for riding and describe the radiographic findings.
3. To estimate the prevalence of hind limb lameness after flexion test of the tarsus in the Icelandic riding horse population and to assess the association between RS and lameness after flexion test.
4. To compare the rate of culling between horses with and without RS and lameness after flexion test and thus to determine the prognostic value of these diagnostic methods.
5. To evaluate intrinsic and environmental risk factors associated with RS and lameness after flexion test.
6. To estimate the heritability of RS and lameness after flexion test.

Material and methods

Specimens (Paper I)

The left CD joints, including the Tc and the T3, from 111 horses in the age range of 6 months to 6 ½ years were collected post-mortem at the slaughterhouse. The bones were sectioned with a bandsaw into 8-mm thick slabs in the frontal plane, dorsal to the mid-line of the central tarsal bone, for high detail radiography. Specimens from horses younger than 5 years (n=82) were then selected for histology. The majority of the horses were not broken to saddle. They were culled because of poor conformation, gaits or pedigree.

Horses (Paper II – VI)

By an official advertisement, horse owners in the south, west and north of Iceland were invited to submit horses to a survey. The age range was 6-12 years and all of the horses were saddlebroken and in use for riding. Offspring from 17 selected sires that were in use for breeding in the years 1982-1989 and having a breeding index (BLUP) higher than 105, based on more than 50 offspring, were requested. This provided 420 horses. Additionally 194 horses, meeting the same criteria but sired by unselected stallions, were also included. The paternity was known for 144 of them but unknown for 50 horses. Together, the material consisted of 614 horses, 24 (3.9%) stallions, 403 (65.6%) geldings and 187 (30.5%) mares. The mean age was 7.9 years. Two horses presented with forelimb lameness were excluded from the study. The analysis of the heritability of RS and lameness after flexion test, by the non-linear sire model in paper V, and the heritability of age-at-onset of RS in paper VI were based exclusively on the 420 horses in the progeny groups. In paper III, the 614 horses were followed up five years later.

Histology (Paper I)

Bone sections including the distal part of the Tc bone and the proximal part of the T3 were decalcified, trimmed, embedded in paraffin, cut into approximately 6-µm thick section, coded and stained with hematoxylin & eosin and toluidine blue. The degree of articular cartilage lesions was graded as mild (a focal loss of the extracellular stain and chondrocytes, with formation of chondrocytes in clusters adjacent to the area), moderate (diffuse chondronecrosis containing more cluster formations) or severe (marked chondronecrosis with loss of cartilage, often together with fibrosis and areas of fusion of the Tc and the T3) in the lateral and medial parts of the CD.

High detail radiography (Paper I)

Bone sections, 8 mm in thickness, including the CD joint were radiographed using high detail film and corresponding high detail intensifying screen (mammography system). The CD was evaluated on the high detail radiographs for sclerosis of the subchondral bone, defects of the subchondral bone plate, narrowing of the joint space and periarticular osteophytes (Table 2). The locations of the abnormalities were recorded separately for the Tc and T3 bones and the medial and lateral parts of the bones. The origins of osteophytes were noted.

	Sclerosis
0	no changes
1	peripheral thickening of the trabecular bone
2	all trabecular bone thickened or developed into compact bone
	Defects
0	no changes
1	one or two separate points of lysis
2	more than a half joint surface with a thin zone or coalescing points of lysis
	Narrowing
0	no changes
1	narrowing without ankylosis
2	narrowing with ankylosis

Table 2.
Grading of high detail radiographs.

Radiographic examination (Papers II – VI)

The radiographic examination consisted of latero-5°-proximal-mediodistal (L5Pr - MD), dorso-35°-lateral-plantaromedial oblique (D35L - PlMO) and plantaro-45°-lateral-dorsomedial oblique (Pl45L - DMO) projections of each tarsus. These were described to be the most sensitive projections for detecting OA in the distal tarsal joints (Eksell *et al.* 1999). Strict intra-articular diagnostic criteria were used for RS: rarefaction of the subchondral bone, narrowing or collapse of the intertarsal joint spaces (Figure 5). The location of the radiographic findings was identified by the specific joints involved and the extension of the lesions was graded as mild (radiographic signs in one or more of the distal intertarsal joints, in total up to a half joint space), moderate (in total between half and one joint space) or severe (in total more than one joint space). Presence of periarticular osteophytes on the dorsomedial aspect of the distal tarsus was recorded, primarily for comparison with palpation abnormalities at the same location. The radiographic findings of active bone remodelling, defined as irregular and poorly demarcated bone proliferations (Butler *et al.* 2000 a) were noted as absent or present. The radiographs were coded and evaluated by two radiologists together. Equivocal findings were graded as the less severe alternative.

