A NEW SKELETAL DEFECT IN SHEEP

H.T. Blair and K.G. Thompson
Institute of Veterinary, Animal and Biomedical Sciences, Massey University,
Palmerston North, New Zealand.

SUMMARY
A new skeletal defect in Texel-cross sheep is described. The defect is tentatively categorised as chondrodysplasia, and is characterised by dwarfism and deformed forelimbs. Preliminary evidence suggests an autosomal recessive inheritance, but breeding trials to be conducted during 2003 are needed to confirm this hypothesis.

Keywords: Dwarf, skeletal, cartilage, genetic, defect

INTRODUCTION
Inherited diseases in production animals can cause both economic losses to the owner and (sometimes) animal suffering. Consequently, significant research effort is often expended in an attempt to elucidate the genetic cause of the disease, which may lead to a means by which animals carrying defective genes can be removed from the gene pool. The majority of simply inherited diseases show a recessive pattern of inheritance, although some genes show either dominant or overdominant modes of inheritance. In the past, test mating of potential nucleus males has been the only effective method of identifying carrier males. However, because of the expense and time delay, few breeders use test matings. A more practical action has been to cull both the sire and dam if known (and possibly near relatives) whenever an undesirable inherited condition arises. More recently, the development of molecular DNA techniques has led to the use of either DNA markers or gene probes as a means of removing heterozygous animals from the population.

A wide range of inherited skeletal defects have been reported in humans and animals, although only a small number have been reported in sheep in New Zealand (Jolly et al. 2003). Arthur et al. (1992) reported on the occurrence of osteogenesis imperfecta in Romney sheep and West et al. (1992) the occurrence of Spider Syndrome in Suffolk sheep. This paper describes a new defect not previously reported in sheep.

MATERIALS AND METHODS
Animals. All Texel cross sheep used in this study are sourced from a single commercial farm in New Zealand. All affected lambs had Texel genes on both sides of their pedigree. In addition to the commercial property providing animals for this study, affected lambs have been reported on one other commercial property and on a stud farm which provided rams to both commercial properties.
The second commercial property no longer uses Texel rams, and no recent occurrences of affected lambs have been reported.

An unusual phenotype (Figure 1) was first brought to the attention of the authors in late 2001, although the farmer and a local veterinarian had been aware of the condition for the two previous years. Unfortunately, all rams used in the 2001 mating were unavailable by late 2001. However, 11 afflicted lambs and 3 normal lambs which were supposed co-twins to afflicted lambs were tentatively identified to a pool of 12 dams. Blood samples were obtained from all animals for DNA parentage testing. The 11 afflicted lambs (5 ewes and 6 rams) were transported to Massey University in May 2002 for breeding studies.

Figure 1. Photograph of an affected lamb.

Nine afflicted lambs from the 2002 mating were identified on the same property. Blood samples for DNA parentage testing were obtained from 11 sires, 9 dams and afflicted lambs and 4 normal lambs born as co-twins to the afflicted lambs. In addition, 2 of the ewe lambs transferred to Massey University produced lambs (sires unknown). One produced a single lamb dead at birth caused by dystocia, another produced twins, one of which died 2 days post-partum and the second died at 3 weeks post-partum.

Parentage. DNA parentage testing was undertaken by SignaGen, Rotorua, New Zealand. Fourteen multi-allelic loci were typed for each animal.
Pathology. All tissue studies were undertaken in the Pathology Unit at Massey University.

RESULTS AND DISCUSSION

Phenotype. The phenotype has tentatively been described as a chondrodysplasia characterised by dwarfism and deformity of the forelimbs (Figure 1). Affected lambs appear normal at birth, but by 2 weeks of age show evidence of reduced growth rate, shortened neck and legs, forelimb deformities and a progressive reluctance to walk. With increasing age, the rib cage becomes increasingly widened under the forelimbs resulting in a bulldog-like appearance. It is not known whether this is caused by the animals having to lie down in a ventral position, thereby causing a mechanical expansion in the ribcage or whether the ribs grow in an inherently abnormal fashion.

