



Equine Lung Function Testing Device

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# Table of Contents

<b>Authorship Page</b> .....	v
<b>Acknowledgements</b> .....	vi
<b>Abstract</b> .....	vii
<b>Executive Summary</b> .....	viii
<b>Table of Figures</b> .....	x
<b>Table of Tables</b> .....	xi
<b>Chapter 1: Introduction</b> .....	1
<b>Chapter 2: Literature Review</b> .....	5
2.1 Equine respiratory system .....	5
2.2 Respiratory disorders of horses .....	6
2.3 Recurrent airway obstruction (RAO) .....	7
2.4 Inflammatory airway disease (IAD) .....	7
2.5 Other disorders .....	8
2.6 Diagnosing disorders .....	8
2.7 Pulmonary function tests .....	10
2.8 Equine pulmonary function tests .....	11
2.9 Imaging .....	12
2.10 Sampling .....	14
2.11 Special laboratory diagnostics .....	17
2.12 Additional methods .....	18
2.13 Cummings School Gold Standard .....	20
2.14 Complications when dealing with horses .....	26
2.15 Significance of developing devices for horses .....	27
2.16 Conclusion .....	28
<b>Chapter 3: Project Strategy</b> .....	30
3.1 Initial Client Statement .....	30
A) Initial Project Objectives .....	30
3.2 Project Constraints .....	31
3.2.1 Design Constraints .....	31
3.2.2 Function Constraints .....	31
3.2.3 Safety Constraints .....	32
3.2.4 Code and Regulations .....	32

3.3.1	Revised Project Objectives .....	33
3.4	Project Approach .....	34
3.4.1	LabVIEW Code Approach .....	34
3.4.2	Mask Design and Prototyping Approach .....	35
3.4.3	Material Selection Approach .....	35
3.4.4	Design Validation and Testing.....	36
<b>Chapter 4:</b>	<b>Methods and Alternative designs.....</b>	<b>37</b>
4.1	Needs Analysis .....	37
4.1.1	Current Design Limitations .....	37
4.1.2	Equine Respiratory Testing Limitations .....	37
4.1.3	Design Pairwise Analysis .....	38
4.2	Functions and Specifications.....	40
4.3	Feasibility Study .....	41
4.4	Conceptual Designs.....	41
4.5	Preliminary and Alternative Designs.....	42
4.6	Material Selection .....	46
4.6.1	3D printer material.....	46
4.6.2	Carbon Fiber .....	47
4.6.3	Stainless Steel.....	47
4.6.4	Plastic Molding .....	48
4.6.5	3-Ply Medical Grade .....	48
4.6.6	Neoprene Fabrics .....	49
4.7	Mask Testing .....	49
4.7.1	Mechanical Testing .....	49
4.7.2	Interior Mesh Testing.....	50
4.8	Sensor Selection.....	50
4.9	LabVIEW Code Methods .....	52
<b>Chapter 5:</b>	<b>Design Verification and Results .....</b>	<b>53</b>
5.1	Material Selection and Decisions.....	53
5.1.1	Structural Material Considerations .....	53
5.1.2	Internal Mesh Material Considerations .....	54
5.1.3	Final Material Decisions .....	54
5.2	Material Testing .....	55

5.2.1	3D Printed Material Testing .....	55
5.2.2	Internal Mask Material Testing .....	55
5.3	Design Optimization.....	58
5.4	Design Modeling .....	58
<b>Chapter 6:</b>	<b>Discussion .....</b>	<b>59</b>
6.1	Results and Objectives .....	59
6.2	Economics .....	59
6.2.1	Sensor Purchasing Cost .....	60
6.2.2	Mask Design Cost .....	60
6.2.3	Material Component Cost.....	60
6.2.4	Total Cost .....	60
6.2.5	Mass Production Cost .....	61
6.3	Environmental Impact.....	61
6.4	Societal Influence .....	61
6.5	Political Ramifications .....	61
6.6	Ethical Considerations.....	62
6.7	Health and Safety Issue.....	62
6.8	Manufacturability .....	62
6.9	Sustainability.....	62
<b>Chapter 7:</b>	<b>Final Design and validation .....</b>	<b>63</b>
7.1	Final Mask Design .....	63
<b>Chapter 8:</b>	<b>Conclusions and Recommendations.....</b>	<b>66</b>
8.1	Future Recommendations .....	66
8.1.1	Component Selection and Mass Production.....	66
8.1.2	Wireless Connectivity.....	67
8.1.3	Integration of RIP Bands .....	67
8.1.4	Display Software and Operation .....	68
Chapter 9:	References.....	69
Chapter 10:	Appendices.....	76
<b>Appendix A:</b>	<b>Mask Drawings .....</b>	<b>76</b>
<b>Appendix B:</b>	<b>Bag Drawing.....</b>	<b>87</b>
<b>Appendix C:</b>	<b>LabVIEW Front Panel .....</b>	<b>88</b>
<b>Appendix D:</b>	<b>Human Mask .....</b>	<b>89</b>

**Appendix E: Mask Instructions ..... 92**  
**Appendix F: Low flow wind tunnel SOP ..... 93**  
**Appendix G: SOP for single calibration LabVIEW program ..... 96**  
**Appendix H: Cost Breakdown and Budget ..... 103**

## Authorship Page

<b>SECTIONS:</b>	<b>WRITTEN BY:</b>	<b>EDITED/REVIEWED BY:</b>
TITLE PAGE	JLS	ALL
TABLE OF CONTENTS	BDH	ALL
AUTHORSHIP PAGE	ADW	ALL
ACKNOWLEDGMENTS	DLF	ALL
ABSTRACT	JLS, BDH	ALL
TABLE OF FIGURES	ADW	ALL
TABLE OF TABLES	BDH	ALL
CHAPTER 1 — INTRODUCTION	All	ALL
CHAPTER 2 — LITERATURE REVIEW	All	ALL
CHAPTER 3 — Project Strategy	JLS,DLF	ALL
CHAPTER 4 — Methods and Alternative Designs	ALL	ALL
CHAPTER 5 — DESIGN VERIFICATION - RESULTS	JLS,DLF	ALL
CHAPTER 6 — DISCUSSION	ALL	ALL
CHAPTER 7 — FINAL DESIGN AND VALIDATION	ADW,JLS	ALL
CHAPTER 8 — CONCLUSIONS AND RECOMMENDATIONS	JLS,DLF	ALL
REFERENCES	ALL	ALL
APPENDICES	ALL	ALL

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## **Abstract**

The Cummings School of Veterinary Medicine at Tufts University is the only facility in New England with a non-invasive device for diagnosing equine respiratory problems. Their first rendition of the device, while functional, was very cumbersome and expensive, leading to a partnership with Worcester Polytechnic Institute (WPI) to improve the aspects of this design. Following the work of a previous WPI design team and that of Dr. Mazan of the Cummings School of Veterinary Medicine, our team refined the display and functionality of LabVIEW code for analysis, and developed significant improvements to the mask design in order to house a Rev C sensor, which is used for data acquisition. The result of this project is a lightweight, cost effective, and reproducible mask design capable of producing consistent and accurate measurements of respiratory function.



## Executive Summary

# Equine Lung Function Testing

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**Abstract-- The Cummings School of Veterinary Medicine at Tufts University is the only facility in New England with a non-invasive device for diagnosing equine respiratory issues. Following the work of the previous WPI design team and that of Dr. Mazan of the Cummings School of Veterinary Medicine, our team refined the display and functionality of the LabVIEW codes used for analysis, and made significant improvements to the mask design. The result of this project is a design capable of producing consistent and accurate measurements of respiratory function that is both lightweight and cost effective.**

## I. INTRODUCTION

80% of stabled horses experience lung disorder. Due to their living environment, many stabled horses suffer from inflammatory airway disease [1]. Roughly 70% of competition horses that are kept in athletic facilities experience pulmonary disorders [2]. Poor air quality in stables leads to an increased risk of these diseases, and is typically caused by airborne hay, dirt, excrement, and dust.

The current method for testing equine lung function is an invasive procedure that takes pressure measurements using esophageal balloons. Additionally bronchoalveolar fluid samples are taken for clinical testing for respiratory disorders. These testing methods are expensive, and potentially traumatizing for the horse. These procedures are often ineffective in providing a prompt diagnosis for potentially life threatening pulmonary diseases such as COPD or Asthma [3]. The Fleisch pneumotachograph itself cost \$8,000. The remaining system components

cost approximately \$10,000 resulting in a total system cost of approximately \$18,000 [4].



**Fig. 1: Current Fleisch Pneumotachograph**

We continued upon the testing from last year's MQP to create an improved, non-invasive diagnostic device that would be a cost effective tool for the data collection and data analysis of horse lung function testing. The previous year's device used a hot wire anemometer, comparable to the fleisch pneumotachograph, but significantly more lightweight and inexpensive. Our MQP team validated the sensor and developed a mask housing system to be mounted on the horse during respiratory testing. Additionally we improved upon the existing LabVIEW and excel outputs for live data monitoring and data analysis.

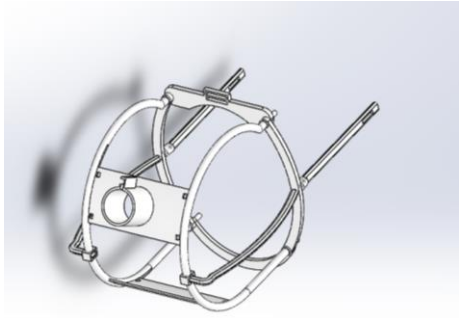
## II. DESIGN APPROACH

To meet Dr. Mazan's requirements, the design needed to be lightweight, attachable to a standard bridle, breathable, moisture absorbent, and easily applied and cleaned. In addition to the mask design, the LabVIEW code needed to be restructured and redesigned for better user interface (UI). The labview code needed to be updated to better reflect the respiratory patterns of a horse. Preliminary designs included a kinetics model on a replica horse and Solidworks models designed to fit a standard bridle.

We tested several materials for the framework of the mask which involved a comparison of material properties versus weight and price. The internal materials were tested for water absorption, breathability, and ability to direct airflow through the sensor housing tube. Our LabVIEW code provides a simplified monitoring display with minimal user inputs. The color scheme and layout of the individual graphs were altered for improved visibility and comparison. We removed global variables from the code, which improved the speed of the code, reduced file size, and limits errors when running tests on different computers.

### III. FINAL DESIGN

The final design consisted of a frame made of 3D printed acrylonitrile butadiene styrene (ABS) and a neoprene mesh suspended within the frame. Expired air is directed through the neoprene mesh into the ABS tube on the front of the mask. The air then passes over the Rev C sensor which is connected to a computer which uses LabVIEW software to run our LabVIEW code for data analysis. Figure 2 below illustrates the final Solidworks model for the design.

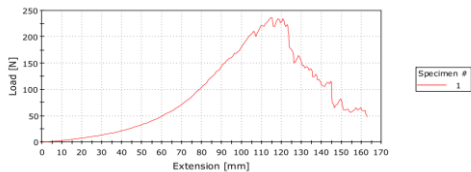


**Fig. 2: Final Respiratory Mask Design**

The LabVIEW display was updated and simplified in design and operation. The display presented a simplified grey background with two displays for the breathing rate in respect to velocity and in relation to volumetric breathing rate. The raw data is extracted to a local file on the user's hard drive, and may be reflected for additional display and peak ranges through an Excel or Matlab code.

### IV. TESTING

Various materials were tested with an Instron 5543 in a 3pt bending testing (ABS mask design) for compressive and bending stresses, and tensile testing (neoprene mesh). Figure 3 below indicates the Load-Extension curve of the Neoprene mesh.