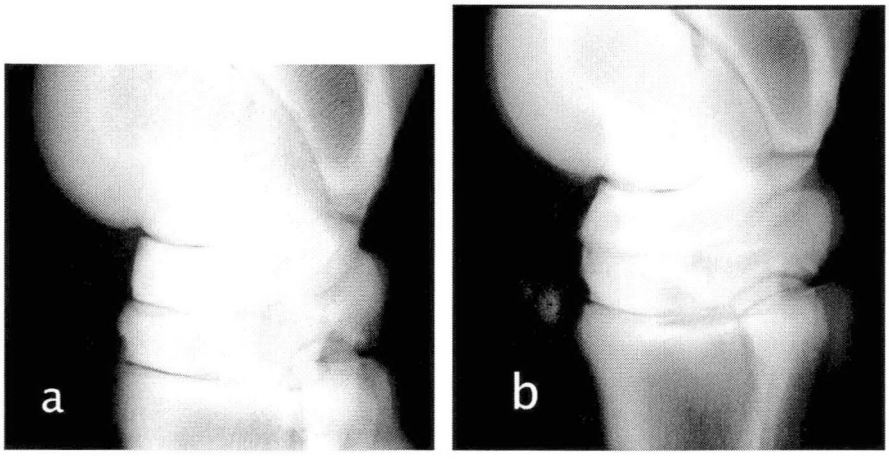

Figure 5. Lateral projections of a) a normal tarsus and b) tarsus with narrowing and collapse of the CD joint and subchondral bone lysis.

Clinical examination (Papers II – V)

Hind limb lameness was first evaluated while trotting the horse by hand on a firm surface 25 - 30 meters straight away from the examiner and back, after which a flexion test was performed by flexion of each tarsus for one minute and repeating the above motion evaluation. Lameness before and after the flexion test was graded as mild, moderate, severe, very severe or non-weight bearing.

Palpation of the medial aspect of the distal tarsus preceded the motion evaluation. Firm, subcutaneous tissue swelling and indistinct margins of the dorsal tarsal joint were considered as palpation abnormalities.

Conformation (Paper IV)

The sturdiness of the frame was classified as light, intermediate or heavy. Hind limb conformation was evaluated from the side (classified as normal, sickle or straight) and from behind (classified as normal, hock narrow or hock wide) (Stashak 1987). Body measurements included the height at the withers and the croup, the width between the thighs, thickness of the right tarsus and the tarsal angle (the angle between the axis of the tibia and the third metatarsal bone).

Interview (Papers I – II)

Information on registration number, age, gender and pedigree was obtained from the owners (Paper II). Multiple choice questions regarding riding qualities included gaits, temperament (during breaking period and at present time) and fore limb action. Management-related questions included; place of birth, type of housing the first two years of life, age when broken to saddle, if saddle and riding training were performed by an amateur or professional and if entered at the national stud show. Additional questions to determine workload concerned weekly training intensity (summer and winter), competition activity and if in use for tour trekking.

In the five year follow-up the owners were interviewed by telephone and asked if the horses were still used for riding. If not, they were asked when and why the horses were sold, selected for breeding or culled (Paper I).

Data analysis

Bivariate and multivariate logistic regressions were used to examine the effect of age, gender and potential risk factors on RS and lameness after flexion test, and the association between the findings (Paper II). Also the effect of age on lesions found by high detail radiography and histology and their association were examined by these methods (Paper I). Chi Square test and Chi Square for linear trend were used to analyse the effect of age on categorical dependent variables (details of radiographic findings) and their association to lameness after flexion test in the same limb (Paper II). The minimum level of significance was chosen as $P<0.05$.

The survival function and the culling rate was estimated by the Kaplan-Meier estimator or the Product limit estimator (Klein and Moeschberger 1997) (Paper III). The association between the hazard function and the explanatory variables (RS and lameness after flexion test) was analyzed by Prentice and Glockler's (1978) models for grouped data approximated by an exponential regression model including a time dependent explanatory variable (Ducrocq 1999) (Paper III).

The heritability was analysed by two statistical models based on the threshold liability concept, a non-linear sire model and a linear animal model (Paper V). Survival analysis with Prentice and Glockler's (1978) model was used to estimate the heritability of age-at-onset of RS (Paper VI).