There is a range in the degree of deformities in the forelimbs. The most severely afflicted die within the first 4 months of life, most likely from an inability to move freely for grazing. However, several animals exhibiting a less severe phenotype have survived to at least 18 months. In addition to the above limb deformities, one farmer has reported that afflicted lambs exhibit laboured breathing. It is not yet known as to whether this is caused by a change in shape of the chest or whether there is an underlying deformity in the respiratory system.

Thompson et al. (2003) reported that post-mortem examination of two severely affected 3-month-old lambs born in 2001 revealed extensive loss of articular cartilage and exposure of subchondral bone on the weight-bearing surfaces of the proximal humeri and femurs (Figure 2). Articular and physeal cartilages were thicker than normal, suggesting delayed or impaired endochondral ossification. Histologically, there was disorganisation of chondrocytes in articular and physeal cartilage of all bones examined. In addition, there were multiple foci of chondrolysis, which coalesced in some areas to form large clefts. The chondroid matrix surrounding chondrocytes had an abnormal fibrillar appearance. One of the twin lambs born at Massey University in 2002 showed early signs of the disease but died of an unrelated cause at 3 weeks of age. This lamb did not show erosion of articular cartilage but had the characteristic microscopic lesions in articular and physeal cartilages. The above phenotypic descriptions are not consistent with other reported chondrodysplasias. Sires and dams of afflicted lambs appear to be of normal phenotype.
Inheritance. All lambs presenting with the dwarf condition have Texel genes appearing on both sides of their pedigree. Both commercial properties experiencing afflicted animals sourced their Texel rams from the same nucleus flock. Parentage testing on the 11 afflicted and 3 normal lambs born in 2001 was able to accurately assign 6 afflicted and 2 normal lambs to 8 dams. The remaining 6 lambs could not be assigned to any of the remaining 6 ewes presented as putative dams. Also, no lambs could be confirmed as genetic twins. Given that identification of lambs to dams had occurred at about 4 months of age, this degree of inaccuracy in parentage assignation is unsurprising. After accounting for the dam alleles in the parentage test, it appeared that 4 of the 6 afflicted lambs that could be assigned to a dam were most likely sired by one ram. Thus, at least 2 sires generated the afflicted lambs in 2001.

The 3 lambs born to the afflicted ewe lambs moved to Massey University in 2002 are somewhat uninformative regarding the possible inheritance of the condition. Two ewes became pregnant to uncontrolled matings. All 3 lambs died, with 2 lambs being presented for post-mortem. One lamb died at 2 days and showed no signs of the condition, however it would have done little walking and there may not have been sufficient activity to cause erosion of the cartilage. The second lamb which died at 3 weeks showed lesions consistent with an early onset of the condition.

The evidence available to date favours an autosomal recessive genetic aetiology for this new dwarf condition in sheep. Studies on the genetic and biochemical basis of the disease are continuing. In 2003, 10 afflicted ewes and 9 possibly carrier ewes will be mated to an afflicted sire. An afflicted
sire will also be mated to c.150 unrelated ewes to generate c.75 daughters who will be mated back to
their sire in 2004. If the condition is recessive, 50% of the offspring of the sire by daughter matings
should be dwarfs. In purposely generating these dwarf lambs, due concern will be taken of their
welfare, as required by the Massey University Animal Ethics Committee. Any animals showing
signs of suffering will be humanely euthanased.

**Candidate genes.** Given the unusual structure of the collagen observed during histopathological
examination, possible candidate genes may be one of the 40+ collagen genes (OMIM, 2003). The
most common form of collagen in cartilage is type II. Mutations in the collagen type II alpha 1 gene
are known to cause several growth disorders in humans. Cartilage also contains large amounts of
glycosaminoglycans, and there is also a possibility that one of the many genes involved in its
manufacture may be at fault.

**ACKNOWLEDGEMENTS**
The trial has been funded by Massey University.

**REFERENCES**
The trial has been funded by Massey University.

**REFERENCES**