**Fig. 3: Tensile Testing Neoprene Fabric**

Additionally, the breathability and water resistance of the mesh were tested by using a contact angle test and breathability testing. We concluded from testing that ABS 3D printed material is the ideal material based on weight and cost, and neoprene is the ideal material for the internal mesh based on design specifications and cost.

### V. FUTURE WORK

Future recommendations for the continuation of this project include the incorporation of respiratory Inductance Plethysmography (RIP) bands to the system and LabVIEW code, as well as designing a wireless alternative for mobile testing through the use of an Arduino, or other device capable of data acquisition. We recommend testing this sensor and code on live horses to gauge response to the system in action.

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## Table of Figures

<b>Figure 1:</b> Airflow into the horse during inspiration.....	6
<b>Figure 2:</b> A horse being tested with the passive Fleisch pneumotachograph device .....	21
<b>Figure 3:</b> A schematic of the current device and how it works.....	21
<b>Figure 4:</b> Placement of abdominal and thoracic RIP bands.....	22
<b>Figure 5:</b> Examples of graphs used for diagnosis.....	23
<b>Figure 6:</b> Representative data from the RIP bands and the Fleisch pneumotachograph.....	24
<b>Figure 7:</b> Cummings School of Veterinary Medicine FOM device.....	25
<b>Figure 8:</b> Schematic of FOM method.....	25
<b>Figure 9:</b> Kinects Model.....	42
<b>Figure 10:</b> Bridle Parts Description.....	43
<b>Figure 11:</b> Preliminary Cage Design.....	44
<b>Figure 12:</b> 3D Printed Preliminary Design.....	44
<b>Figure 13:</b> Third Iteration Mask Design.....	45
<b>Figure 14:</b> Exploded Third Iteration Mask Design.....	46
<b>Figure 15:</b> Neoprene Force vs. Displacement.....	55
<b>Figure 16:</b> Neoprene Hydrophobicity Test.....	57
<b>Figure 17:</b> Hydrophobicity Test after 5 Minutes.....	57
<b>Figure 18:</b> Final mask design.....	63
<b>Figure 19:</b> Final mask.....	64
<b>Figure 20:</b> Drawing of final side support.....	76
<b>Figure 21:</b> Drawing of final horizontal support.....	77
<b>Figure 22:</b> Final mask views.....	78
<b>Figure 23:</b> Drawing of final mask extension.....	79
<b>Figure 24:</b> Drawing of left nose hoop.....	80
<b>Figure 25:</b> Drawing of right nose hoop.....	81
<b>Figure 26:</b> Drawing of mask support.....	82
<b>Figure 27:</b> Drawing of neck bar.....	83
<b>Figure 28:</b> Drawing of nose rest.....	84
<b>Figure 29:</b> Drawing of the sensor housing holder.....	85
<b>Figure 30:</b> Drawing of the sensor housing.....	86
<b>Figure 31:</b> Final bag drawing.....	87
<b>Figure 32:</b> Front panel of the LabView program.....	89
<b>Figure 33:</b> Human mask.....	90
<b>Figure 34:</b> Human mask.....	91
<b>Figure 35:</b> Human mask.....	92
<b>Figure 36:</b> Reducers attached.....	93
<b>Figure 37:</b> Reducers unattached.....	93
<b>Figure 38:</b> Threaded nipple.....	93
<b>Figure 39:</b> Balls valve connected to rotameter.....	93
<b>Figure 40:</b> Balls valve connected to regulator.....	94
<b>Figure 41:</b> Regulator in closed position.....	94
<b>Figure 42:</b> Balls valve in closed position.....	94
<b>Figure 43:</b> Male quick disconnect.....	94
<b>Figure 44:</b> Rev C in wind tunnel.....	95

<b>Figure 45:</b> Completely open balls valve.....	95
<b>Figure 46:</b> DAQ Box.....	96
<b>Figure 47:</b> Sensor with pins on left.....	97
<b>Figure 48:</b> DAQ Box ports with labels.....	97
<b>Figure 49:</b> Rev C sensor schematic.....	97
<b>Figure 50:</b> Sensor in mask.....	98
<b>Figure 51:</b> Plug in outlet.....	99
<b>Figure 52:</b> DAQ box connected to computer via USB.....	99
<b>Figure 53:</b> Ringer used to choose which program is running.....	99
<b>Figure 54:</b> Different programs.....	99
<b>Figure 55:</b> Run arrow.....	100
<b>Figure 56:</b> Desired start conditions.....	100
<b>Figure 57:</b> Desired end conditions.....	100
<b>Figure 58:</b> Ringer setting.....	101
<b>Figure 59:</b> Define file path.....	101
<b>Figure 60:</b> Start/stop saving.....	101
<b>Figure 61:</b> Stop program.....	101
<b>Figure 62:</b> Excel warning message.....	101

## Table of Tables

<b>Table 1:</b> Air-fluid patterns.....	13
<b>Table 2:</b> Cells present in disorders.....	15
<b>Table 3:</b> Airway reactivity.....	20
<b>Table 4:</b> Pairwise analysis.....	39
<b>Table 5:</b> Neoprene Tensile Test Data.....	56
<b>Table 6:</b> Cost breakdown and Budget.....	103

## **Chapter 1: Introduction**

As many as 80% of stabled horses experience lung disorders. Due to the environment in which they live, many stabled horses suffer from inflammatory airway disease (Cummings Veterinary Medical Center, 2016). Roughly 70% of competition horses that are kept in athletic facilities experience pulmonary disorders (Robinson, 2003). Most stables have poor air quality due to hay, dirt, excrement, and dust, leading to an increased risk of these diseases. Horses are the key component of many well-established industries. Equine industries contribute approximately \$39 billion to the U.S. economy, and support 1.4 million full-time jobs, (American Horse Council, 2017). Maintaining the horse's health is important to the survival of these industries. Because respiratory issues are so prevalent, diagnosis, treatment, and prevention are critical. This report focuses on improving the diagnostic device that is used for equine respiratory diseases.

A current method for testing equine lung function is an invasive procedure that takes pressure measurements using esophageal balloons; it takes bronchoalveolar fluid samples for clinical testing of respiratory disorders. These testing methods are expensive, and potentially traumatizing to the horses. These procedures are often do not provide a prompt diagnosis for life threatening pulmonary diseases such as Chronic Obstructive Pulmonary Disorder and Asthma (Mazan, Personal Communication, 2017). Delayed prognosis and diagnosis of these diseases compromise the veterinarian's ability to prevent permanent damage to the respiratory system (Mazan, Personal Communication, October 24, 2017). Two alternatives to this method are a non-invasive passive airflow device and a forced oscillatory mechanic (FOM) device.

Dr. Melissa Mazan is a veterinarian from the Cummings School of Veterinary Medicine at Tufts University, specializing in the analysis of equine lung function. She utilizes both the

passive airflow device and the FOM through a Fleisch pneumotachograph to measure flow rate, lung pressure, and lung capacity of horses. The pneumotachograph outputs data through a virtual interface, displaying the measured results. Additionally, Respiratory Inductance Plethysmography (RIP) bands are strapped on the thoracic region of the horse. These measure the change in output volume through the same virtual interface (Mazan, Personal Communication, September 9, 2016). From this data, Dr. Mazan interpolates the possible respiratory diseases based on the variations in graph slope and distribution. The interface and device were developed by Dr. Andrew Hoffman of Tufts University Cummings School of Veterinary Medicine, another equine expert.

The passive device is used frequently in testing and diagnosis due to its simplicity of operation and because it is available for use with all race horses, regardless of age or condition. The FOM device can only be used on young racehorses and sport horses. Older horses or severely affected horses cannot use this device because their breathing rates too closely matches the frequency of the sine waves to be distinguishable, (Mazan, Personal Communication, October 24, 2017). Although the passive device has proven to be an effective testing mechanism, it poses some concerns that need to be addressed. The Fleisch pneumotachograph used for the current device is no longer in production, making it difficult to replace. The current device is also expensive. The Fleisch pneumotachograph itself cost \$8,000 and can only be calibrated to an accuracy of  $\pm 3.33\%$ . The remaining system components cost approximately \$10,000 resulting in a total system cost of approximately \$18,000 (Mazan, Personal Communication, September 9, 2016). The current device is also heavy, approximately 3 lbs., and protrudes from the horse's muzzle by 12 in., which poses the risk of head injuries to the human operators due to a horse's tendency to swing it's head. The costs, risks, and inconveniences of using the device in the field

makes the Fleisch pneumotachograph inaccessible to other veterinarians. Thus, Cummings School of Veterinary Medicine at Tufts is the only location in the Northeast that uses the Fleisch pneumotachograph (Mazan, Personal Communication, September 9, 2016).

Last year, a team of WPI students was tasked with creating an improved, non-invasive diagnostic device that would be a cost effective solution to the data collection and analysis of horse lung function testing. They determined that a hot-wire anemometer would be comparable to the current system's Fleisch pneumotachograph, while being significantly less expensive. Additionally, they focused on creating an output display in LabVIEW that would respond to the live feed of the system, so that veterinarians can view the abnormalities present in the breathing rate and volume. The work of the previous team provided a basis to improve the equine lung function test, however before this is fully investigated and utilized in the field, a number of primary objectives need to be met to improve functionality and safety of the device.

Our sponsor, Dr. Mazan, provided us with a client statement in order to improve the design of the sensor housing and mask. The limitation of the current design is that it is large and cumbersome, and is a danger to the people operating the device. Dr. Mazan herself was hospitalized due to the current device. Additionally to the safety concern, the device is heavy, weighing approximately 3 lbs. This requires an assistant to hold the device upright while the horse is undergoing testing because the horse is not able to support the weight of the device. This is a significant limitation as normal activities cannot be measured such as running and jumping over obstacles. Beyond the scope of the physical limitations of the current design, financially, the current design is not feasible for most veterinarians interested in testing equine lung function. The current model costs upwards of \$18,000, and is no longer in production, making diagnosis of

equine lung function, and the repair of the system costly (Mazan, Personal Communication, September 9, 2016).

Our team evaluated the current mask design, and produced a lightweight, form-fitting mask that adjusts over a standard bridle and houses a hot-wire anemometer. Dr. Mazan indicated sanitation as a major consideration in the design, as this system is used interchangeably with each horse. Another priority is to design the mask to be easily cleaned.

We prototyped potential mask designs based on cost effectiveness, strength, and weight. Through our literature review, we concluded that the anemometer must be exposed to direct flow from the nose of the horse. With this in mind, we created a wireframe support structure leading from the clips on the side of the bridle. The design is sealed to the horses face with a rubber sheath, fitting over the horse's nose. The wireframe is velcroed into place, and protrudes 1 inch from the horse's nose. The air is directed downwards through a hole in the inferior segment of the mask, while providing a spit release so no moisture accumulates.

Our device was tested through the use of a wind tunnel, which simulated the speed and volume of a horse. We calculated the weight of our designed unit and found that it is 0.91 lbs. From this, we determined that our system is a significant improvement on the current system, given the reduction in weight, reduction in price, and similar effectiveness when compared to the old system.

This report illustrates our understanding of the design considerations necessary to develop an improved equine lung function testing apparatus, and the limitations of current designs on the market.