Results and discussion

The early signs (Paper I)

Histological examination of the centrodistal joint (CD) collected from young horses at slaughter revealed chondronecrosis of the articular cartilage from the age of 6 months with an increasing frequency up to the age of 4 ½ years, in total 33% of the specimens. The lesions were found both in the medial and the lateral parts of the joints without significant difference between the two locations. Sclerosis of the subchondral bone detected by high detail radiography was commonly found in the medial part of the joints with an increasing frequency up to the age of 6 ½ years (Figure 6). As it was not associated with the presence of chondronecrosis, but strongly related to age, it was considered to be an adaptation to dynamic strain (Kawcak 2001). However, in the lateral part of the joint, sclerosis of the subchondral bone was an infrequent finding. In all cases with lateral bone sclerosis, chondronecrosis was also found, but chondronecrosis could be present without bone sclerosis. These findings suggest that lateral bone sclerosis is secondary to, or not related to the degeneration of the articular cartilage. Hence, subchondral bone sclerosis did not appear to be a primary factor in the development of OA in the CD joint but is a result of an uneven distribution of biomechanical forces within the joint. Radiographic defects of the subchondral bone plate were on the other hand significantly associated with chondronecrosis in the corresponding articular cartilage.

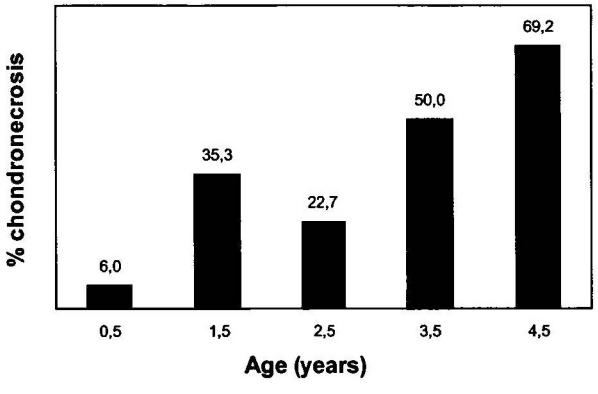

Figure 6. The frequency of chondronecrosis in the centrodistal joint

Radiographic findings (Paper II)

Radiographic signs of OA in the distal tarsal joints (RS) were recorded in 30.3% of the horses (n = 186) and the total number of affected limbs was 306. The prevalence of RS was strongly correlated to age (OR = 1.3 / year, P<0.001), increasing from 18.4% in the 6-year-old horses up to 54.2% in the 12-year-old horses, or by 6% as an average for every year in the age range. There was no significant difference in frequency of RS between stallions, mares and geldings. The results correspond well to radiographic and clinical findings of bone spavin reported from Icelandic horses in Sweden (Eksell *et al.* 1998), taking in account the difference in the mean age. The RS were found bilaterally in 65% of the affected horses and the unilateral findings were evenly distributed between the left and the right limbs. Most commonly the CD was the only joint affected (n = 159), or the CD together with the TMT (n = 124). The TMT joint was seldom affected alone (n = 19) and the PIT was only affected in four limbs. The frequency of bilateral appearance of RS was not influenced by age, but the number of affected joints in the same limb increased significantly with age. In most limbs (n = 260), the extent of the RS was graded as moderate or severe and there was a linear trend with the grading increasing with age.

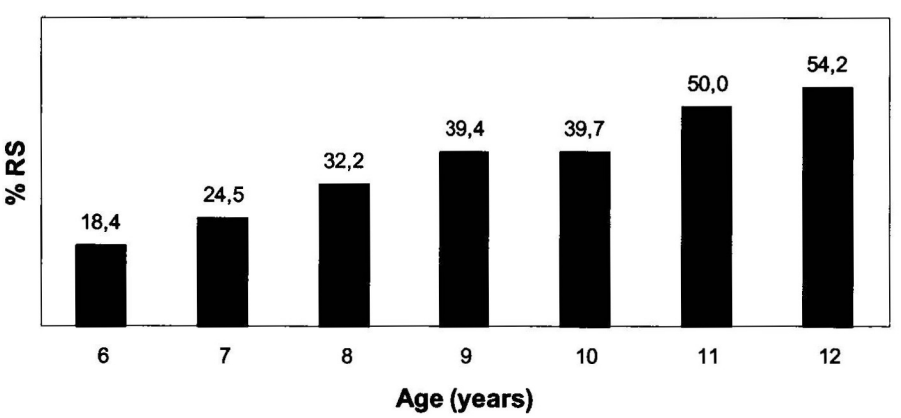

Figure 7. The frequency of radiographic signs of OA in the distal tarsal joints.

Clinical findings and their relation to RS (Paper II)

Hind limb lameness after flexion test of the tarsus was found in 32.4% of the horses (n = 199) and 6.7% (n = 41) of these were lame at presentation. The lameness after flexion test was most often unilateral (85.0%), equally distributed between left and right limbs, and graded as mild (88.6%). The prevalence of lameness after flexion test was not significantly correlated with age and not influenced by gender.

