# HOW NORTH RONALDSAY SHEEP SURVIVE EXILE ON UK MAINLAND

**Author :** SUSAN HAYWOOD, DAVID BRITT

**Categories :** Vets

**Date :** September 8, 2008

**SUSAN HAYWOOD** and **DAVID BRITT** conclude this two-part article, with Dr Britt introducing Dr Haywood's explanation of the challenges this rare breed of sheep faces

**IN part one of this series (VT38.32) we discussed the origin and survival of the ancient North Ronaldsay breed of sheep on the eponymous island of North Ronaldsay, and their restriction to the foreshore of the island, where they were compelled to live on seaweed.**

We highlighted the threats to their survival from marine oil pollution and the subsequent removal of a subpopulation to the more sheltered island of Linga Holm.

The animals thrived for 20 years on Linga Holm, only to be moved to the UK mainland to avoid contravening EU animal welfare regulations in 2000. In part two, we give an account of their fate up to the present day, detailing the hazards they faced and, in particular, we demonstrate the interest of this ancient breed to biomedical science on account of their unusual mineral metabolism, particularly copper.

## Mainland experience

Despite a possible health risk from copper, North Ronaldsay sheep have been established on the mainland for several years. The breeders that formed the North Ronaldsay Sheep Fellowship (NRSF) are the main drivers of this.

These animals are registered with the Rare Breeds Survival Trust (RBST) and are of guaranteed genetic purity. However, despite this assertion, a genetic study a few years back at the University of Liverpool demonstrated that the mainland flock differed from the island sheep and that some adulteration had probably taken place in the recent past. David Britt had established a small flock at Leahurst (University of Liverpool) in 1980 for parasitological studies (later disbanded). By restricting copper intake, principally by not feeding commercial rations, the sheep survived and bred successfully, although deaths from copper toxicosis did occur from time to time.

Susan Haywood had been interested in copper toxicosis in animals and became alerted to the unique interest of this breed when differences between the pathology of Ronaldsay copper toxicosis (RCT) and classical copper poisoning of domesticated sheep became apparent. RCT had more in common with copper toxicosis (CT) in Bedlington terriers and a genetic condition in some Caucasian children, known as idiopathic copper toxicosis (ICT)[1]. When Dr Haywood became aware of the disbandment of the Linga Holm stock, she, along with Sandy Mackenzie (Harper Adams Agricultural Institute – HAAI), bid for some of the flock for study and conservation purposes.

With the collaboration of two paediatricians (Wilfred and Thomas Müller of Innsbruck University), Dr Haywood and Dr Mackenzie acquired funding from the International Copper Association (ICA) to study these sheep in relation to the childhood disease. The money allowed Dr Haywood to establish a small flock at her home in North Yorkshire, together with deer-proof fencing (the breed is notoriously agile), from which to breed for conservation purposes and to provide small flocks for Leahurst and HAAI for study.

The story now moves on to Dr Haywood explaining her experiences of breeding and maintaining these sheep, together with all the assaults from foot-and-mouth disease (FMD), scrapie and bluetongue, along with her studies in collaboration with colleagues at the University of Liverpool, the University of Aberdeen and the University of York.

## Survival and bureaucracy

So, what became of the sheep transferred from Linga Holm? As the sheep were dispatched to their new homes, the journey was deemed a success.

However, problems began almost at once – large losses were experienced in the first few years, chiefly from bacterial and viral infections not encountered previously in the breed, and from copper toxicosis. Sheep keepers complained about the “wildness” of these sheep compared to homebred animals. Their feral nature meant that they never truly adapted to their new environment, but those that survived bred successfully, and the next generation were much more manageable.

Most of the Linga Holm sheep have been put to mainland animals, and completely pure Linga Holm subset sheep are now somewhat rare, although Dr Mackenzie and I have maintained two such flocks.

As the island sheep are not registered by the RBST, these Linga Holm mainland representatives are the most pure examples of the breed.