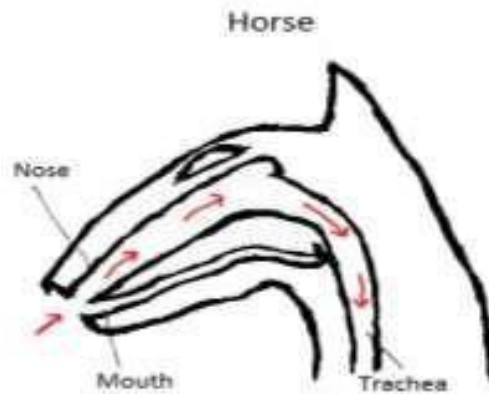


## Chapter 2: Literature Review

### 2.1 Equine respiratory system

The respiratory system is the pathway to exchange oxygen and carbon dioxide. Air travels into the horse's pulmonary system through the upper respiratory tract (URT) and then the lower respiratory tract (LRT) (Davis, 2013; Crabbe, 2007). The URT consists of nostrils, nasal passages, pharynx, larynx, and the trachea. The LRT consists of the structures in the lung including the bronchi, bronchioles, and alveoli (Davis, 2013).

In the URT, Cartilage rings inside the nostrils can expand to allow increased airflow, which is necessary during exercise (Crabbe, 2007). Air continues through the nostrils and nasal passages to the pharynx. The pharynx in a horse has two purposes: facilitate airflow to the larynx and transport food to the esophagus from the oral cavity (Davis, 2013; Crabbe, 2007). The soft palate separates the oral cavity from the pharynx and only allows airflow through the oral cavity when the horse is swallowing (Davis, 2013). The epiglottis also assists in keeping food from entering the larynx by separating the trachea and esophagus. When air is flowing into the trachea the epiglottis blocks the esophagus by lying flat over the esophagus. When the horse is swallowing food, the epiglottis blocks the trachea using the same mechanism (Crabbe, 2007). Together the soft palate and epiglottis cause horses to be obligatory nose breathers (Davis, 2013; Crabbe, 2007). Figure 2.1 shows airflow as the horse inhales, and displays that the horse is an obligatory nose breather because the soft palate location does not allow airflow from the mouth to the trachea.



**Figure 1:** Airflow into the horse during inspiration.

As air flows through the trachea and enters the LRT through two bronchi (Davis, 2013; The British Horse Society, 2011; Crabbe, 2007). One bronchi branch enters the left lung and the other to the right lung. The two bronchi branches proceed to branch further forming into bronchioles. At the end of the bronchioles are alveoli, also known as alveolar sacs. In the alveoli, oxygen in the air diffuses into the pulmonary capillary circulation to be absorbed by the blood and carbon dioxide diffuses into the alveoli (Davis, 2013; The British Horse Society, 2011). This process of diffusing oxygen from the air into the blood is called oxygen exchange (Raven & Rashmir-Raven, 1996). The carbon dioxide in the alveoli is then exhaled out of the horse, which concludes one breath of airflow through the respiratory system (Davis, 2013).

## **2.2 Respiratory disorders of horses**

Equine respiratory disorders are quite common. Horses can have a number of disorders including recurrent airway obstruction, inflammatory airway disease, and other less common disorders. Diagnosing the disorders is problematic as differentiating between the many disorders is difficult. Unlike with other animals, the symptoms and results of specific tests do not lead to one specific diagnosis. Veterinarians have to stay up to date with frequently changing disorder

definitions. A correct diagnosis is also difficult because the disorders are often subclinical, so the horse may suffer for extended periods of time before a test is performed or a clinical level disorder is detected. Wrong diagnoses can be serious because different treatment methods are used for each disorder. Incorrect treatment can cause the disorder to worsen.

### **2.3 Recurrent airway obstruction (RAO)**

Recurrent airway obstruction (RAO) is commonly seen in older horses that are experiencing airway obstruction, inflammation, mucus accumulation, or tissue remodeling. RAO is the most commonly diagnosed lower airway disease in horses and is very similar to non-eosinophilic asthma in humans. RAO is believed to be caused primarily by an allergic reaction to inhaled molds.

Many horses live in closed barns where hay is stored. It is common for hay to develop a dusty and moldy living environment, which aggravates the respiratory system of horses, causing diseases such as RAO. The most common sign of RAO is frequent labored breathing. Fortunately, RAO is reversible if correctly diagnosed early on. The most common steps that can be taken to reverse the effects of RAO are to reduce the dust in the horses living environment and administer a bronchodilator (Kutasi, Balogh, Lajos, Nagy, & Szenci, 2011).

### **2.4 Inflammatory airway disease (IAD)**

RAO and inflammatory airway disease (IAD) are similar, but they can be differentiated at the clinical level. IAD is a non-septic inflammation of the lower airways that is common in young sport horses and can be caused by many different factors. These factors can include dust and mold spores in their living environment, immunological factors, and infectious agents. If

IAD is untreated it can progress into RAO. IAD is commonly untreated because most cases have subclinical symptoms that go unrecognized by the owner.

## **2.5 Other disorders**

Pulmonary disorders caused by infections can affect horses, however they are less common than RAO and IAD. These disorders can be caused by bacterial, viral, fungal, or parasitic agents. Infections are typically seen in older horses that have been subjected to increased stresses including long distance travel or strenuous exercise (Kutasi, et al., 2011).

Pulmonary hemorrhaging is the second most prevalent disorder found in young racehorses after IAD. Exercise-induced pulmonary hemorrhaging is common in racehorses and sport horses, but most commonly in racehorses who have to over exert themselves for short periods of time. This most commonly occurs because of inflammation in the upper and lower airways that applies excessive stress to the pulmonary circulatory system, (Kutasi, et al., 2011). These hemorrhages should be treated as soon as they are detected, however symptoms are often minimal so frequently they go undetected. Lastly, while rare, horses can be diagnosed with granulomatous, neoplastic disease, or pneumonia (Kutasi, et al., 2011).

## **2.6 Diagnosing disorders**

Veterinarians commonly encounter horses with lung function disorders. One of the first tasks a veterinarian will complete is checking the contagious nature of the disorder. Horses often live in close proximity of other animals, and risk of spreading contagious infections should be minimized. The horse's age, breed, sex, origin, environment, herd or group history, vaccination, deworming, and medical history are all required information the veterinarian will ask the client (Kutasi et al., 2011). These questions provide insight into the potential causes behind any disorders. For example, a horse living in a barn that stores damp hay is an environment that

makes horses more susceptible to respiratory infections (Robinson, 2003). The veterinarian will also inquire about any symptoms the horse might be displaying. These include:

- Cough
- Nasal and or ocular discharge
- Exercise intolerance
- Respiratory distress
- Sneezing
- Abnormal respiratory noise
- Elevated breathing rate
- Abnormal respiration pattern
- Depression
- Fever
- Anorexia

Before any further testing, the condition of the horse will be examined. This includes noting the manner of movement, demeanor, body condition, abdominal movement, presence of nostril flare, and respiratory rate. The horse will be further examined, looking at mucus membranes, any swelling, abnormal nasal discharge, signs of pain, or swollen glands. A stethoscope is used to see if any abnormal breathing sounds can be heard. A test known as the brown bag exam is used to determine if the lower airways are obstructed. During the bag rebreathing exam, wheezes and crackles could be a sign of an obstruction and tracheal rattling could be mucus accumulation in the lower airways, (M. Mazan, Personal Communication, September 30, 2016).

Coughing while the bag is on or prolonged recovery time after the bag is removed are signs of a respiratory disorder (Katusi et al, 2011). For IAD, oftentimes the blood chemistry is completely normal, but accumulation of bacteria in the trachea could be a sign of the disease (Robinson, 2003). After understanding the horse's past, further testing can be completed to determine if a lung function disorder is present.

## 2.7 Pulmonary function tests

Pulmonary function tests (PFTs), or lung function tests, are tests employed to determine the quality of the respiratory system's performance (U.S. National Library of Medicine, 2015). Most tests focus on measuring lung function through defining lung capacity, respiratory rate, and proficiency of oxygen exchange to the blood (U.S. National Library of Medicine, 2015).

Often the first step for diagnosis using PFTs is a physical examination with a stethoscope (Myers & Bass, 2010). Doctors listen with a stethoscope for any abnormal respiratory sounds (Myers & Bass, 2010; Yu, Tsai, Huang, & Lin, 2013). Doctors generally listen for wheezing, commonly associated with asthma, difficulty breathing, restricted airways, or other obstructions passing through the respiratory system. (Myers & Bass, 2010; Yu, et al., 2013). When wheezing becomes severe enough, it is heard without a stethoscope (Myers & Bass, 2010). Hearing these obstructions through a stethoscope is not enough to provide a diagnosis of asthma, instead other PFTs must be conducted to fully determine the presence of asthma or other pulmonary disorders.

Spirometry is a common PFT to determine the presence of different lung diseases. It measures the amount of air a person exhales and the speed of exhalation (U.S. National Library of Medicine, 2015). This test is dependent on compliant breathing, a person's ability to follow directions to breath at a specific time with a certain amount of effort (U.S. National Library of Medicine, 2015). Often spirometry is conducted with a person postured in a sitting position with a mouthpiece to breathe in (U.S. National Library of Medicine, 2015).

Methacholine tests use spirometry to determine lung function while breathing in specific agents such as methacholine or histamine (American Thoracic Society, 2009). When people with asthma breathe in methacholine, their airways tighten, further restricting breathing, (American Thoracic Society, 2009). Since patients without asthma will not have their airways tightened with

exposure to those specific agents, this method is extremely useful in diagnosis (Scope, Contraindications, & Training, 1999).

Spirometry and spirometry with methacholine challenge tests require compliant breathing. Human infants and animals are unable to follow directions to provide maximum exhalation (Rozanski & Hoffman, 1999). Tidal breathing flow-volume loops, a pulmonary function test that does not require compliant breathing, was initially designed for human infants, but was determined useful for pulmonary disorders in animals such as dogs and cats (Rozanski & Hoffman, 1999). As the infant or animal breathes into this device, it measures respiratory rates through a pneumotachograph with a pressure transducer (Rozanski & Hoffman, 1999). This process takes several minutes because the flow-volume loops require time to appear consistent in shape and there needs to be breathing patterns without crying, purring, or panting (Rozanski & Hoffman, 1999).

As described in the previous section, other tests and questionnaires are completed before a non-compliant animal is tested for a lung function disorder. Lung function testing is only performed as a last resort if no other testing methods provide a clear diagnosis, (PetWave, 2015). Once all of these methods are exhausted and a diagnosis is not identified, lung function testing is considered. Typically, lung function testing is invasive, expensive, and has many limitations as described in section 2.5.

## **2.8 Equine pulmonary function tests**

There are many techniques for testing lung function in horses to include imaging, taking samples, laboratory diagnostic techniques, and newer methods that focus on the actual breathing patterns of the horse. Each one of these techniques has different advantages and disadvantages,

so they are used in different situations, which is investigated and discussed in the following sections.

## **2.9 Imaging**

Imaging is typically used for horses that have clear symptoms of a pulmonary disorder. Most of these techniques are invasive, but they can provide a proper diagnosis with high levels of accuracy and precision. The key imaging techniques that are used currently include endoscopy, radiography, and thoracic ultrasonography.

Respiratory tract endoscopy is commonly used for diagnosing horses who are experiencing abnormal nasal discharge, coughs, or poor performance during exercise. Endoscopy allows for imaging of the upper respiratory tract and the proximal lower respiratory tract. This procedure is performed by inserting an endoscope through the nares (nostrils) of the horse into the upper respiratory system (Pusterla, Watson, & Wilson, 2006). RT Endoscopy provides an accurate diagnosis and it does not always require sedation, but it is an invasive procedure, (Kutasi, et al., 2011).