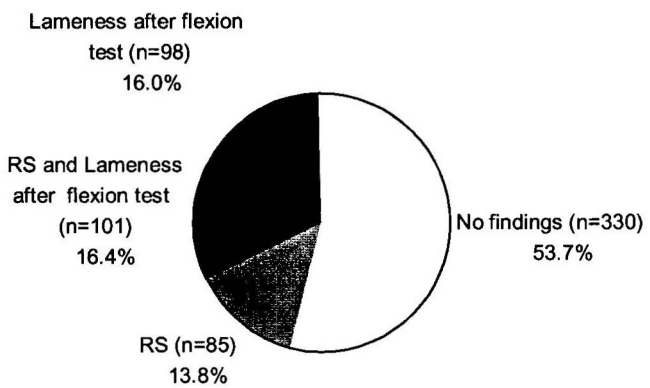

Figure 8. The distribution of radiographic signs of OA in the distal tarsal joints (RS) and lameness after flexion test in 614 Icelandic horses.

The combination of RS and lameness after flexion test was found in 16.4% of the horses, 13.8% had RS exclusively and 16.0% showed only lameness after flexion test (Figure 8). The association between RS and lameness after flexion test was strong (OR = 4, P<0.001) as lameness after flexion test was found in 54.3% of the horses with RS, compared to 22.9% of the horses without RS. The absence of periarticular osteophytes reduced the risk of lameness after flexion test from 54.3% to 30.0% while other details of the radiographic findings: the joints involved, the extent of the RS, and signs of active bone remodelling were not associated with lameness in the same limb.

Palpation abnormalities of the medial aspect of the distal tarsal joints were found in 31.1% of the horses, significantly associated with the prevalence of RS (OR = 4.3, P<0.01) and lameness after flexion test (OR = 3.55, P<0.001). The palpation abnormalities were considered to be caused by soft tissue proliferation rather than a periosteal reaction as periarticular osteophytes were seldom (23%) identified radiographically on the corresponding aspect of the joint.

Eksell (2000) described two different patterns of radiographic bone spavin according to joints involved and the presence of periarticular osteophytes, in 98 Icelandic horses in Sweden, raising questions that two aetiologies might exist with different clinical significances. In the Icelandic material a similar pattern was identified. However, horses with RS in both CD and TMT were significantly older than horses with one of the joints affected, suggesting that the different radiographic appearance is a result of progression of the disease. The CD joint was involved in 93% of the affected limbs hence the degenerative changes are most likely to start there. The involvement of the TMT might be due to the same reasons as for the CD, but the presence of a communication between the two joints cavities and a development of synovitis or capsulitis are probably important factors. The limbs with two joints involved were more frequently positive on flexion test compared to limbs with only one affected joint. Multivariate analysis, including other details of the radiographic findings, revealed that the difference was explained by the more frequent presence of periarticular osteophytes when two joints were involved.

Interpretation of the above findings (Papers I – III)

Radiography is considered to be a specific method to detect OA, revealing the bone reaction and repair processes. Allowing only an indirect evaluation of the articular cartilage thickness the method is, however, not sensitive for detecting the initial phase of the disease. Bone density must vary considerably from normal to be detected on radiographs (Butler *et al.* 2000 a) and superimposed bone loss and sclerosis may be balanced in such a way that they "cancel out" one another radiographically (Hanson *et al.* 1996). A reaction on the flexion test of the tarsus may be due to lesions within the soft tissues of the joint or to early bone changes not detectable on radiographs. A positive flexion test of the tarsus is not even pathognomic for OA in the distal tarsal joints as many anatomical structures within other parts of the limb are put under pressure. It is therefore likely that some of the horses with lameness after flexion test that did not have RS were reacting to early OA of the distal tarsal joints and others (with RS and without RS) were reacting to pain from non-progressive soft tissue lesions or lesions in other parts of the limb. However, the radiographic diagnosis is considered to be specific for OA in the distal tarsal joints and once present, the RS persist, undergoing bone remodelling over time. In contrast, the reaction to the flexion test tends to have an intermittent course. The repair process may succeed in limiting the joint damage, in part by altering the biomechanics, resulting in stabilisation of the disorder, as occurs in younger humans (Dieppe 1995). This is probably a common course of the OA in the distal tarsal joints of Icelandic horses, explaining the presence of RS without lameness after flexion test.

Histology is a more sensitive for detecting early OA compared with radiology, as shown by a higher frequency of chondronecrosis in the articular cartilage from the young horses than the prevalence of RS in 6-12 year horses (Papers I and II). Although the two materials are reflecting sub-populations that might have different frequencies of OA in the distal tarsal joints, the results indicate a progressive nature of the disease from young age. However, if one assumes that all the chondronecrotic lesions will eventually progress to RS, the period required must be extremely variable.