I have lost most of the original conservation flock of five ewes and one ram over the years. The first ewe was lost due to copper toxicosis within 18 months, despite monitoring all feed intake and water supply, rigorously avoiding commercial feed, feeding of zinc licks and incorporating diets with a high iron content (such as beet pulp) into their winter diet.

However, I still have a lone survivor of the original disbanded flock that retains its intensely suspicious nature. The homebred progeny are much more tractable and although I still have occasional losses, on the whole they do seem to have acquired some physiological and/or genetic adaptation to copper.

The first conflict with officialdom arose in 2001 with the FMD outbreak, which raged around the northern counties and came to within four miles of Swaledale, my home. Despite an application to DEFRA to have my animals vaccinated (which was permissible by EU rules), this was turned down. However, the present policy will allow rare breeds to be vaccinated in a successive outbreak.

The mainland North Ronaldsay flocks survived on the whole, but worse was looming. Scrapie, following the bovine spongiform encephalopathy (BSE) debacle, assumed a higher profile and selective breeding for resistant stock was assisted by genetic testing. Five alleles with linkage to the prion protein of scrapie were identified as ARR, AHQ, ARQ, ARH and VRQ[2]. Sheep that inherit the ARR allele from both parents (ARR/ARR genotype) are highly resistant, whereas the VRQ/VRQ genotype group is extremely susceptible. The ARQ/ARQ genotype group also has little resistance.

In 2003, EU regulations for the control of scrapie were incorporated into the National Scrapie Plan, which heralded a rolling programme for the elimination of infected flocks and then the culling of rams with a scrapie susceptible genotype, such as those in the possession of VRQ and ARQ alleles. The eventual aim was to have a scrapie-resistant national flock.

This posed a challenge for breeders of primitive sheep, since the majority were of the ARQ/ARQ genotype – said to be the ancient ovine genotype. In fact, the North Ronaldsay sheep possessed this genotype almost exclusively and have, on this basis, been designated the most pure of the primitive breeds.

The breed was apparently saved by a departure from the most draconian measures of control, which could have obliterated them, along with other primitives. The reason for this appeared to be the discovery of an atypical form of scrapie in European flocks, which turned conventional wisdom on its head, in that the most susceptible flocks were the ARR haplotype and VRQ conferred resistance[3].

Having survived two possible mass extinctions, it might well have been wondered what this small

ancestral breed of sheep had to offer the modern world, and why anyone should go to all the trouble of attempting to save it? As with all primitive breeds, they allow us to see the ancestral form with an almost full complement of genes.

The North Ronaldsay sheep are small, with often a more goat-like or even deer-like head that shows a common ancestry with other ungulates. They occur in a wide variety of coat colours, ranging from albino to black, and with all shades of brown, gold or grey in between. The coat colour inheritance pattern is complex and almost impossible to predict from any one mating encounter. The lambs, when they appear, are “rainbow hued”, in contrast to the uniformity of their domesticated cousins.

It is said that the brain is bigger in relation to the body size than domesticated sheep. Certainly, they possess a canniness that denotes their more feral nature. I think this trait would allow them to live better in the wild than their often highly modified counterparts. In this context, it is interesting to observe their behaviour and limited ability to “flock” or to be driven as such – *One Man And His Dog* would be gravely disadvantaged with these sheep. Their strategy, using the element of surprise, is to turn a full 180° on wouldbe herders and drivers, and run and jump their way out of perceived danger.

Apart from these tendencies, which make shepherding more difficult than it would be normally, North Ronaldsay sheep show considerable individual diversity and charm. This is particularly noticeable during the summer months when, in the evenings, the sheep appear to have races, with older sheep as well as lambs getting involved. I have seen them jump and twist rather like impalas. There appears to be no reason for this, except from a superfluity of energy – it's just for fun.

North Ronaldsay sheep are also browsers, in a similar manner to goats. They are never happier than when nosing around in shrubs or weeds and, in this capacity, are quite excellent in removing docks and ragwort from horse-grazed pasture and generally clearing overgrown ground.