Radiography is another common imaging method used for diagnosing lung function disorders in horses. Radiography is key to locating the cause of a disease by identifying fluid-air lines in the lung. This equipment is advantageous because it can image small areas of the lung including the paranasal sinuses, the guttural pouches, and the retropharyngeal area that the other imaging technologies cannot access. A major disadvantage with radiography is that it has very limited usage due to the fact that it is not readily available (Pusterla, et al., 2006).

When analyzing a horse using radiography veterinarians are looking for one of four common patterns, which include the alveolar pattern, the interstitial pattern, the reticular pattern, and the bronchial pattern. These are typical patterns to look for in any species when using



radiography, but unlike in other species, horses do not have one diagnosis that matches with each distinct pattern. For horses, each pattern represents a range of possible diagnoses that often overlap with each other. The major limitation of diagnosing by fluid-air line patterns is that the most common pattern, the interstitial pattern, does not clearly define any specific disorders. Table 2.1 illustrates the overlapping definitions that veterinarians need to be aware of when caring for a horse with a pulmonary disease.

<b>Pattern</b>	<b>Disorders</b>
Alveolar	Pulmonary edema, hemorrhage, lung consolidation, or neoplastic infiltration
Interstitial	Variety of diseases, has no clear definition of diagnosed disorders
Reticular	Most common with viral, bacterial, and fungal infections Also, present in horses with pulmonary edema, interstitial pneumonia, and pulmonary fibrosis
Bronchial	Bronchitis or bronchiolitis

**Table 1:** Air-fluid patterns common in horses and what disorders they represent.

Thoracic ultrasonography is more readily available than radiography, so it is used more often especially if pleural effusion, pulmonary consolidation, pulmonary or mediastinal abscesses, tumors or granulomas are being detected. The main limitations of ultrasonography are the lengthy process to prepare the horse and the ease of doing something improperly. These limitations combined can lead to an inefficient test. Ultrasonography also has a very limited number of disorders that it can diagnosis (Pusterla, et al., 2006).

## 2.10 Sampling

Multiple sampling methods are used to diagnose equine respiratory disorders including tracheal wash, bronchoalveolar lavage (BAL) fluid cytology and culture, thoracentesis, and percutaneous lung biopsy. Similar to imaging, each one of these techniques is invasive.

Tracheal washes detect different disorders by collecting a sample from the distal trachea. This is done using an endoscope or a percutaneous tracheal wash. The percutaneous tracheal wash requires surgical skin preparation and has a risk of infection at the insertion site, but if the sample needs to be cultivated for diagnosis, this method is required.

Endoscopy can acquire the sample, but it will be contaminated by the nasopharyngeal bacteria, so it can only be used for cytological examination. Acute inflammation, bacterial pneumonia, crecence, fungal infections, viral infection, and non-septic inflammation can be detected with this method of sampling. Table 2.2 below shows what cells are present during the different disorders that can be diagnosed (Pusterla et al., 2006).

<b>Disorder</b>	<b>Cells Present</b>
Acute inflammation	Neutrophils
Bacterial pneumonia	Neutrophils showing signs of degeneration
Credence	Intracellular bacteria
Fungal infection	Neutrophilic infiltration, large number of eosinophils and macrophages
Viral Infection	Increase in lymphocytes and epithelial cell injury
Non-septic inflammation	Non-degenerative inflammatory cells with no evidence of etiologic agents

**Table 2:** Cells present in disorders.

BAL is the most common sampling method used by veterinarians testing for diffuse inflammatory disorders in horses. An endoscope is used to retrieve a sample of the fluid lining in the distal airways in the alveoli. This sample is then used in cytological examination or quantitative culture techniques. Quantitative culture techniques must be used so that contamination due to the nasopharyngeal bacteria can be ignored. The BAL sample cell distribution is compared to a normal cell distribution to determine the disorder (Pusterla et al., 2006). Veterinarians can use a similar method to diagnose the disease using the cell types listed in Table 2.2.

Thoracentesis can be completed quickly and easily with little equipment, so it is the preferred method for many veterinarians. Once the sample is collected both culture and cytology analyses can be conducted, along with the analysis of the odor, color, and consistency of the sample. A normal sample should be odorless, transparent, and slightly yellow, so if the sample taken does not appear normal, then there is an abnormal cell present meaning the culture and cytology examinations should be conducted. This sampling method is used to easily and quickly

diagnose disorders such as; pulmonary abscesses, pneumonia, chronic obstructive lung disease, pulmonary granulomata, equine infectious anemia, systemic mycosis, traumatic penetration of the thorax, and primary and secondary thoracic neoplasms. There are a few risks because it is an invasive procedure, with the exceptions being the chance of pneumothorax, cardiac puncture, intercostal artery or vein laceration, and patient collapse due to rapid removal of large amounts of fluid. Although these results are very uncommon, they can occur, so this method is typically only used if other diagnostic methods do not work (Pusterla et al., 2006).

The last sampling technique used is the percutaneous lung biopsy, which is extremely invasive and has many complications. These complications include epistaxis, pulmonary hemorrhage, tachypnea, respiratory distress, pneumothorax, collapse, and potentially death. Since there is such a high risk for this procedure, it is typically a last resort and is only used when all less invasive diagnostic methods have failed to provide an accurate diagnosis. This procedure can be conducted in non-sedated, standing horses, but is commonly done on a restrained horse in the stock. To try to reduce the risk of the complications, ultrasonography evaluations are conducted before the procedure to map the major organs to avoid puncture while accessing the desired location. The percutaneous lung biopsy is typically used to diagnose diffuse lung disease or undetermined etiology (Pusterla et al., 2006).

Sampling techniques allow for both sensitive and accurate results if contamination is taken into account, but each technique is invasive and has a risk of serious complications. Therefore, veterinarians are moving towards less invasive methods that are just as sensitive and accurate. They do have special laboratory diagnostic techniques that they can use, but they are only used for very specific disorders, which are discussed in the following section.

## **2.11 Special laboratory diagnostics**

Special laboratory diagnostics may be used when trying to diagnose very specific disorders or when imaging and sampling do not provide a clear diagnosis. These laboratory techniques include hematology, immunodiagnostic testing, and molecular diagnostics.

Hematology is a very sensitive and time dependent method of determining if the pulmonary disorder is infectious or noninfectious based on the increases of cell types over time. The limitation of this method are that the changes in cell type is miniscule, making effective analysis difficult unless it is a chronic disorder. This method can be used to detect inflammation quite accurately because inflammation is dependent on plasma concentration (the higher the plasma concentration, the higher the levels of inflammation), which is easier to quantify than the small changes in the different cell types. Hematology is commonly only used to determine if inflammation is present, but if records are kept well and the test is conducted cautiously, information on the infectious versus noninfectious nature of the disorder can be determined (Pusterla et al., 2006).

Immunodiagnostic testing is a serologic test that is conducted to determine the presence of specific antibodies. The antibodies are detected by using enzyme-linked immunosorbent assay (ELISA), radioimmunoassay, or immunofluorescence methods. This type of testing can be used to determine the disease progression, detect if the patient is a carrier of a disease, and to distinguish between vaccination, exposure, and disease. A limitation of this test is the veterinarian needs to have a solid understanding of what the results of each test mean. A positive test may mean an active disease, but it often does not. Instead, the positive results may indicate the carrying ability of the subject for the specified antibodies. However, a negative result does not mean that the horse does not have the disease. Veterinarians need a strong understanding of

the sensitivity and specificity of the test to interpret results correctly. Another limitation of this method is the age of the horse can affect the results. Older horses may exhibit higher levels of antibodies, providing false-positive results. Since the test does not give clear results, it is difficult to use for accurate diagnoses and is not reliably repeatable (Pusterla et al., 2006).

Lastly, molecular diagnostics can be used to diagnose infections caused by pathogens that are difficult to cultivate. For this method, Polymerase Chain Reaction (PCR) is used to amplify the sample and ELISA is used to determine if antigens are present. This method is still in the development phase, but its applications have been increasing. For it to be widely used the ease of use, safety, cost efficiency, sensitivity, reproducibility, and automation need to be improved. The speed and reliability of molecular diagnostics are advantageous to other diagnostic methods, but it is paired with the disadvantage of producing false positives due to PCR contamination. These special laboratory diagnostic techniques are used primarily for infectious disease diagnostics. Infectious disease makes up a minimal portion of all pulmonary disorders in horses, but if these methods are made easier and more reliable, they might be applied more frequently in the future to test for infectious diseases before testing for other disorders.

## **2.12 Additional methods**

Veterinarians have begun to use less invasive methods for diagnosing equine lung function disorders, such as conventional mechanics, flowmetric plethysmography, histamine challenge, bronchodilator challenge, and forced oscillatory mechanics.

Of the invasive methods, the conventional mechanics method is considered the gold standard for lung function testing, but it is invasive. A balloon-tipped esophageal catheter is placed in the thoracic esophagus to measure the pleural pressure. This pleural pressure is measured at the same time as the flow at the nostrils. The flow at the nostrils is measured with a

pneumotachograph. Software is used to find the resistance, dynamic compliance, and end expiratory work from the measured airflow, pressure, and respiratory rate. One limitation of this device is the invasiveness causes the horse to swallow frequently, causing pressure readings to be inaccurate. It also has low sensitivity, making it difficult to detect small airway obstructions.

The low sensitivity is due to low resistance in small airways at normal breathing and changes in resistance and compliance as frequencies change. This method is applied in severe cases, but can be made more sensitive when coupled with a histamine challenge (Mazan, & Hoffman, 2003).

The histamine and bronchodilator challenges are bronchoprovocation methods to detect low-grade airway obstruction. Horses suffering from low-grade airway obstruction have airway hyperactivity, meaning the airway is more responsive to a mild stimulus than healthy functions would be. The causes of this hyperactivity may range from airway thickening caused by inflammation, mucus, hyperplasia of the epithelial cells, and high acetylcholine or defective neural response. Histamine challenges are conducted more frequently than bronchodilator challenges; in this test, forced oscillatory mechanics (FOM) is used to measure the resistive friction (RRS). A baseline is set with FOM and histamine is administered in 2 mg/mL doses until the RRS increases more than 75%. Table 2.3 displays the level of obstruction based on the histamine dosage reactivity occurs at.

<b>Histamine dosage where 75% reached</b>	<b>Airway Obstruction Classification</b>
less than 2 mg/mL	Severe reactivity, probably has signs of heaves
2 mg/mL - 4 mg/mL	Moderate airway obstruction
4 mg/mL - 6mg/mL	Mild airway obstruction
6 mg/mL	Considered healthy and normal

**Table 3:** Airway Reactivity based on Histamine.

When a horse reacts to low doses of histamine, a bronchodilator challenge is typically performed. This measures the obstruction and determines if a bronchodilator treatment is right for the horse. Albuterol is the bronchodilator of choice because it has a shorter wait time after administering, (15-minute wait time), but Ipratropium bromide (45-minute wait time) may also be used if time is not a concern (Mazan, & Hoffman, 2003).

Cummings School of Veterinary Medicine at Tufts University uses a combination of flowmetric plethysmography and a Fleisch Pneumotachograph to quantify obstructions experienced by the horse. This method is a sensitive, non-invasive test that provides an accurate diagnosis. This method and a similar forced oscillatory mechanics (FOM) method are described in significant detail in section 2.6.