Prognosis (Paper III)

In the five year follow-up study, information about the rate of culling was obtained for 508 of the 614 horses originally examined in the survey (Paper II). The rate of culling was low up to the age of 11 years. The presence of RS affected the survival function in the 5 years period significantly and the difference was highest for 14-year-old horses. The risk ratio of culling was twice as high in horses with RS compared to horses without RS ($P< 0.001$). The most common disease as cause of culling was hind limb lameness and the risk ratio of culling because of hind limb lameness was 5.5 times higher for the horses with RS ($P< 0.001$). Lameness after flexion test as the only finding in the survey had lower prognostic value than RS exclusively but the presence of both RS and lameness after flexion test had the highest risk ratio for culling (2.5 times higher than for horses without findings, $P<0.001$). For culling because of hind limb lameness the risk ratio was 10 times higher ($P< 0.001$).

Predisposing factors (Paper IV)

Several potential risk factors for RS and lameness after flexion test were studied separately, which included both intrinsic (age, gender, sire, conformation, gaits, temperament, forelimb action) and environmental variables (place of birth and examination, management and workload).

The final multivariate model for RS included: age, tarsal angle and birthplace. Horses with a larger tarsal angle had a lower prevalence (OR/degree = 0.83, $P<0.05$) confirming that the tarsal conformation is associated with OA in the distal tarsus, probably by altering the biomechanics of the distal tarsal joints. The small difference in the tarsal angle between horses with and without RS (0.8°) limits the clinical application of the finding in designing investigations to prevent the disease. Horses born in the north and south regions of Iceland had a lower prevalence of RS (OR = 0.27, $P<0.001$ and 0.41, $P<0.05$ respectively) compared with the other parts of the country. This is most likely an indirect genetic effect because of clustering of dams in the specific regions.

The final multivariate model for lameness after flexion test included: sires, age when broken to saddle, entered at stud show, height at croup and gaits. Two progeny groups had significant higher (OR = 8.26, $P<0.05$ and OR = 8.93, $P<0.05$ respectively) and one significant lower (OR = 0.05, $P<0.05$), indicating genetic predisposition. Breaking to saddle at a young age and especially entering stud show at a young age is expected to result in high workload on relative young (4-6 year) horses. However, horses broken to saddle at 6 years or older had a higher

prevalence of lameness than horses broken to saddle at 4 years of age (OR = 12.07, P<0.001) as well as horses not entered at stud shows (OR = 3.74, P<0.001). These results indicate that the workload does not contribute to the development of the disease. The lack of a significant effect of the training intensity and competing status on any of the dependent variables, RS or lameness after flexion test supports this. The mean height for sound horses was 6 mm higher than for horses with lameness after flexion test. Although significant, the difference is too small to be of value. Four gaited horses (walk, trot, *toelt* and gallop) was the only gait group having a significantly lower prevalence of lameness after flexion test (OR = 0.30, P<0.001) compared with the group of pace-like *toelters*. The effect of gaits is difficult to interpret, as the ability to perform the different gaits may be a consequence of the disease rather than a predictor. In any case, there was no indication of *toelt* or other riding qualities being a risk factor for the disease.

Heritability (Papers V and VI)

The heritability analysis according to the linear animal model resulted in the following estimates on the underlying scale: for RS, $h^2 = 0.10$ (SE = 0.06) and not significantly different from zero. For lameness after flexion test, $h^2 = 0.42$ (SE = 0.13), and for the combined trait RS and lameness after flexion test, $h^2 = 0.22$ (SE = 0.08) (Paper V). The non-linear threshold sire model yielded similar results but higher standard errors. The estimated genetic correlation between RS and lameness after flexion test was of the order of 0.70. The phenotypic correlation was estimated as 0.30 and the corresponding environmental correlation was 0.22. The high genetic correlation estimate supports the assessment that lameness after flexion test was most often caused by OA and using the flexion test as a selection criteria would reduce the prevalence of bone spavin. The different heritability estimates of RS and lameness after flexion test can probably be explained by the different effect of age on the two dependent variables. If the effect of age was partly genetic, including it as a fixed effect in the linear model can have removed genetic effects as well as environmental effects and caused an underestimation of the heritability estimates of RS. Exclusion of age from the model would on the other hand have caused an overestimation of the heritability, since the progeny groups were unevenly distributed across the age classes (Paper V).

