

FINAL STATUS REPORT “SLUTT REPORT” AS OF NOVEMBER, 2013.

Prosjektleder: Eric Strand, NVH with support from Susan J. Holcombe and Heather Chalmers

Prosjekttittel: «Larynx funksjon hos Norsk og Svensk kaldblodstraver – årsaksforhold for dynamisk larynx kollapse assosiert med nakkefleksjon»

Funding: Norwegian/ Swedish Foundation for Equine Research / Norges Forskningsråd

Our research group again thanks the scientific committee for funding our above titled research project(s) for the period May 1st 2010 to May 1st 2013!

I Below is a list of our original objectives (5 different tasks or research projects):

Primary Objective (Main Task): attempt to determine the pathogenesis of Dynamic laryngeal collapse associated with poll flexion in the Coldblooded Trotter (CT) racehorse.

Secondary Objective (Task 1): To develop additional diagnostic imaging tests to compliment high-speed treadmill videoendoscopy.

Secondary Objective (Task 2): To perform a detailed comparative anatomical description of the laryngeal region of affected CTs, normal CTs, and normal Standardbred racehorses.

Secondary Objective (Task 3): To further develop and test prototype racing equipment that will limit head flexion, yet retain steering control of the horse during training and racing.

Secondary Objective (Task 4): Determine whether it is possible to develop an experimental model of the disease.

Secondary Objective (Task 5): Determine whether a bitless bridle reduces the severity of dynamic laryngeal collapse associated with poll flexion in horses

Addition research tasks were initiated during the time period of this study and are also reported below.

II. Status of tasks identified above as of November 2013

Primary Objective (Main Task): attempt to determine the pathogenesis of Dynamic laryngeal collapse associated with poll flexion in the Coldblooded Trotter (CT) racehorse.

We have developed a much greater understanding of this disorder which affects the airways of harness racehorses, especially the Coldblooded trotter. The results are presented in one defended PhD (publication # 8 below) and one upcoming PhD defense in spring 2014 (#10 below) and one already awarded Master of Science degree in August 2012 (#6 below). Our research has impacted a human medicine group pioneering evaluation and treatment of dynamic upper airway disorders in humans.

Secondary Objective (Task 1): To develop additional diagnostic imaging tests to compliment high-speed treadmill videoendoscopy.

Completed and published – see # 7 below

Secondary Objective (Task 2): To perform a detailed comparative anatomical description of the laryngeal region of affected CTs, normal CTs, and normal Standardbred racehorses.

Completed publications # 4 & 5 (endoscopic evaluation) and #9 below (histologic evaluation).

Secondary Objective (Task 3): To further develop and test prototype racing equipment that will limit head flexion, yet retain steering control of the horse during training and racing.

Completed and published – see # 3 below

Secondary Objective (Task 4): Determine whether it is possible to develop an experimental model of the disease.

Despite exploring different avenues, so far we have not been able to develop an experimental model of the disorder. Work is ongoing, but at this point we are not sure if this goal is technically possible. We have however learned a lot which is explained in PhD's (publications #8 and 10).

Secondary Objective (Task 5): Determine whether a bitless bridle reduces the severity of dynamic laryngeal collapse associated with poll flexion in horses

This study is almost finished and has resulted in a MSc. Thesis for DVM Zoe Fretheim-Kelly. We have technical problems with our tracheal pressure measuring system and need to test ca. 4-

5 more horses with the protocol. A manuscript will be submitted to *Equine Veterinary Journal* in 2014

Additional publications were made possible by this grant:

Publications # 1 and 2.

List of peer reviewed publications and MSc. and PhD Theses resulting from this research grant:

1. Fjordbakk CT and Strand E. Lidelser i øvre luftveger hos hest (Disorders of the Equine upper respiratory tract). *Norsk Veterinærtidsskrift (Norwegian Veterinary Journal)* 2010; 7: 634-644.
2. Hanche-Olsen S, Rannem L, Strand E. Bilateral dynamic laryngeal collapse associated with collection in “high poll flexion” in a gaited Icelandic horse. *Pferdeheilkunde (German)* 2010; 26 (6): 810-813.
ISSN:0177-7726. Accession number: WOS:000284250500007
3. Fjordbakk CT, Holcombe SJ, Fintl C, Chalmers H, and Strand E. A novel treatment for dynamic laryngeal collapse associated with poll flexion – the modified air-check. *Equine Veterinary J.* 2012; 44 (2) 207-213. DOI:10.1111/j.2042-3306.2011.00388.x
4. Strand E, Fjordbakk CT, Sundberg K., Spangen L, Lunde H, & Hanche-Olsen S. Relative prevalence of upper respiratory tract obstructive disorders in 2 breeds of harness racehorses (185 cases: 1998-2006). *Equine Veterinary J.* 2012; 44, 518-523. DOI: 10.1111/j.2042-3306.2011.00517.x
5. Strand E and Skjerve E. Complex dynamic upper airway collapse: Associations between diagnosis in 99 harness racehorses with one or more dynamic abnormalities. *Equine Veterinary J.* 2012; 44, 524-528. DOI: 10.1111/j.2042-3306.2011.00516.x
6. Zoe Fretheim-Kelly, Master of Science (MSc.) Thesis
“Does tongue and consequently hyoid apparatus position play a role in dynamic laryngeal collapse associated with poll flexion in Norwegian coldblooded trotters.” MSc. student with University of Edinburgh. Thesis awarded August 2012 from University of Edinburgh. Eric Strand - Thesis supervisor.
7. Fjordbakk CT, Chalmers HJ, Holcombe SJ, Strand E. Results of upper airway radiography and ultrasonography predict dynamic laryngeal collapse in affected horses. *Equine Veterinary J.* 2013; 45, 705-710. DOI: 10.1111/evj.12066

8. Eric Strand, PhD Thesis (dr. philos) (ISBN 978-82-7725-248-3)
A study of upper respiratory tract obstruction during exercise in 3 breeds of racehorses.
Thesis defended on June 20 and 21, 2013 at Norwegian School of Veterinary Science. Opponents were Professor Paddy Dixon, University of Edinburgh and Professor John-Helge Heimdal, Haukeland University (human) Hospital, Bergen, Norway. Thesis is 111 pages + 6 published manuscripts.
9. Muscle fiber characteristics of selected intrinsic laryngeal muscles in horses affected with dynamic laryngeal collapse associated with poll flexion. Fjordbakk CT, Goodwin D, Revold T, Piercy RJ. To be submitted to ***Equine Veterinary Journal*** by November 2013.
10. Cathrine Fjordbakk, Thesis for the degree *Philosophiae Doctor* (PhD):
Dynamic Laryngeal Collapse in harness racehorses: pathogenesis, diagnostics and treatment. To be submitted to the PhD committee Norwegian School of Veterinary Science by March 2014. Includes 4 peer reviewed manuscripts

Other publications reporting our research results

- 1) Strand & Fjordbakk. «Lidelser i øvre luftveier» Trav og Galopp Nytt. Årsrevy 2009
- 2) Fjordbakk C.T. - “Kaldblodssyndrom” – hva vet vi så langt? (Dynamic laryngeal collapse – where are we now?) *Husdyrforskmøtet (bi-annual national farm animal research meeting)* 15.02 2011, Lillestrøm, Norway. Abstract published in proceedings; s 562- 565
- 3) Review of equine respiratory research by our research group presented in journal “*International Innovation: disseminating science, research and technology*” July 2012, pages 54-56.
- 4) Trådløst endoskop for luftveisundersøkelse. Strand and Fjordbakk. Trav og Galopp Nytt 14/2012.

Presentations of our research results to veterinarians, human medicine groups, horsemen/ breeders, and racing authorities.