However, it is their peculiar adaptation to an unusual mineral diet on their native island that has given them scientific interest.

## Copper and arsenic

The “marine” diet of the island sheep has an unusual complement of trace elements. Seaweed, the mainstay of their diet, has been shown to be low in copper (less than 5ppm) and molybdenum (less than 0.5ppm), but relatively rich in zinc (more than 55ppm)[4]. It had already been realised that North Ronaldsay sheep transferred to the mainland were at risk from copper toxicosis[5]. Another finding has been that certain species of seaweed contain higher than normal concentrations of arsenic, apparently without the North Ronaldsay sheep suffering any adverse effects. This has prompted the study of arsenic metabolism in this breed[6].

My own interest has focused on the unusual copper metabolism of these sheep in relation to disease. As a species, sheep are notoriously susceptible to copper toxicosis on account of their limited ability to excrete excess metal. The North Ronaldsay breed has proved to be the most susceptible of all, which is related to their efficient absorption of dietary copper – we have shown a 10-fold increase in ability compared to a domesticated breed. This ability has exceptional usefulness in a copper-depleted environment, but is of limited value elsewhere.

Supported by the ICA, we established in a retrospective study that RCT was very similar in its pathological features to ICT, so we simulated the conditions in artificially fed North Ronaldsay lambs[7,8].

Unfortunately, although a founder had been established for the human condition, the actual gene mutation has not yet been established beyond it being shown not to be a variant of the Wilson disease gene, nor the same as the gene responsible for Bedlington terrier copper toxicosis. We await the sequencing of the sheep genome to take this work further.

Robert Beynon (veterinary preclinical sciences, University of Liverpool) and I obtained funding from the Wellcome Trust to investigate differences in the response to copper challenges in the North Ronaldsay breed, compared with a domesticated (Cambridge) breed. Deborah Simpson, using proteomic techniques, found the pattern of changes (fibrosis) was consistent with the greatly enhanced susceptibility of North Ronaldsay sheep to copper-induced oxidative stress. Moreover, we established possible biomarkers that could be of use in the childhood condition and in animal species susceptible to copper[9], [10], [11].

At the present time, funding from the RCVS Trust has allowed us to look at another peculiarity observed in North Ronaldsay sheep, which is the ability to take up copper into the brain[12]. The blood-brain barrier is notoriously resistant to metal uptake and a complex system of underexplored transporters appear to be responsible. We have hypothesised that over-expression of the copper transporters, which allow for the facilitated uptake of copper from the intestine, are also operative at the blood-brain barrier in North Ronaldsay sheep. This is a possibly important avenue of inquiry, now that the plaque protein that characterises Alzheimer's disease has been established as a copper-binding protein. The question is open as to how such metal transference occurs. It is also possible that copper is a risk factor in the translation of PrP to $PrPs^{C}$, the abnormal form found in scrapie, BSE and Creutzfeldt-Jakob disease – an area of investigation well studied by David Brown, of the University of Bath, and summarised in VT33.02[13]. We hope that North Ronaldsay sheep studies will answer some of these questions, or at least enable others to do so.

## Heroism

In conclusion, the story of the North Ronaldsay sheep and their remarkable survival and environmental adaptation, from probably the last ice age to the present day, possesses a certain amount of heroism. Furthermore, these little primitive sheep are a flagship for the whole

conservation movement.

The scrapie experience, outlined in this article, has established an important principle – that in a world in which the environment is undergoing considerable change, to reduce the genetic complement of our domesticated animals is to court disaster. In other words, to maintain haplotype diversity is an essential pursuit. This principle can be extended to the wider world, in that we disrupt threatened ecosystems at our peril.

The work of my colleagues and I with these sheep has shown unexpected revelations into adaptive mechanisms of mineral metabolism, and we hope it will instill further understanding into important diseases in both humans and animals.