An alternative way to analyse the data of RS was to apply survival analysis for censored data (Paper VI). The horse's age at examination was treated as a discrete time scale variable and the presence of RS was registered as the age-at-onset (failure) while negative findings represented censored data. The heritability estimates of the age-at-onset of RS (failure time) yielded the effective heritability estimate of $h^2 = 0.33$. Simulations of greater data sets provided strong evidence for the conclusion that this estimate is far less biased than the low heritability estimates of RS obtained by the binary threshold model.

Although reliable results from genetic analysis would have required much larger data than were available for this study, these results strongly indicate that the age-at-onset of RS, which reflects the predisposition for OA in the distal tarsal joints, is a trait with medium-high heritability.

General discussion

The material of the survey reflects the population of active riding horses in Iceland (Papers II - VI). A randomised material was not possible to obtain as the registration of horses in Iceland, at the time of the investigation, included an overrepresentation of breeding horses. Official advertisement was therefore considered to be the best way of providing horses to the study. The horse owners that decided to participate in the project presented all horses they had fulfilling the selection criteria. A possible bias to the study due to selection of horses with a history of hind limb problems was tested. However, excluding these horses did not alter the results significantly. Offspring from 17 selected sires, representing all the major breeding lines, were selected to allow heritability estimates as well as the prevalence assessment. Results from the heritability assessments indicated that the dams represented a random sample (Paper V). The slaughter house material did not reflect the riding horse population but was applicable to detect the first morphological lesions compatible with OA in the distal tarsal joints of Icelandic horses.

The high prevalences and the characteristics of chondronecrosis in the CD joint (Paper I) and RS in the CD and TMT joints (Paper II) confirm that bone spavin is a common disease in Icelandic horses that starts at young age. High frequency of similar histological lesions has been found in young horses of other breeds (Barneveld and van Weeren 1999, Laverty *et al.* 1991) but comparable information about the prevalence of RS in mature horses of other breeds is not available.

The increasing frequency of chondronecrosis and RS with age is most likely due to accumulation of affected horses within the population rather than an increased hazard rate. The variation in time-of-onset of RS is proposed to reflect a variance in the predisposition for the disease within the breed. Comparison of the frequency of histological findings in the young horses to the frequency of radiographic findings in the mature horses strongly indicates that the chondronecrosis will in most cases progress to radiographic changes. The effect of age on the grading of RS and the number of joints involved also demonstrate the progressive nature of the disease. This relationship would probably be stronger if the exact age-of-onset was known.

Flexion of the tarsus provoked a pain reaction in many horses with RS (and in some without RS), independent of the stage of the radiographic changes. Positive flexion test as the only finding had, however, a lower predictive value for culling in general and culling because of hind limb lameness, compared with RS. According to the follow-up study, horses are seldom culled because of hind limb lameness before the age of 13 years and many of the horses with RS or lameness after flexion test can be used for riding for many years without becoming clinically affected (Paper III).

It can be concluded that OA in the distal tarsal joints is often subclinically manifested in Icelandic horses. However, some horses become severely lame because of bone spavin. This is probably due to further progression of the disease causing more destructive lesions of the bone and inflammation of the soft tissues of the joints. A radiographic study of 60 Icelandic horses presented with clinical suspicion of bone spavin (Sigurdsson 1991) support this. The horses were older

(mean age 10.1 year) and the radiographic abnormalities were found to be more extensive with the PIT and the TMT joints more frequently involved, in 25% and 81.7% respectively.

Workload in young age or in older age was not found to be a risk factor for OA in the distal tarsal joint (Paper IV). This was supported by the frequent histological findings in the young horses, strongly suggesting that the initiation of the disease is unrelated to the use of the horses for riding (Paper I). The characteristic gait "*toelt*" was ruled out as a risk factor. (Paper IV). In agreement with other rapports (Rooney 1969, Morgan 1972, Gabel 1980, Barneveld 1983, Wyn-Jones 1988, Eksell, 1998) reduction in the tarsal angle predisposed for the disease. Although the mean tarsal angle was smaller than 150° for both horses with RS and without RS, indicating sickle hocks to be a common conformation in the breed, the grade of the conformational defect was of importance (Paper IV). It can, however, not be excluded that the small reduction in the tarsal angle for horses with RS, is a consequence of the disease rather than a risk factor.

The genetic predisposition for the disease stands out as the most important aetiological factor. It was presumed that the presence of RS is a quantitative threshold trait with an underlying normal distribution of multigenetic effect. The genetic contribution can be, at least partly, via the conformation of the hock or the shape of the distal tarsal joints. The pattern of subchondral bone sclerosis, demonstrating an uneven distribution of biomechanical forces in the CD joint, support this. It is suggested that the medium high heritability estimate reflect an inheritable variation in conformation or stability of the distal tarsal joints, resulting in predisposition to the disease.

