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# An investigation of the building blocks (mucins) of lung mucus in horses with Recurrent Airway Obstruction

An exploration of the properties and sites of production of lung mucus, which is in excess and blocks the airways, in horses with heaves.

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# Reasons why the study was performed



- RAO is a lung disease of horses similar to asthma in humans, which is usually worse when horses are stabled than kept outside.
- RAO can severely affect athletic performance and quality of life.
- There are increased amounts of mucus in the lungs of horses with RAO. This mucus blocks the airways and makes breathing more difficult.
- We wanted to investigate the building blocks (mucins) that make up the mucus, to see if there are any differences to the mucus of normal horse airways.
- This may help us to identify novel treatment options for management of the disease in the future.



# RAO and the Thoroughbred



- RAO affects 15% of the UK horse population.
- This lung disease can severely impact on athletic performance if poorly managed.
- The majority of thoroughbred horses are housed inside of at least part of the day.
- RAO is usually worse in horses affected by it when they are housed rather than being kept in a paddock, but can occur outdoors.
- Management of the disease often involves the use of inhalers (including steroid inhalers) and reducing dust in the environment.
- In the thoroughbred racehorse, turnout is often impractical and medications are not permitted on raceday.





# What are mucins?

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- Mucins are a family of high molecular weight proteins that are manufactured by epithelial cells, such as those lining the respiratory tract.
- Mucins' key characteristic is their ability to form gels; therefore they are a key component in most gel-like secretions, serving functions from lubrication to cell signalling to forming chemical barriers.
- Mucins are a component of the mucus that is found in increased quantity in the trachea (windpipe) of horses with lower airway disease.



During an endoscopic exam of a coughing horse, mucus is found in the trachea.

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# Project Aims & Objectives

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The long-term goal of this research project was to understand the role that mucus plays as part of the disease recurrent airway obstruction (RAO), by fulfilling the following aims:

- Measuring the amounts of mucins that make up mucus in samples from horses with RAO across a spectrum of disease
- Determining the sites of production of mucins in the horse airway.



# Project Aims & Objectives

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We also wanted to:

- Determine whether airway cells collected from RAO-horses can be grown in an experimental model system and produce mucus as they would do in the live animal, to enable study of mucus production in RAO-animals under experimental conditions and without the need for experimentation on live animals.
- Investigate ways to alter mucin production and therefore mucus properties after treatment of these cells in culture with therapeutic agents.



# Summary of what was done



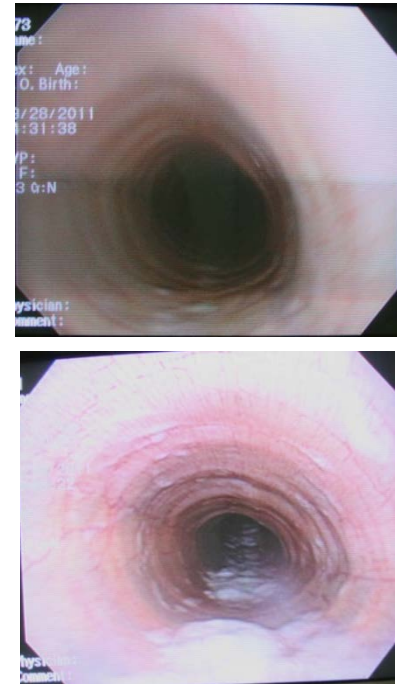
- Investigation of the mucins present in mucus samples from RAO horses and healthy control animals. Samples were collected from horses' airways when they were kept stabled and also when they were kept out at pasture.
- Investigation of the location, size and number of cells that make mucins in the horse airway by analyzing tissue samples: this was first undertaken in samples from healthy horses to establish "normal" before then comparing tissue samples from healthy horses to RAO horses that had been kept stabled inside and out at pasture.
- Refinement of the methods for growing airway cells collected from RAO-horses in an experimental model system.