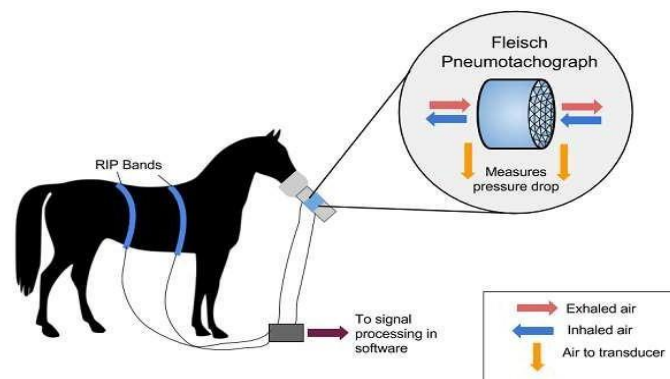
**2.13 Cummings School Gold Standard**

Cummings School of Veterinary Medicine measures equine lung function utilizing a Fleisch pneumotachograph. This is a flow meter relating the velocity of breath from the horse to time. Increasing the flow through the pneumotachograph creates a linear relationship when calibrating the equipment, and accurately measures the breathing rate of the horse. The pneumotachograph is based off of Poiseuille's Law, stating that under capillary conditions in a



rigid tube, the flow is proportional to the pressure loss per unit length. This is particularly beneficial in ensuring an accurate translation of flow velocity and pressure for diagnostics. (2.2)

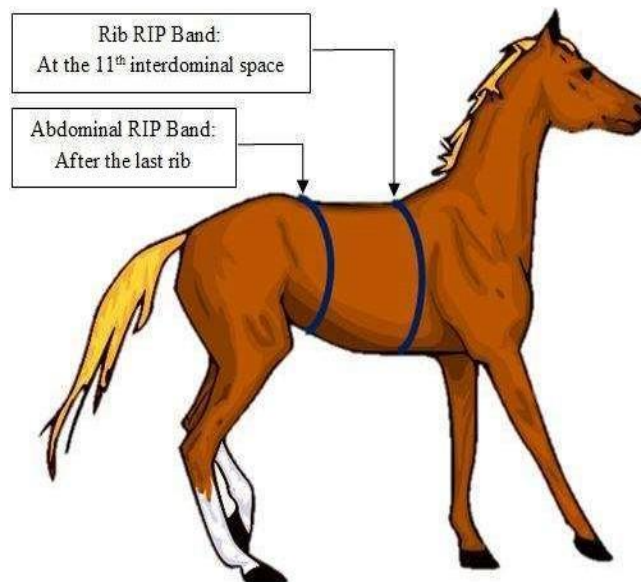
shows a Fleisch pneumotachograph during testing and a schematic of the current device.



**Figure 2:** A horse being tested with the passive Fleisch pneumotachograph device; **Figure 3:** A schematic of the current device and how it works.

The arrows in Figure 2.2(B) represent the flow of air through the device. The pressure drop is detected and measured through the capillary bed in the Fleisch pneumotachograph. The pneumotachograph is calibrated using a 3 liter syringe, forcing a specified quantity of air through the system over a specific amount of time. The pressure loss, or difference in pressure between two points, creates a curve that represents velocity of the air flowing (Vitalograph, 2016). Several capillary tubes direct the airflow to reduce turbulence in the tube, inducing laminar flow.

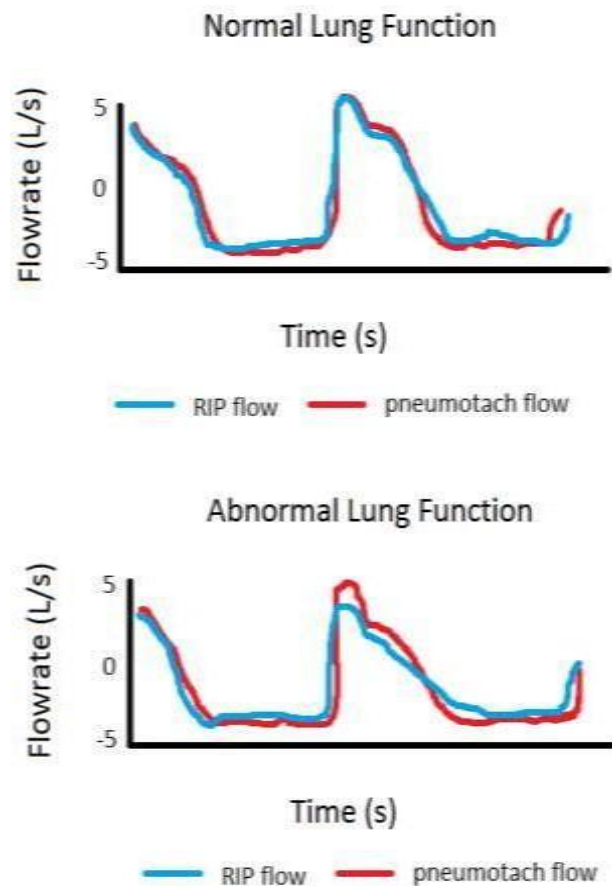
This creates a simplified characteristic equation set based on laminar fluid mechanic properties. A transducer is included in the device, which collects a voltage signal from the pressure drop and converts it to a signal displayed using the Open Pleth software, designed for the particular transducer used in the device. Along with the pneumotachograph, Respiratory Inductance Plethysmography (RIP) elastic bands are wrapped around the thorax and abdomen to collect lung volume data as shown in Figure 2.3.



**Figure 4:** Placement of abdominal and thoracic RIP bands (Howell, 2011)

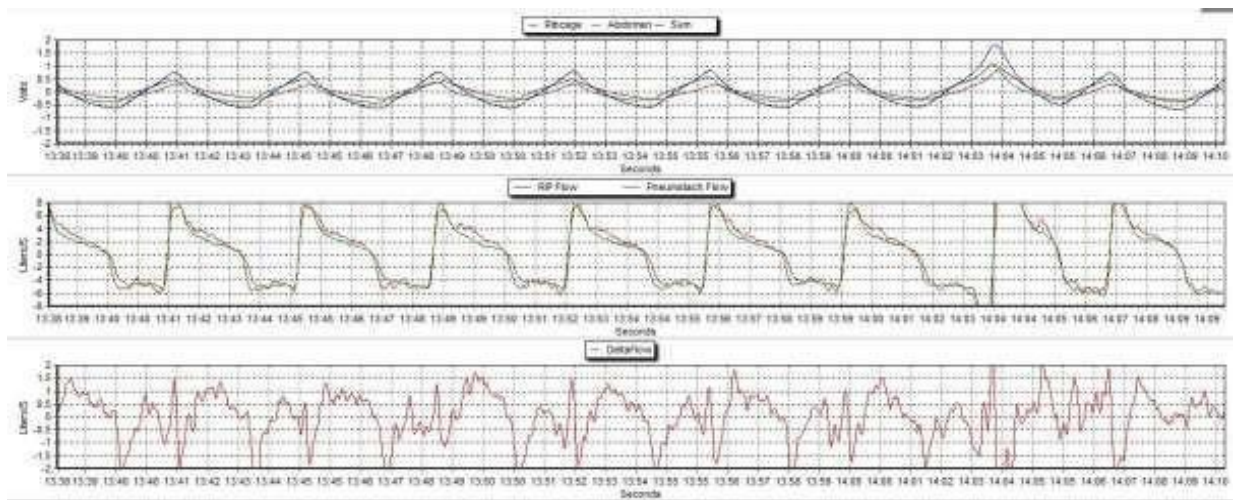
RIP bands are calibrated to the horse using the Fleisch pneumotachograph data and set to zero voltage when no force is present on the sensors. The bands will increase in voltage as the horse's body expands during breathing, and decrease as the horse exhales. The data from the pneumotachograph and the bands are collected simultaneously by a transducer, processed, and displayed on the same screen. Both signals are used in conjunction to diagnose possible pulmonary disorders, by checking for any characteristic deformations in the graph (Hoffman, 2002). For example, if the peak of inhalation is sporadic and at a low voltage, there is high

likelihood for an obstruction in the pulmonary system. An example of graphs used to diagnose disorders are shown in Figure 2.4, where the graph on top represents normal lung function and the one below it represents abnormal lung function.



**Figure 5:** Examples of graphs used for diagnosis.

The slight peak in the pneumotach flow in the bottom image of (2.4) represents a lower respiratory obstruction. A series of graphs displaying the data of both the RIP bands and the Fleisch pneumotachograph measurements are displayed in (2.5).

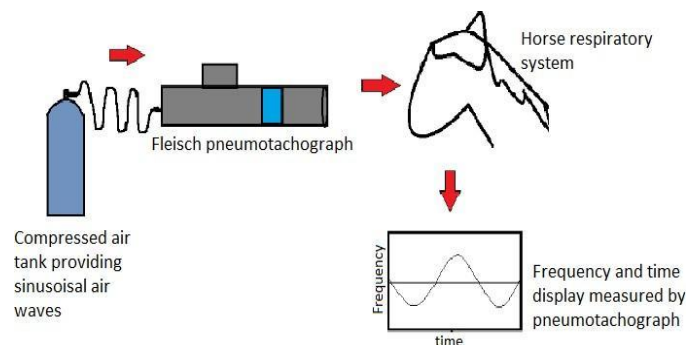


**Figure 6:** Representative data from the RIP bands and the Fleisch pneumotachograph in Open Pleth.

The topmost graph indicates the voltage readings from the RIP bands, the middle graph indicates the voltage in terms of volumetric flow after conversions, and the bottom graph indicates the difference between the volumetric flow data and the data from the RIP bands/Fleisch pneumotachograph.

The Fleisch pneumotachograph has the lowest resistance to horse's breathing during rest, which provides a significant advantage in producing accurate results and larger pressure differentials. However, this comes with the limitation that there is a high resistance during exercise, making the results during those trials invalid. Fleisch pneumotachographs are also capable of displaying collected data as a graph with a linear output, making the analysis of data and diagnosis more efficient. The pneumotachograph is attached to the horse using a facemask, adding stability and guiding airflow through the sensor. For young horses or less affected horses, FOM is used when collecting data to show how the air moves through the respiratory system. Through FOM, sinusoidal waves of air are directed into the horse's nostrils and through the system, creating sinusoidal pressure waves. Through the OpenPleth software, natural pressure fluctuations are filtered out (Hoffman & Mazan, 1999). The main output of FOM is impedance,

which is the ratio of driving pressure to flow. The lower the flow, the higher the impedance, and vice versa. Impedance signals change based on resistance, elastance of the lungs, and inertance. Elastance contributes to impedance at low FOM frequencies, whereas, inertance dominates at higher frequencies. There is a revealing frequency value that can signify lung function abnormalities, with a normal horse at approximately 2.5 Hertz. This will increase given possible airway obstructions or abnormalities in breathing rate (Hoffman & Mazan, 1999). FOM is advantageous because testing is not time consuming or invasive. Figure 2.6(A) shows the FOM device the Cummings School of Veterinary Medicine uses, and Figure 2.6(B) is a schematic depicting how the system works.



**Figure 7:** Cummings School of Veterinary Medicine FOM device, **Figure 8:** Schematic of FOM method where sinusoidal air waves are forced through the pneumotachograph to the horse's respiratory system.

If the horse is older or has a severe breathing disorder, the respiratory rate too closely matches the FOM signals, making the testing method obsolete. Instead, veterinarians utilize a passive device by first nebulizing the horse using histamine to restrict the airways and increase flow velocity from the lungs through the sensor (M. Mazan, Personal Communication, September 30, 2016).