Selection based on radiographic examination and flexion test of the tarsus can be expected to be useful in reducing the prevalence of bone spavin in the Icelandic horse population. The lack of specificity of the flexion test makes the radiographic examination preferable. It seems most important that sires and dams that develop RS early in their life are excluded from the breeding stock as they are expected to have the highest predisposition for bone spavin. The late appearance of RS will, however, reduce the expected profit as RS will in many cases not be detected until the sires have been used for breeding for many years. Identifying conformational traits with a strong genetic correlation to RS, would therefore be of great importance. The subclinical manifestation may have prevented a natural and artificial selection against the disease and as health control has not been required in connection to the stud shows in Iceland, the predisposition for the disease is probably "stronger preserved" in Icelandic horses compared with other breeds.

The cause of the focal necrosis within the articular cartilage can not be clarified in this study. Static compression to the articular cartilage can cause a mechanically induced death of the chondrocyte releasing metalloproteinases that further destroy the cartilage matrix (Luccinetti *et al.* 2002). Changes in the subchondral bone have been stated to be integral to the arthrotic process (Radin 1995). Kawcak and co-workers (2001) suggested that static strain to the bone, which can be produced by instability models, induce articular cartilage necrosis prior to changes in the subchondral bone. They also suggested that a dynamic strain would result in a primary bone sclerosis.

Sickle hock and narrow hock conformations might result in abnormal loading of the distal tarsal joints. From the caudal view, 77% of the horses in the survey were found to have narrow hock conformation, but none was classified as wide hock (Paper IV). Although the narrow hock conformation was not significantly associated with the presence of RS, it has not been ruled out as risk factor for bone spavin. A more precise grading of the conformation may detect an effect lost in the coarse grading "narrow hock" used here. As the initiation of the disease occurs in the first years of life in many cases (Paper I) medial instability due to laxity of periarticular support structures in foals (Auer 1999) and following valgus deformity should also be considered as an etiological factor.

It is suggested that the conformational defects, probable together with poor intra-articular or extra-articular architecture of the distal tarsal joints contribute to static strain laterally and instability medially. Depending on the severity of the deformity, an attempt at stabilisation would result in proliferation of the periarticular soft tissue and formation of periarticular osteophytes, preferable on the medial side of the joints. The immobilisation in the lateral part (or the whole joint after stabilisation) would favour primary bone healing with resorption of the subchondral bone plate and spongiosa, resulting in fibrous and bony ankylosis as described by Pool (1996). In a radiographic and scintigraphic study, Eksell and Carlsten (2001) found the dorsolateral part of the distal tarsus to be the predilection site of bone spavin in Icelandic horses, indicating that the reparative response of the bone starts there in many cases.

Two pathogenic pathways have been outlined for articular cartilage degeneration of equine osteoarthritis (McIlwright 1996). 1) Abnormal stress on normal cartilage and 2) normal stress on abnormal cartilage. In conclusion of the results from the present study, the following route is hypotheses for OA in the distal tarsal joints of Icelandic horses:

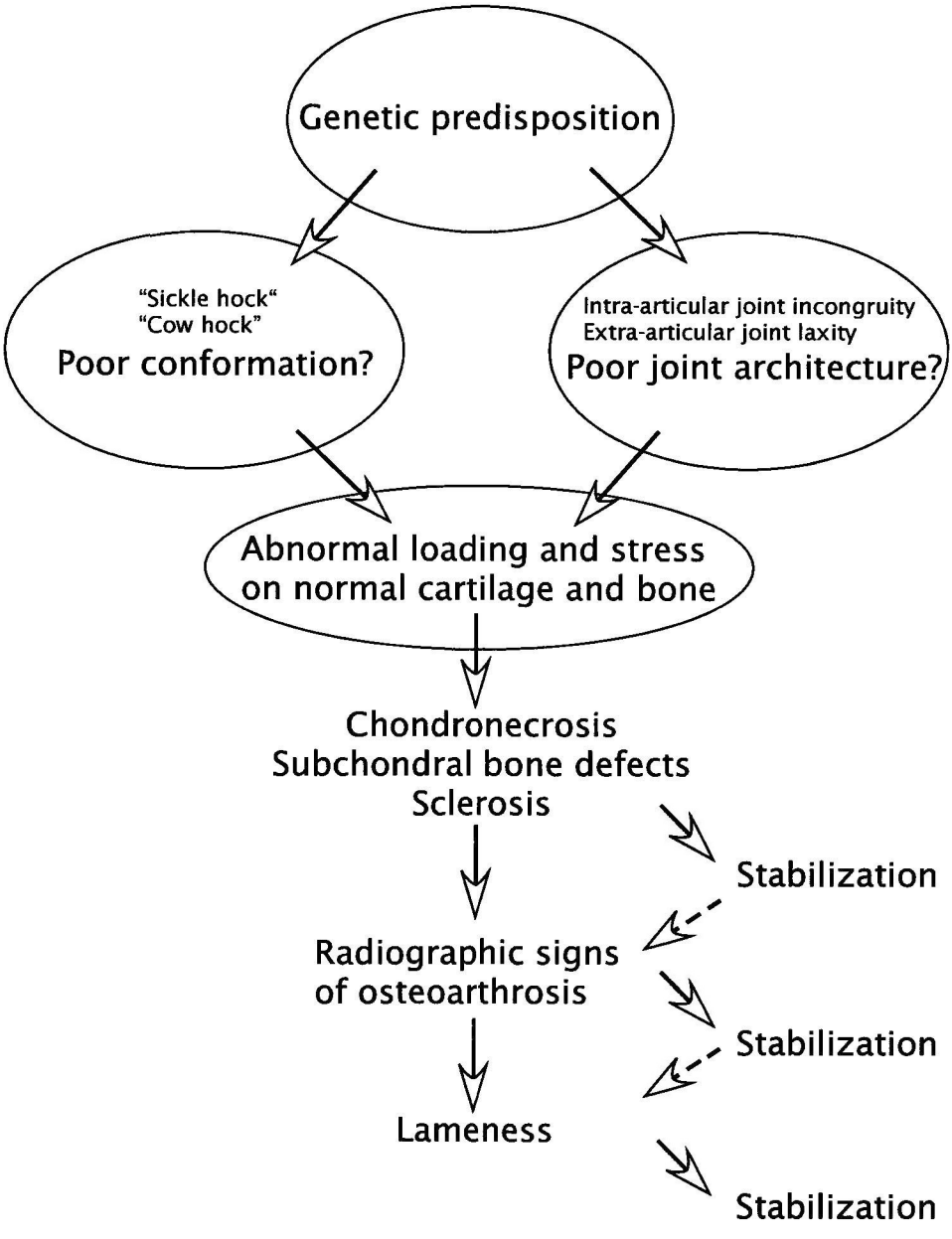

Figure 9. Flow chart showing hypothesised progression of bone spavin in Icelandic horses based on findings of this thesis.

Conclusions

1. In young horses (1-4 year-old), chondronecrosis of the articular cartilage was commonly found on histology, both medially and laterally in the CD joint. The characteristics of the histological findings strongly indicated early degenerative joint disease. The pattern of radiographic subchondral sclerosis indicated asymmetrical distribution of biomechanical forces within the joint.

2. The prevalence of radiographic signs of OA in the distal tarsal joints (RS) was 30.3% in the population of 6-12 year-old Icelandic horses in use for riding, and was strongly correlated to age.

3. The prevalence of hind limb lameness after flexion test of the tarsus was 32.4% in the population There was a significant correlation between RS and lameness after flexion test and 16.4% of the horses had both of them.

4. The presence of RS and lameness after flexion test affected the survival function significantly in a five years period, with strongest effect in the age range of 12 – 16 years. As the only finding, RS had higher prognostic value than lameness after flexion test, but the presence of both RS and lameness after flexion test had the highest prognostic value.

5. The intrinsic factors age and tarsal angle were significantly associated with RS. Birthplace, which was considered to be an indirect genetic effect because of clustering of dams, was also associated with RS. Workload and other environmental factors tested did not influence the prevalence of RS. Lameness after flexion test was influenced by sire and inverse related to the environmental variables age when broken to saddle and entered at stud show. The gait *toelt* was ruled out as a risk factor.

6. The heritability of age-at-onset of RS, reflecting the predisposition of OA in the distal tarsal joints, was estimated to be $h^2 = 0.33$ and the estimation of the heritability of lameness after flexion test yielded $h^2 = 0.42$. Together, the results suggest a medium high heritability of OA in the distal tarsal joints.

Further studies

Based on the heritability estimates of the current study, an expected reduction in the prevalence of bone spavin needs to be calculated for different possible breeding regimes. The inclusion of radiographic examination in the breeding programme would provide database for continuous improvement of the genetic analysis. Genetic studies on the molecular level in order to identify a genetic marker for the disease would be of interest.

The influence of the hind limb conformation and the architecture of the distal tarsal joints (objective measurements) on the biomechanic of the distal tarsal joints needs to be investigated, preferably by locomotion analysis in young horses. Then, the correlation of these factors to degenerative changes in the articular cartilage can be studied by radiography and histology.

In the future, Magnetic Resonance Image should be used to determine the initiation and progression of the disease in a longitudinal study *in vivo*.

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