# Results and Conclusions: 1



- RAO horses have more mucus in their airways than control animals, whether they are housed inside or kept at pasture.
- The mucins that make up the mucus in the abnormal horses are the same as the ones in healthy horses, but they are present in greater amounts.
- The properties of the mucins from RAO horses do not change depending on where the horse is housed (inside or outside).



Images taken from the windpipe of a healthy horse (top) and an RAO horse (bottom). The white mucus is more abundant in the windpipe of the RAO horse.



# Results and Conclusions: 2



- Mucins are made in the cells lining the airway and in deeper glands.
- The size and number of these cells varies greatly between individual horses, whether they are healthy or suffering from RAO.
- In any individual horse, the distribution of mucin-producing cells in the surface lining is consistent along the length of the windpipe.
- There are fewer glands deeper in the lung tissue compared to the windpipe.
- The surface lining mucin-producing cells are larger in horses that were housed outside compared to horses housed inside, irrespective of health status.
- Mucin-producing cells in the deeper glands are larger in horses with RAO than in healthy control animals.

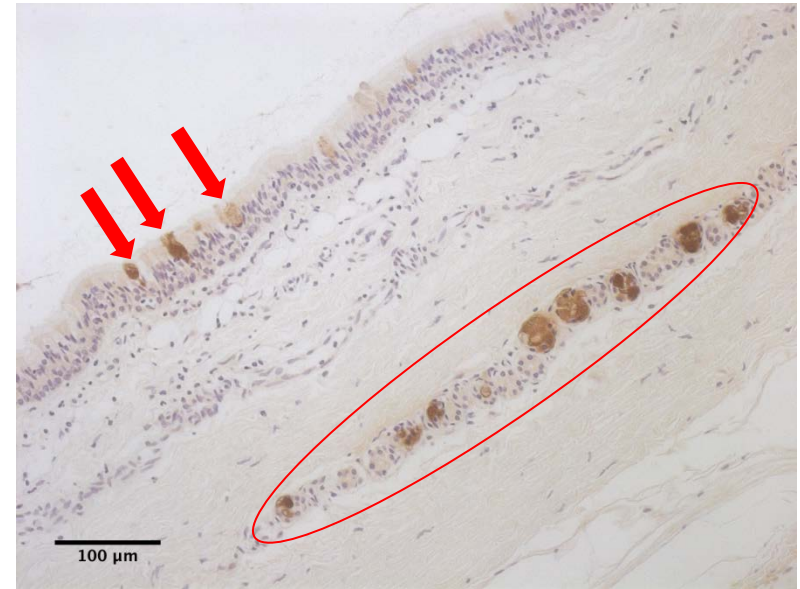


Image of a section of horse airway with a special stain to show the mucins that make mucus in brown. Red arrows point to mucin-producing cells in the airway surface lining, while the oval highlights mucin-producing cells in the deeper glandular tissue.

# Results and Conclusions: 3



- It is possible to grow cells collected from horse airways in a culture model. The cells are collected from the live animal on a brush that is repeatedly rubbed up and down the windpipe.
- It is also possible to freeze the cells after collecting them to enable them to be stored for later use.
- The cells that grow secrete mucins.
- Unfortunately the procedure is fraught with difficulties such as fungal and bacterial growth that kill the airway cells.
- The technique needs further refinement before experiments can be performed analysing and manipulating the mucus these cells produce.



A typical brush used to collect cells for the culture model

# Impact on the Thoroughbred

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- This project has provided greater understanding of the pathology involved in the disease RAO so that future research can be translated into new therapeutic targets.
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# Potential next steps

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- Further refinement of the cell culture model using airway cells from horses with RAO, in particular to address the issue of fungal and bacterial contamination.
  - Employ airway cell cultures to study and manipulate the mucins and mucus they produce with the long-term aim of finding a therapy that can help combat the excess mucus produced in horses suffering from this disease.
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To find out more about lower  
airway disease in racehorses

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Lower Airway Disease, now and in the  
future, KC Smith

[http://onlinelibrary.wiley.com/doi/10.1111/j.  
2042-3306.2011.00375.x/full](http://onlinelibrary.wiley.com/doi/10.1111/j.2042-3306.2011.00375.x/full)

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