Some challenges associated with the current setup is saliva accumulating in the device, interfering with the sensors which alters the calibration, imbalance of the flow transducer, and small amounts of added resistance from the pneumotachograph (Hoffman, 2002). Additionally, the data gathered from this passive system is noisy, and hard to decipher by veterinarians easily, costing valuable time. To determine which breaths to actually analyze, inclusion criteria were developed by Dr. Andrew Hoffman created inclusion criteria to determine what breaths displayed are valid for analysis and diagnosis. For example, if FOM is used, the data will filter out frequencies that are not between 5 and 30 Hz per minute, and inspiratory to expiratory volume ratios that are not between 0.7 - 1.3. Criteria can also be included that removes tidal volumes below 2 L and inspiratory flows less than 1 L/sec. The criteria will not filter out every unusable data point and some are still removed manually. The facemasks used on the horse can also cause irregular breathing and pressure swings based on minor adjustments and a lack of form fitting.

#### **2.14 Complications when dealing with horses**

Being that horses are very large animals, working around them causes a potential hazard to equipment, other animals, and veterinarians in close proximity. Additionally, studies indicate that horses may exhibit behavioral problems such as crib biting, weaving, chewing wood, box-walking, and various other aggressive behaviors (Moore, Millar, Matsuda, & Buckley, 2003).

People working around or on horses, regardless of previous experience or training, may become victims to bites and kicks without warning. Horse bites can inflict muscle rupture, fat necrosis, and severe hematoma depending on the severity of the bite (Moore et al., 2003). In a survey completed by 216 Swiss veterinarians, 75% of the vets were kicked by a horse one or more times per year (Hausberger, Roche, Henry, Visser, 2008). When introduced to new stimuli, horses typically perform one (or multiple) of the following actions: stepping sideways, swinging their head, kicking in the direction of the stimuli, or moving backwards. Beyond their behavioral characteristics and unpredictable nature, horses are non-compliant to human commands, and thus cannot follow particular breathing patterns as opposed to humans, that can be directed to take a deep breath in, or to exhale fully. These aforementioned complications make testing, diagnosing, and working with horses much more difficult.

### **2.15 Significance of developing devices for horses**

Chronic obstructive pulmonary disease (COPD) is caused by the delayed hypersensitivity response and inflammation of the bronchial tubules, resulting in particle accumulation in the lungs, reduced respiratory rate, and ultimately decreased oxygenation of the blood. The delayed hypersensitivity response occurs from antigen formation and frequent particle inhalation (Robinson, Derksen, Olszewski, & Buechner-Maxwell, 1996). Stabled horses suffer from exposed risk to inhaling large amounts of particles given the recirculation and poor ventilation of stables. The humidity in the summer causes antigens such as thermophilic molds and actinomycetes to grow in the hay, and when horses breathe in these antigens, neutrophils attack the lung causing an inflammatory response (Knapp, Holt, & Lechtenberg, 1975). The antigens formed through humid conditions in confined stables, obstructs the airways and causes

nonspecific hyper responses. Mucus accumulates in the airway along with the antigens, causing stabled horses to wheeze and cough frequently (Robinson et al., 1996).

80% of stable horses suffer from Inflammatory Airway Disease (IAD) (Cumming Veterinary Medical Center, 2016). Early diagnosis and therapy treatment for young horses with IAD is crucial in preventing coughing and heaving to prevent permanent tissue damage, especially in racehorses (Wood, Newton, Chanter, & Mumford, 2005). The performance levels of race horses with pulmonary disorders, especially in younger horses, significantly decreases (Sanchez, Couetil, Ward, & Clark, 2005). The race horsing industry is directly impacted by the performance of horses, and the multi-billion dollar industry requires horses to perform at optimal levels. Besides the tremendous amount of money through this industry alone, equine veterinary care is also costly. Performance race horses require annual veterinarian/medical, with costs ranging from \$500 to \$1,400 per horse (Gordon, 2009). In the state of Kentucky, the amount of money that is bet daily on horse races can rise up to \$1.2 million, if not higher, for a single race track. A 3.5% tax in the United States is issued on horse race bets, providing the government significant revenue. This exorbitant amount of money reflects a significant emphasis on the importance of the health of racehorses, sourcing a clear need for diagnosing and preventing possible diseases and permanent damage.

## **2.16 Conclusion**

IAD and other pulmonary disorders can greatly impact the performance and health of all horses. Current diagnosis methods are complex, invasive, and expensive, making it challenging for horse owners to receive adequate diagnosis and treatment for their horses suffering from subclinical lung function disorders. The Cummings School of Veterinary Medicine at Tufts developed a non-invasive method to test for lung function abnormalities. This device has proven



to be successful, but has some disadvantages as well. The device is heavy and protrudes far off the face of the horse, causing a risk of injury to the operator. The device also uses a Fleisch pneumotachograph component that is expensive and no longer produced. Our team was tasked with developing an improved method of measuring lung function of horses. In the following chapter, we discuss our design process to develop an improved method for measuring equine lung function.

## Chapter 3: Project Strategy

### 3.1 Initial Client Statement

During the first meeting with Dr. Mazan, our team discussed the needs of the Cummings School of Veterinary Medicine: an improved and efficient respiratory testing apparatus. This follows the work of WPI's 2017 Equine Respiratory Function MQP team. The initial client statement was to develop a lightweight respiratory monitoring system, capable of performing with equivalent precision to Tuft's Fleisch pneumotachograph, and to incorporate RIP band data into the LabVIEW program. The following subsections reflect the objectives for the project, revised client statement, and overall strategy for completion.

#### *A) Initial Project Objectives*

The overall project objectives after multiple meetings and revisions were compiled into a comprehensive list included below:

1. Validate the Rev C sensor, and test the sensor in controlled environments to simulate equine respiratory tests
2. Validate and update LabVIEW code to convert Rev C sensor outputs to wind speed and breathing rate
3. Incorporate RIP bands in the LabVIEW code to quantify expansion of the diaphragm
4. Design and test multiple masks meeting the guidelines of Dr. Mazan, and the safety/comfort of horses
5. Research and design a wireless, portable system capable of running the respiratory test in the field, without having to be attached to a computer

## **3.2 Project Constraints**

In the initial meetings with Dr. Mazan, project constraints and concerns were discussed, along with the most critical factors to measure and ensure in the design process. The main constraints were split into 3 areas of focus: Design constraints, Function Constraints, and Safety/Comfort constraints. While some of these topics overlap and relate to each other, each one is addressed individually in the following subsections.

### *3.2.1 Design Constraints*

The first set of constraints comes from the overall mask design. The current fleisch pneumotachograph, as mentioned in the Literature Review section is expensive and limited in manufacturing. In addition to its expense and manufacturing struggles, the fleisch pneumotachograph is heavy, weighing 10 lbs, which poses a risk to people and equipment nearby. Additionally a heavy design is impractical as a horse's neck cannot support the weight on its own.

### *3.2.2 Function Constraints*

The next stage of constraints are the functional constraints of the current design and the required testing outputs in order to be used in clinical applications. The first function required for the data output is the lung velocity vs. time during resting. This is measured through the Rev C sensor, but requires calibration to minimize sensor noise and to display accurate lung volume displacement. In addition to the velocity functionality of the design, it also has to be able to attach to a standard halter or bridles for multiple breeds of horses, while still directing airflow over the sensor. This is crucial in the design, because if the mask is not capable of adjusting size or permeates a significant amount of air, then all results will indicate respiratory conditions. The mask design is required to collect spit and moisture accumulation. This encasement must be

easily maintained and cleanable. The whole system is required to be sterilized and cleaned after each use, while still maintaining form and mechanical properties.

### *3.2.3 Safety Constraints*

Safety is a primary concern for both the horses during trials and any surrounding personnel conducting the test. The mask must not have any pointed protrusions on the interior or exterior of the mask, potentially leading to injury. The mask's interior must not contain jagged edges or rough composites that could lead to cuts and abrasions on the horse's head. For additional safety, the mask must not be heavy, as this would strain the horse's neck. Keeping the mask lightweight also prevents serious injury to surrounding personnel if the horse swings its head around. The mesh on the inside of the mask must direct airflow over the sensor, but not restrict breathing, swaying results or causing difficulty breathing for the test subjects.

### *3.2.4 Code and Regulations*

Due to the limited manufacturing and regulations required for the mask design, there are no specified codes and regulations for the creation of this project, however, for our project we operated under the assumption that we were developing a class 1 medical device, as would be the case if we were developing this product for human use. Good Manufacturing Practices are required for mass manufacturing of the mask design. When working with horses, it is important to consider the fact that they are living beings that are responsive to external stimuli, including light, sound, and touch. In the design of the mask housing unit for the flow sensor, those considerations must be taken into account. It is important to design all interfaces between components and the horse are comfortable and cause no danger from electrical components or abrasions.

### 3.3 Revised Client Statement

After discussing and evaluating the constraints of the project, we sat with Dr. Mazan and redefined the client statement to meet the current needs. This revised client statement is to develop a lightweight respiratory monitoring system, capable of performing with equivalent precision to Tuft's Fleisch pneumotachograph, adhering to the safety protocol and design constraints explained in the previous sections.

#### 3.3.1 Revised Project Objectives

The revised project objectives are concentrated to provide guidance to the project goals, and structure for the completion of the project. The concentrated objectives allow for increased understanding of the individual components, integral to the design, and allow the full analysis and comparison of various materials, designs, and approaches for the optimal project outcome.

1. Validate the Rev C sensor, and test the sensor in controlled environments to simulate equine respiratory tests
  - Test multiple Rev C sensors to evaluate accuracy
  - Use compressed air over sensor to test limits of sensor output
  - Compare test airflow with breathing rate by standard rate
2. Validate and update LabVIEW code to convert Rev C sensor outputs to wind speed and breathing rate
  - Compare simulated outputs to controlled flow over sensor
  - Redefine variables and equations to ensure calibration and outputs are consistent with Fleisch pneumotachograph outputs
  - Improve User Interface (UI) for broader application and less confusion

3. Design and test multiple masks meeting the guidelines of Dr. Mazan, and the safety/comfort of horses
  - Research and analyze material properties for the exterior mask design and interior mesh
  - Create rough designs and rapid prototype models for application

### **3.4 Project Approach**

The project approach was broken down into three separate approach categories to be addressed throughout the entire project timeline. Below are descriptions for the approach of the LabVIEW code, mask design and fabrication, material selection, and the testing of the final design.

#### *3.4.1 LabVIEW Code Approach*

The first stage of the project was to improve the previous LabVIEW code. Prior to our project team's continuation of the Equine Lung Function Testing MQP, we met with the previous team to transfer all data and tools so we could build from their foundation. During this meeting, we received a large syringe to simulate the lung capacity of a horse, the final report, and a Rev C sensor as their final choice in an affordable respiratory measuring tool.

Firstly, the LabVIEW code required updated user interface (UI) to benefit the operators in a clinical setting. To do so, we reduce clutter and overlapping text on the screen, redefine sizes of textboxes and user directed inputs. By changing the colors and orientation of the system, and increasing the output graph displays, the user experiences less confusion, and will overall lead to optimal performance in the field.

In addition to the UI of the LabVIEW code, we focused on updating the code to eliminate redundancies and enhance performance. We eliminated the use of global variables between test

cases and the operating program. Program efficiency was improved, which lead to more accurate results. Beyond the UI and the function updates, we send the results of the code to an Excel file, with appropriate naming conventions for data analysis.

### *3.4.2 Mask Design and Prototyping Approach*

We first investigated the client needs and discussed the potential limitations and focuses of the mask designs and prototypes. We used Solidworks as the platform for designing mask components and fitting it for full size dimensions. We used the 3D printing facilities for prototyping and fitting components. We purchased a life-size model head of a horse to ensure proper fit and function. Each iteration of the mask was shown to our advisors and sponsor for input on potential improvements. The mask was tested to ensure flow can pass through it under high pressure conditions. It was tested to ensure that it is comfortable on the head of a horse, and that there would be no interference with any components needed for data acquisition.

