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I have never seen a CAT (CT or computed axial tomography) scan of a cow. Although the veterinary machines are big, they aren't cow big; however, they are calf big. So when given the opportunity to CAT scan a calf with a potential genetic defect, we jumped at the chance.

One of the most important things to consider when identifying a genetic mutation is to make sure all samples used for DNA analysis are taken from calves with the same abnormality. Put differently, if you were looking for the gene responsible for red you would start with red calves, not black calves, because all the red calves should be homozygous for the red gene. Likewise, if you are looking for the gene that causes a specific abnormality, for example digital subluxation (DS), you would want to make sure all your samples came from calves with digital subluxation - you don't want samples from calves with spastic paresis, or hip dysplasia or something else confusing your analysis. Thus, the importance of a physical exam, necropsy, and ancillary testing to fully identify and document the pathology associated with the abnormality.

Over the past couple of years there has been "barn talk" about an abnormality in Shorthorn and Shorthorn cross cattle that affects the lower hind limbs. Calves were born with the abnormality. The defect, much like "fawn calf" (contractural arachnodactyly, CA) in Angus cattle, is variable in presentation. Some calves are so severely affected they are unable to rise, while others are mildly and subtly affected.

By late 2011, seven cases of DS had been reported, samples and pictures submitted - but no x-rays had been taken and no calf had been fully examined or necropsied. The seven were from various regions of the country and shared

## You want to CAT scan a COW??

common ancestors, suggesting that the abnormality was genetic. Further strengthening the notion that this was a genetic defect was that 6 of the 7 were homozygous for a 2.7 MB region of the gene (ie homozygous in a specific size and location on the gene).

The defect affects only the hind limbs below the hock. The dew claws are inappropriately positioned and there is a curvature at the base of the leg that makes walking difficult. While most calves are born alive, severely affected calves cannot stand and are euthanized. Less severely affected calves appear to "improve" with age. The variable phenotype, somewhat like fawn calf, makes accurate diagnosis imperative.

In February 2012, I was contacted about a calf with suspected DS. This presented us with an amazing opportunity to obtain a complete examination of the calf including x-ray and necropsy - and a full body CAT scan of the affected calf. While necropsy of the calf revealed no abnormalities other than the distal hind limb, the x-rays and CAT scan were very revealing.

Special thanks to Dr. Tony Pease and Mark Sellers, radiologists at the Michigan State University College of Veterinary Medicine for creating these images.



The first picture shows the hind limbs of the calf with DS. The calf is on its belly and the left leg is abnormally curved at the metatarsal phalangeal joints (fetlock). The abnormal distal left leg also covers the abnormally curved right leg.



The next picture is an x-ray of a normal bovine distal limb. Note how the bones (phalanges) stack up on top of each other. Photo courtesy of vetmansoura.com



The third picture is an x-ray of the left hind limb taken front to back, just like the previous picture. The curvature of the leg is clearly evident. The bones, which should be stacked on top of each other are clearly not normally oriented and are twisted medially.



The final picture is computer recreated from the CAT scan - the soft tissue (muscles, nerves, ligaments, skin etc) have been removed to reveal only the bones of both legs. While the bones are abnormally arranged, they are normal in size and shape, suggesting that the abnormality is in the collateral ligaments. Although the CAT scan will never be routine for cattle, this information, along with the necropsy findings, will allow us to focus the gene hunt.

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Addition to the DS article - This is what we know DS is inherited as an autosomal recessive (like TH and PHA) - to have DS both parents must be carriers

BUT DS it is kinda complicated

AND there are some differences between DS and TH or PHA

1) Variable penetrance - we know there is variable phenotypic expression (ie some are severely affected and do not survive and some are "almost normal") - this is because the mutation alters a gene that makes a protein - sometimes that protein is not functional and sometimes it is partially functional - this leads to the variability of what we see. Penetrance is defined as the frequency with which a heritable trait is manifested by individuals carrying the principal gene or genes conditioning it. So for DS some homozygous animals are severely affected and some are not

2) Both the DS mutation and the PHA mutation are on the same gene - calves that carry the DS mutation (from one parent) and the PHA mutation (from the other parent) are susceptible to developing the DS phenotype - again it has to do with a functional protein - further these calves are likely to have more severe pathology