- 1) “Dynamic laryngeal collapse – an update” (in Norwegian). CT Fjordbakk. Husdyrforskningsmøtet 2011; Lillestrøm, Norway, February 15 2011
- 2) “Diagnostic work-up of resting upper respiratory disorders” (in Norwegian). CT Fjordbakk. Veterinære Fagdager, Oslo, Norway, May 20 2011
- 3) “Diagnostic work-up of dynamic upper respiratory disorders” (in Norwegian). CT Fjordbakk. Veterinære Fagdager, Oslo, Norway, May 20 2011
- 4) “Surgery of the equine upper respiratory tract” E Strand. Veterinary «Fagdager» (Bi-annual National Veterinary Meeting in Norway) Oslo, May 20, 2011.
- 5) “Relative prevalence of upper respiratory tract obstructive disorders in Warm (Standardbreds) and Coldblooded trotters” E. Strand. 60min presentation to Norwegian and Swedish breeding judges, veterinarians and racing officials. Sikkilsdalen, Norway. August 16, 2011.
- 6) Mini-symposium of exercise induced laryngeal obstruction in humans. E Strand. Presented 40minute talk regarding “dynamic diagnosis, pathology, and surgical treatment of upper respiratory tract disorders in racehorses” to national human medicine specialists at Haukeland hospital in Bergen, Norway April 11th, 2013.
- 7) “Present state of upper airway diagnosis in horses during exercise” Dr. Philos. lecture, E Strand, NVH June 20th 2013.
- 8) “Complications of equine upper respiratory tract surgery” Dr. Philos. lecture, E Strand, NVH June 20th 2013
- 9) “Present state of upper airway diagnosis in horses during exercise” 2 hour lecture to trainers and horse owners. E Strand. Mjøsa Equine Clinic, Stange, Norway, September 25, 2013.
- 10) “Update on research findings regarding dynamic laryngeal collapse in the Coldblooded Trotter” Veikle Balder Meeting associated with 2 day National annual breeding evaluation of Norwegian Coldblooded Trotters. E Strand spoke to ca. 75 breeders, judges and veterinarians at Biri Racetrack, Nov. 8, 2013.
- 11) ‘Luftvegsobstruksjoner hos hest’, CT Fjordbakk. Stevneveterinærkurs i regi av Mattilsynet, Oslo, 14.11.2013
- 12) ‘Lyder i halsen’, CT Fjordbakk. 1 time. Foredrag for Travtrenerskolen, Oslo, 27.11.2013

Awards

- 1) The paper (#7) “Results of upper airway radiography and ultrasonography predict DLC in affected horses” was selected by the Clinical Reviewer of Equine Veterinary Journal as one of the most clinical relevant papers to appear in EVJ’s Early View section in June 2013. As a result, a synopsis of the article was circulated to equine practitioners via BEVA’s e-News and was also sent to other organisations such as AAEP. The article was free to all users online for 10 weeks.

In addition to this, the paper was chosen to feature in a forthcoming issue of Veterinary Clinical Digest, which is a quarterly online publication featuring selected articles from a range of veterinary publications (www.veterinaryclinicaldigest.com) . A synopsis of the paper will appear with a link through to the full paper, which will then be made free permanently.

- 2) Our respiratory research in horses and its impact on human medicine was presented for a 5 minute national news coverage on January 5th, 2013 on NRK: see link <http://tv.nrk.no/serie/dagsrevyen/nnfa02010513/05-01-2013> and go to Chapter 13 (14minutes/ 2 seconds into sending).

The Future

We are currently exploring the possibilities with Professor John-Helge Heimdal, a human airway surgeon who performs dynamic endoscopy on humans at Haukeland University Hospital in Bergen, of having a comparative PhD student together exploring the similarities and differences of upper airway obstruction in humans and horses.

Cathrine Fjordbakk will defend her PhD at NVH in the spring of 2014.

Eric Strand is invited speaker at the Annual Scientific Meeting of the European College of Veterinary Surgeons (ECVS) next July (2014) in Copenhagen to speak on upper respiratory tract problems and to teach a respiratory surgery lab (1 day) to specialists in Equine Surgery.

We have answered many questions regarding upper respiratory tract problems in horses during the 3 year period of this grant, but our research findings have given rise to many new questions which need to be answered. We hope to seek successful funding for new projects in the near future.

Summary of Project

Dynamic laryngeal collapse associated with poll flexion (DLC) is a performance limiting obstructive disorder of the equine upper respiratory tract characterized by bilateral collapse of the vocal folds and arytenoid cartilages during exercise in poll flexion. DLC is the most common dynamic upper airway disorder diagnosed in the Norwegian/Swedish Coldblooded Trotter (NSCT) harness racehorse at the Equine Section at the Norwegian School of Veterinary Science (NSVS). Affected horses have a normal endoscopic appearance of the upper respiratory tract at rest and when exercised with a neutral head position. Bilateral collapse of the vocal folds and arytenoid cartilages manifest shortly after inducing poll flexion.