### *3.4.3 Material Selection Approach*

The material selection was conducted by testing the mechanical properties for the exterior and interior of the max. This was compared to the need statement and each material was chosen with the intent of meeting as many client needs as possible. This includes the comfort, price, weight, mechanical strength, flexibility, and reproducibility.

#### *3.4.4 Design Validation and Testing*

The design was validated and tested using pressurized air, comparison to literature, and client need evaluation. Our final mask housed the Rev C sensor, and compressed air was sent through, mimicking the breathing rate of a horse. The values from this were measured and compared to that from the Fleisch pneumotachograph, and later compared with human breathing trials in a smaller version of the mask. If the design did not measure the same flow rate inserted into the mask, errors were marked, and the mask was altered to address the initial concern causing the error. The mask was validated based on accuracy and reproducibility of accurate readings through the LabVIEW code.



## **Chapter 4: Methods and Alternative designs**

### **4.1 Needs Analysis**

This project requires considerable focus and directed needs analysis to determine materials, process, and design in order to meet the problem statement and client requirements. The following subsections address the process used to evaluate the needs of the client, to help shape our decisions throughout the duration of the project.

#### *4.1.1 Current Design Limitations*

The current design has multiple limitations that are potential hazards to the horses and any personnel or handlers present during testing. The current mask is large, bulky, and heavy, and is a danger to the horse's neck if unsupported, and to people if the horse swings its head. In addition to these limitations, the Fleisch pneumotachograph is expensive, which limits resources and application outside of the hospital. The current need of the project is to reduce weight/size of the mask and provide a cheaper alternative to the current design.

#### *4.1.2 Equine Respiratory Testing Limitations*

The current testing parameters limit the applications of this device. During testing, the horse must be either sedated or in an enclosed area and it must be attached to a computer for data acquisition. The Fleisch pneumotachograph is a wired sensor supported by a veterinary or aide during testing. Therefore, the needs arise to help create a wireless system for data acquisition and lightweight attachment, capable of supporting itself when placed on a bridle or halter.

### *4.1.3 Design Pairwise Analysis*

The Pairwise analysis is a comparative tool used to test specific characteristics between each other to determine the most important traits required for a design/decision. The first row of traits is compared to the columns of traits with a 1 or a 0. A value of 1 indicates the trait of the row is more important in the design process than the column. Since the trait cannot be categorized against itself, it is denoted a null value (X). The totals for each row are totaled and compared at the right side of the table.

Our team utilized a Pairwise analysis based on a discussion with our sponsor, Dr. Mazan, to determine the most important characteristics our mask design must accomplish. Below is the resulting Pairwise analysis, taking into consideration the 6 traits from our discussion.

<b>Characteristic</b>	Lightweight	Cost	Durability	Ease of Application	Reproducibility	Size	<b>Total</b>
Lightweight	X	1	1	1	0	1	<b>4</b>
Cost	0	X	1	0	0	0	<b>1</b>
Durability	0	1	X	0	0	0	<b>1</b>
Ease of Application	0	0	1	X	0	0	<b>1</b>
Reproducibility	1	1	1	1	X	1	<b>5</b>
Size	0	0	0	0	0	X	<b>0</b>

**Table 4:** Pairwise Analysis.

The lightweight trait describes how light the mask design is on the horse; the cost trait describes the total cost of materials, manufacturing, and setup; the durability trait describes the strength of the material and mask design; the ease of application trait describes how easy the mask is to equip on a horse; the reproducibility trait describes the ability to obtain the same results and ability to manufacture with the same resulting fit for the horse; the size trait describes how small the design must be when attached to the horse.

The above table was completed with the assumption that accuracy would be the number one consideration in the design process with the results of this table following. The number one trait determined was reproducibility, indicating that our final design must satisfy an accurate and easily reproducible method. After this, lightweight is the second most important trait for our final

design. With both of these considerations, we focus our design on the premise of a lightweight, and stable device capable of withstanding the movements of a horse during testing.

Extra considerations for the design included whether the horse was stationary during the test vs. exercising. For stationary testing, the ability for the mask/housing unit to be durable in case of flailing and damaging the equipment. While the horse is exercising, the constraint is that the mask must be lightweight to reduce air resistance and feel indifferent on the horse.

## **4.2 Functions and Specifications**

The overarching functions of the updated mask design and testing parameters are created to meet the needs addressed previously in the aforementioned section. A full list of the required functions and specifications are outlined below.

### *A. Required Functions*

- System must relay breathing rate and lung displacement real time for veterinarians to diagnose
- System must output data to Excel for record keeping and displaying graphs
- Sensor must be capable to wirelessly collect data through external software or equipment for future iterations
- LabVIEW or Matlab code must be capable of incorporating RIP bands in future iterations

### *B. Required Specifications*

- Mask must be less than 1 lbs
- Mask must be lightweight with a Young's Modulus less than PVC
- Mask must not protrude more than 1 ft outside of horse's head

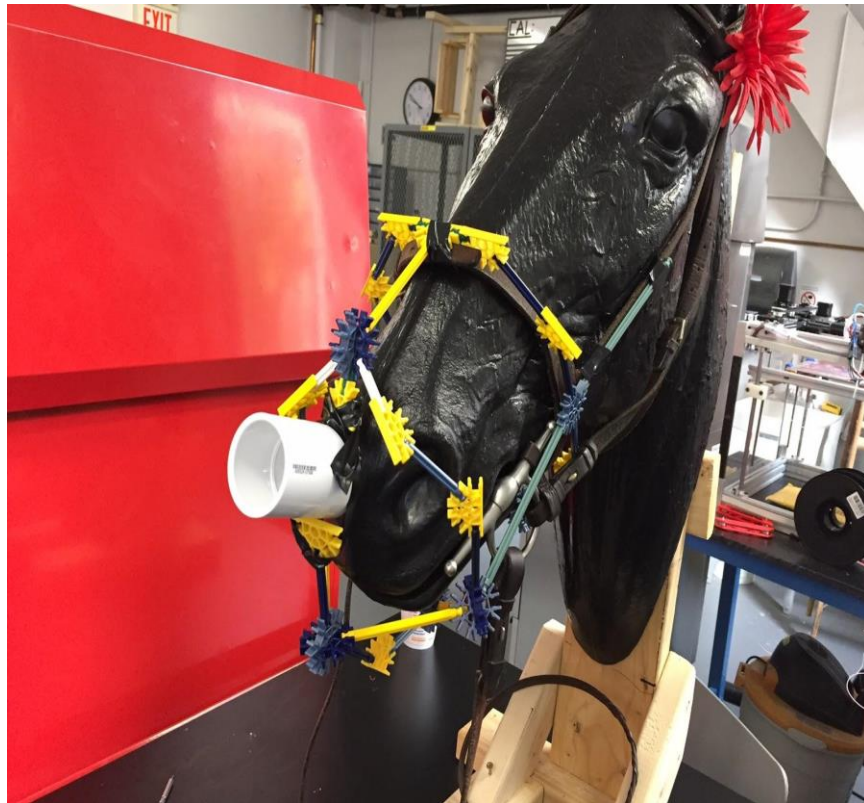
- Sensor must operate with same accuracy of fleisch pneumotachograph (with error of 2.5%)

### **4.3 Feasibility Study**

To determine the feasibility of the proposed design and the ability to complete the revised client statement/objectives, we complete a feasibility study, investigating the cost, the operation parameters, the functions and specifications, and the timeline for manufacturing and completion. The team is budgeted \$1000.00 USD from both the Department of Biomedical Engineering and the Department of Mechanical Engineering of Worcester Polytechnic Institute to complete this project. Due to numerous members of this MQP team pursued double major degrees, the timeline for this project was extended throughout all four academic terms, beginning in August 2017, and concluding on April 20th, 2018 for Project Presentation Day.

### **4.4 Conceptual Designs**

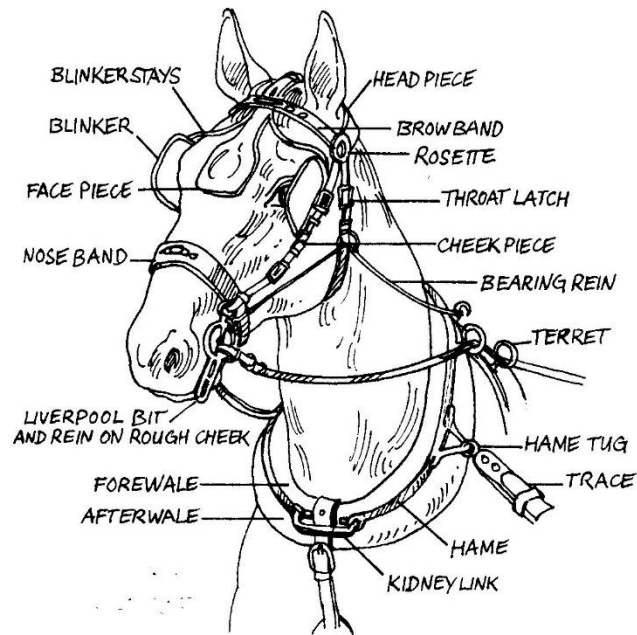
During the first stage of design, our team focused on the functional design of the mask with conceptual designs. We used a Kinects model to illustrate the structure needed to support the mask on a horse. The first mask was built of kinects pieces to give an estimate of the dimensions needed for the upcoming mask iterations. As seen in figures 4.1 (A) and (B), we attached a loop to the nose band and horizontal supports to the cheek piece using electrical tape, making sure that nothing was resting on or behind the nostrils, due to sensitivity in those areas. The pvc tube represents the housing for the Rev C sensor, that is included in the final designs.



**Figure 9:** Kinects Model

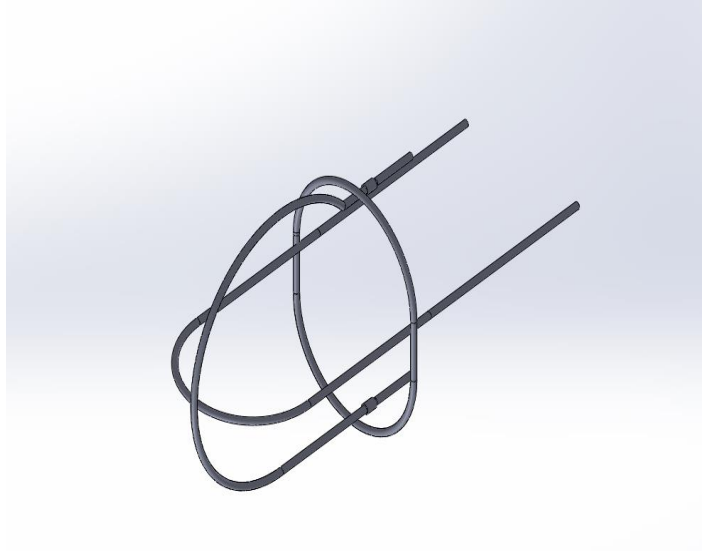
#### **4.5 Preliminary and Alternative Designs**

Based on the conceptual Kinects model for the mask design, we constructed preliminary designs through Solidworks. We planned for the design to be connection to a bridle or halter, allowing for a lightweight, universal design, which is reproducible in its application. Figure 4.3 below indicates the general setup and layout of bridles.



**Figure 10: Bridle Parts Description**

Based on the setup of the bridle, we opted to follow some 3D printed primary designs to fit around the bridle. We 3D printed the first iteration of the kinects design by first converting the components to a Solidworks model. From this model we learned that the horizontal supports that connect to the cheek piece needed to be angled outward to account for the widening of the horses muzzle. We also determined that slots should be put in the horizontal supports to make attachment easier for the user.