I finish with a plea in aid of all primitive sheep that are, like the North Ronaldsays, an endangered breed. The North Ronaldsay sheep have been shown to be at risk on their native island from oil spills, but the threat of global warming and rising sea levels may be the breed's and the islanders' eventual undoing. Not only that, but they are at risk in protected habitats on the mainland – we now have bluetongue to contend with; I've ordered my vaccine.

Their continued existence depends on devoted breeders, such as members of the NRSF, who recognise their importance and attend to their welfare. Anyone who may be interested to take on a flock of North Ronaldsay sheep, despite the hazards, should contact either myself (shaywood@tiscali.co.uk) or the NRSF (www.nrsf.co.uk).

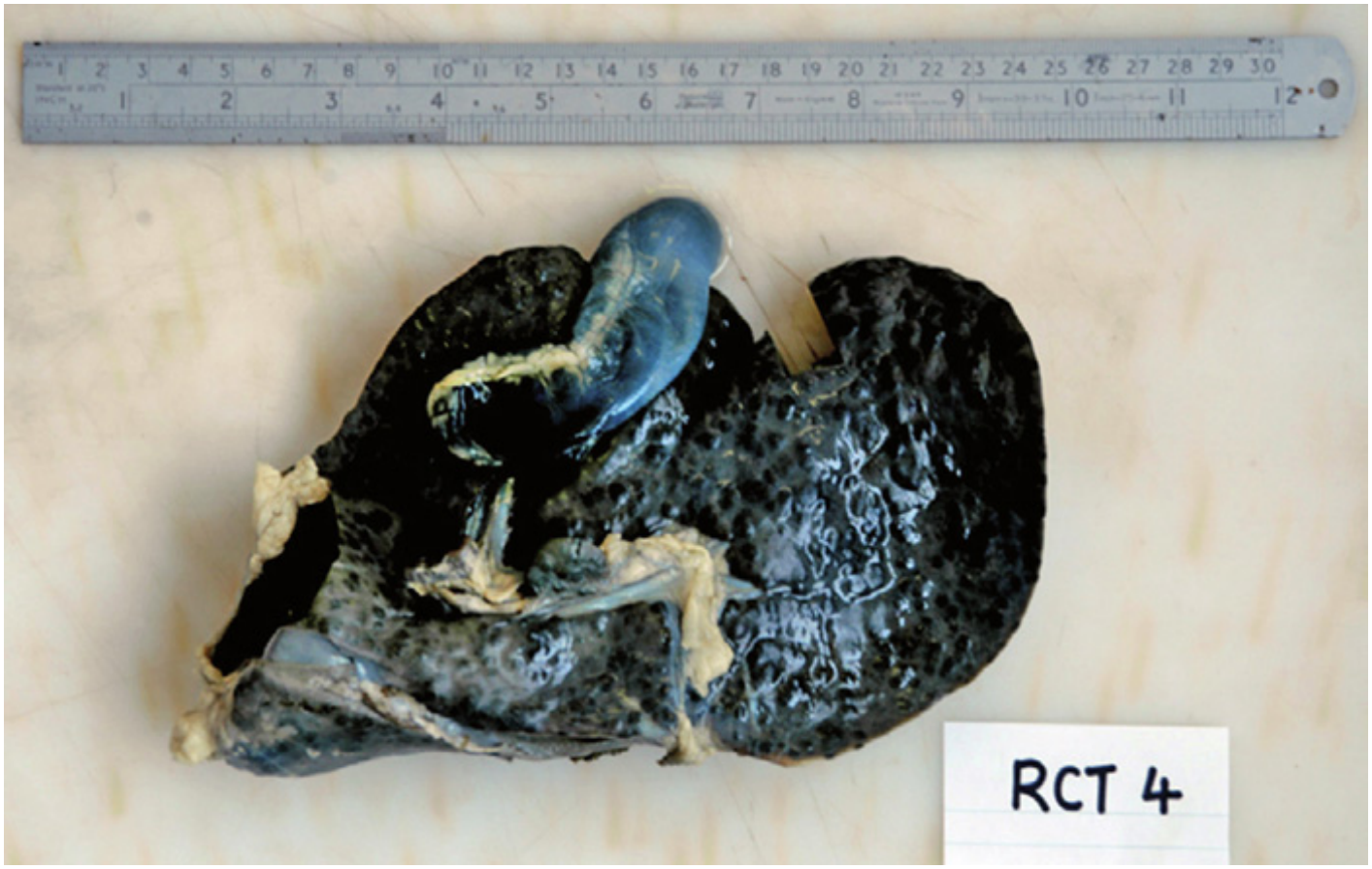
## References


- 1. Müller T, Müller W and Feichtinger H (1998). Idiopathic copper toxicosis, *Am J Clin Nutr* **67** (suppl): 1,082S-1,086S.
- 2. Detweiler L A and Baylis M (2003). *Rev Sci Tech OIE* **22**: 121-143.
- 3. Baylis M and McIntyre K M (2004). Scrapie control under new strains, *Nature*, **432**: 810-811.
- 4. McLachan G K and Johnston W S (1982). Copper poisoning in sheep from North Ronaldsay maintained on a diet of terrestrial herbage, *Vet Rec* **111**: 299-301.
- 5. Weiner G, Field A C and Smith C (1977). Deaths from copper toxicity of sheep at pasture and the use of fresh seaweed, *Vet Rec* **101**: 424-425.
- 6. Hansen H H, Raab A, Francesconi K A and Feldman J (2003). Metabolism of arsenic by sheep chronically exposed to arsenosugars as a normal part of their diet, *Env Sci Technol* **37**: 845-851.
- 7. Haywood S, Müller T, Müller W, Heinz-Erian P, Tanner M S and Ross G (2001). Copper-associated liver disease in North Ronaldsay sheep: a possible animal model for non-Wilsonian hepatic copper toxicosis of infancy and childhood, *J Pathol* **195**: 264-269.