Other than being induced by poll flexion, knowledge about this recently described disorder is limited. Therefore, the aims of this study were to:

- Investigate the effect of poll flexion on airway mechanics in NSCT horses affected with DLC
- Evaluate the effect of an external device as a method of conservative treatment of DLC by limiting poll flexion
- Evaluate the accuracy of conventional diagnostic imaging modalities such as radiography and ultrasonography in predicting DLC
- Investigate potential pathophysiological factors such as laryngochoyoid conformation and positioning in relation to poll flexion and the potential for neuromuscular pathology in selected intrinsic laryngeal muscles of affected horses

From 2007 – 2013, a total of 50 harness racehorses presented to the NSVS were diagnosed with DLC. Presenting complaints were exercise intolerance and abnormal upper respiratory noise. Horses were diagnosed by using a standardized exercise endoscopy protocol which consisted of driving the horses on a treadmill for alternating 1minute periods of neutral head position and poll flexion. To achieve this, horses were fitted with regular racing tack including check and long reins and poll flexion was achieved by applying tension to the reins. From this pool of diagnosed cases, 29 horses were included in the subsequent studies in the current thesis. In the same time period, a total of 30 NSCT free of DLC were recruited as controls.

The extent of vocal fold collapse (VFC) and arytenoid cartilage collapse (ACC) identified was separately graded according to a previously published grading scale (0 = no collapse; 1 = mild collapse, 2 = moderate collapse; and 3 = marked collapse). At the time of diagnosis, 25 of the included horses had moderate or marked VFC and 23 horses had moderate or marked ACC. Endoscopic signs of DLC were only present during periods of exercise in poll flexion. A significant drop in tracheal inspiratory pressures, indicating increased respiratory impedance, was demonstrated in a group of DLC affected horses during poll flexion relative to elite, control racehorses.. The negative pressures recorded were similar to or lower than what is previously reported for experimentally induced recurrent laryngeal neuropathy, demonstrating the magnitude of respiratory compromise caused by this important, newly discovered disorder.

An external device, the modified checkrein, was developed to limit poll flexion while driving the horses with rein tension. Fitted with the conventional checkrein, signs of DLC were evident when the angle between the ventral aspect of the head and the ventral neck decreased by 12°. This degree of poll flexion was not achieved when horses were fitted with the modified checkrein, and endoscopic signs of DLC were significantly improved. Average improvement in endoscopic score was 1.5 degrees for ACC and 1.3 degrees for VFC. The endoscopic improvement was corroborated by recordings of tracheal inspiratory pressures which remained within normal range throughout the exercise test. This experiment proved that poll flexion indeed is the triggering factor for DLC. Also, the external device offers promise for conservative treatment of affected horses by limiting poll flexion during exercise.

Exercise endoscopy is considered the gold standard diagnostic method for dynamic upper respiratory tract disorders including DLC. Due to the low availability of this test on a national level, DLC may be underdiagnosed in the NSCT population. Therefore, conventional diagnostic imaging modalities were assessed as diagnostic tools in predicting DLC. Protocols for obtaining laryngeal radiographs and performing laryngeal ultrasonography in a neutral and a flexed head position were designed. Both modalities proved accurate in predicting DLC and may therefore be used by equine practitioners as selection criteria for referral for final diagnosis. Also, laryngeal radiography and ultrasonography could be implemented as screening tests for DLC in the NSCT population due to the wide availability and low invasiveness of these modalities.

An important finding when assessing radiography and ultrasonography in predicting DLC was the fact that laryngo-hyoid conformation and positioning in DLC horses responded differently to poll flexion than in horses unaffected by DLC. Poll flexion resulted in a further rostral advancement of the larynx in relation to the hyoid apparatus in DLC horses than in controls. Also, the laryngeal lumen width at the level of the vocal folds decreased in DLC horses in poll flexion whereas the lumen width remained unchanged or increased in normal horses. These findings indicate an external mechanical factor superimposed on an anatomic variation in the pathophysiology of DLC.

The pathophysiology of DLC was investigated further by muscle fibre characterization of the laryngeal muscles responsible for abducting the arytenoid cartilages and tensing the vocal folds; the cricoarytenoideus dorsalis and the cricothyroideus muscle. Fibre type grouping which is an early sign of neurogenic atrophy was evident in an equal proportion of DLC cases and controls. However, the changes identified were within the range of abnormal findings reported in clinically normal horses. Therefore, these results do not support a neuromuscular component in the pathogenesis of DLC.

In conclusion, laryngeal conformation and positioning are key elements in the pathophysiology of DLC. Poll flexion triggers clinical signs accompanied by marked derangements in airway mechanics which both can be alleviated by limiting poll flexion during exercise. Conventional diagnostic imaging may predict DLC in affected horses.