- 8. Haywood S, Müller T, Mackenzie A M, Müller W, Heinz-Erian P, Tanner M S, Williams C L and Loughran M J (2004). Copper-associated hepatotoxicosis with hepatic stellate cell

activation and severe fibrosis in North Ronaldsay lambs: an animal model for non-Wilsonian hepatic copper toxicosis of infants, *J Comp Pathol* **130**: 266-277.

- 9. Simpson D M, Beynon R J, Robertson D H L, Loughran M J and Haywood S (2004). Copper-associated liver disease: a proteomics study of copper challenge in a sheep model, *Proteomics* **4**: 524-536.
- 10. Haywood S, Simpson D M, Ross G and Beynon R J (2005). The greater susceptibility of North Ronaldsay sheep compared with Cambridge sheep to copper-induced oxidative stress, mitochondrial damage and hepatic stellate cell activation, *Journal of Comparative Pathology* **133**:114-127.
- 11. Simpson D M, Mobasheri A, Haywood S and Beynon R J (2007). A proteomics study of the response of North Ronaldsay sheep to copper challenge, *BMC Veterinary Research* **2**: 1-12 (www.biomedcentral. com/1746-6148/2/36).
- 12. Haywood S, Paris J, Ryvar R and Botteron C (2008). Brain copper elevation and neurological changes in North Ronaldsay sheep: a model for neurodegenerative disease? *J Comp Pathol* (in press).
- 13. Haywood S and Brown D R (2003). Transmissible spongiform encephalopathies, *Veterinary Times*, **33**(2): 8-10.

*Mainland sheep keepers complained of the wildness of the North Ronaldsay breed compared to homebred animals.*




***A liver displaying the effects of Ronaldsay copper toxicosis.***

*The North Ronaldsay display a wide variety of coat colours, ranging from albino to black, and with all shades of brown, gold or grey in between. The coat cannot be predetermined.*