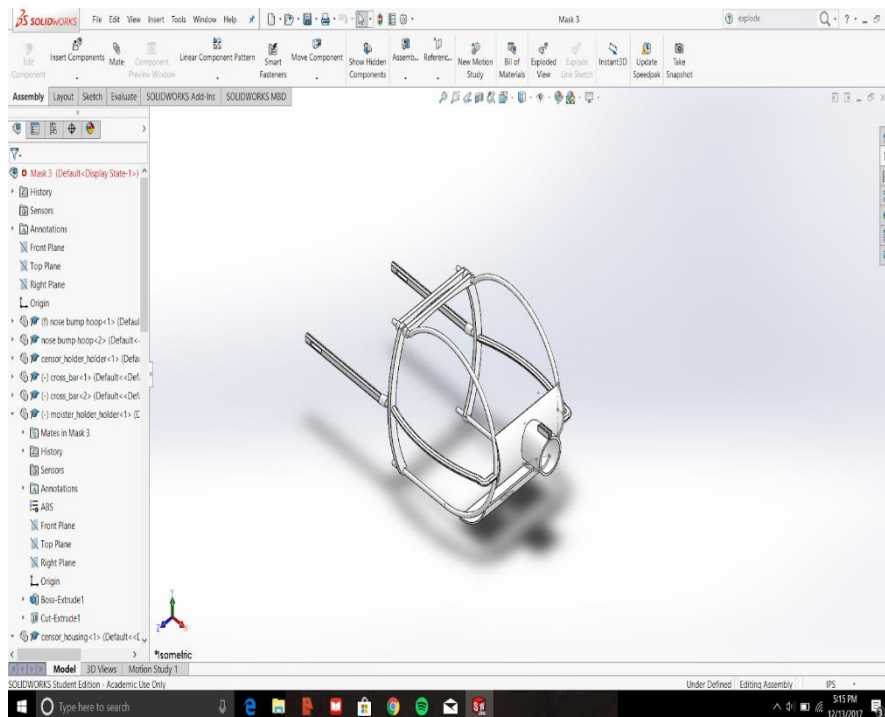
**Figure 11:** Preliminary Cage Design



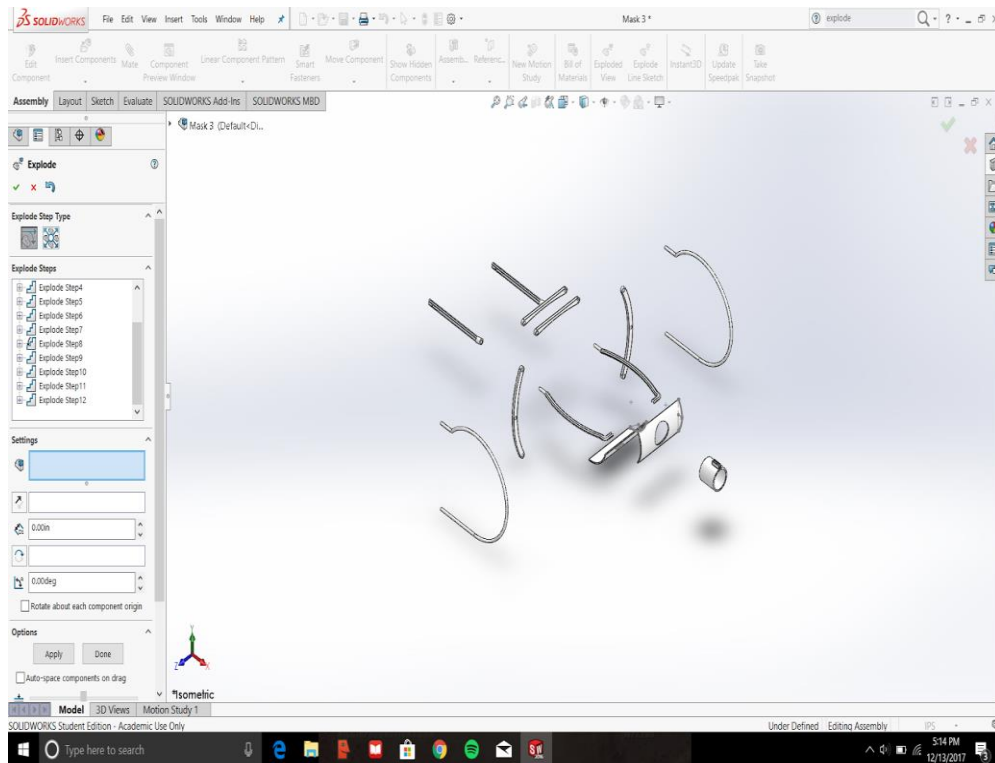
**Figure 12:** 3D Printed Preliminary Design



Our second iteration of the design structured a wireframe cage around the outside of the horse's muzzle. The major difference in this model is the two side hoops that allow for the sensor housing and moisture trap to be more effectively accessed and maintained. This model was designed in ABS material, weighing just over half a pound, fulfilling the lightweight and sturdy requirements. This model also used a more effective connectivity method between pieces, where a rod from one part slides into a slot in another part and then is glued together. This provides a strong adhesive bond, holding the pieces together. Below is the final iteration of the design that was considered before coming to a final design decision.



**Figure 13: Third Iteration Mask Design**



**Figure 14:** Exploded Third Iteration Mask Design

## 4.6 Material Selection

### 4.6.1 3D printer material

Three dimensional printers use a variety of different materials. Acrylonitrile Butadiene Styrene (ABS), Polylactic Acid (PLA), and Nylon are three of the more common materials. ABS is the most common material in 3d printing because of the low costs of the ABS filament. ABS material is resistant to high temperatures and has strong mechanical properties (3dprinting, 2017). The major downfall of ABS is that it is a non-biodegradable toxic material and therefore releases toxic fumes at high temperatures (3dprinting, 2017). Do to the toxicity ABS is not suitable to use with food.

PLA is also a very common material in the 3d printing industry. PLA is made from renewable resources and is nontoxic. PLA allows for high speed printing and is available in many blends such as wood and bamboo (3dprinting, 2017). PLA has moderate prices, but is preferred for smaller objects because post processing is difficult and the material is fragile (3dprinting, 2017).

Nylon 3d printing is also moderately priced. Nylon is very durable but also allows for flexibility in the part. Nylon prints are UV and chemically resistant. Issues includes expiration of the nylon material and a moisture free environment (3dprinting, 2017).

#### *4.6.2 Carbon Fiber*

Carbon fiber is a very strong polymer that is also lightweight. Carbon fiber is five times stronger than steel (ICE, 2015). Although strong, carbon fiber is very lightweight. The material is also chemically resistant, tolerant to high temperatures and has low thermal expansion. Carbon fiber is typically used in the bicycle, automotive and aircraft industries for the reasons listed above (ICE, 2015).

#### *4.6.3 Stainless Steel*

Stainless Steel (SS) has a high elastic modulus and mechanical strength with limited flexibility with a Young's Modulus of 190 GPa (CES Edupack, 2018). In addition to its relative strength, SS is also used in the medical field due to its ease of cleaning and sterilization. Stainless Steel is also waterproof, preventing any seepage to pass through the material support. The disadvantages of this material choice is that it is heavy in comparison to the other materials mentioned in this section, and is costly to prepare and mold to specific fitting. SS is not suitable

for breathability, but has the capability of directing airflow following the path of the material. With this in mind, the only feasible use for this material would be the frame of the mask.

#### *4.6.4 Plastic Molding*

Plastic molding comes in form of heating plastic to an aqueous form and then cooling it to sheets or specified orientations. The benefits of plastic molding and a plastic polymer based material for design is that it is lightweight, shape-fitting to any form, and can easily direct airflow over the material, similar to Stainless Steel. It is significantly weaker than SS, with a Young's Modulus of 160 GPa (CES Edupack, 2018). However, forming plastic molding requires specialized tools and facilities to meet mask component specialization. In addition to this disadvantage, the material is not breathable, leaving the only option of this as a support material for the frame.

#### *4.6.5 3-Ply Medical Grade*

In common medical practices, a 3-ply filter mesh is used as personal protective devices and to prevent flow intake. This 3-ply non-woven mesh offers unidirectional filtered flow, breathable for both phases of the respiratory cycle (3M, 2018). Considering this material is made for controlled breathing and airflow, this material is capable of providing a mesh support leading to the sensor, but does not have the capability of preventing water accumulation or directing airflow over the sensor.

#### *4.6.6 Neoprene Fabrics*

Neoprene fabrics are used frequently in scuba materials and wind resistant jackets due to its hydrophobicity and multilayer woven form. The high number of layers and material composition create a solid barrier to the external environment, preventing significant wind from passing through, and providing protection from water. This material is high in tensile strength, and requires hand washing.

### **4.7 Mask Testing**

#### 4.7.1 Mechanical Testing

To measure the effect of the mask, we test various materials to determine the structural integrity, the shape capability, and the weight of the structure. Firstly, we measured the mechanical properties for the external support of the mask using a 3pt bending test in an Instron 5543, provided by WPI Department of Biomedical Engineering. Through this testing, we examine the Young's Modulus, the fracture resistance, the pliability of the material, and the force displacement of the material. Primarily, we compare the strength of the material of the Young's Modulus and the weight to examine possible support material. The optimal material is then selected after all of the materials are compared. After the support material is tested and selected, we use tensile testing with the Instron 5543 to measure the mesh's mechanical strength and flexibility.

#### 4.7.2 Interior Mesh Testing

Beyond the flexibility and tension test, we conduct a contact angle test on the mesh materials, checking for water hydrophobicity to prevent water accumulation and increased humidity in the mask. When the contact angle test was finished, we created a human sized mask to mimic the full size horse mask, and use it to check comfort and breathability. A syringe mimicking the lung capacity of horse was used to pass air through a stretched portion of the mesh while it was covering the mask to simulate live breathing conditions. This was done to test if a significant amount of air could pass through the mesh without passing through the sensor, which would result in the material needing to be re-evaluated in order to find a more suitable material.

#### 4.8 Sensor Selection

This year's design team used a hot-wire anemometer sensor to continue where last year's team left off. The previous year's team had looked into 7 different sensor types before coming to this conclusion, these included:

- Improved Fleisch Pneumotachograph
- Three-cup anemometer
- Hot-wire anemometry
- Mesh strain gauge
- Venturi meter
- Pilot tube
- Silicon airflow sensor

A few of these sensors were promising with the initial research they conducted, however each had their issues ultimately leading to the choice of a hot-wire anemometer. The issue for hot-wire anemometry is the effect humidity can have on the sensing element. (Durst, Noppenberger, Stil, & Venzke, 1996). Research shows that not incorporating humidity will result in an error in the velocity reading of 1-5%. To adjust for humidity, there is a correction factor to Nusselts number using Reynold's number and temperatures as shown in the following equation:

$$Nu = (0.24 + 0.56*Re*0.54) [ \frac{T_f - T_a}{T_f} ]^{0.17} [ 1 + Ax + Bx^2 ]$$

Despite humidity being the major concern of our mechanical advisor, the literature illustrates that humidity is not a concern for hot-wire anemometry measurements and provides an equation to correct for humidity. The literature provided the team with the ability to pursue this design by addressing the major concern of our mechanical engineering advisor.

The sensor is the Rev C wind sensor for the Modern Device due to its low cost, compacted size, arduino integration, and testing performance. Calibration of this specific sensor is within the code provided by Modern Device. This sensor measures temperature changes that are converted to wind speed in MPH (Modern Device LLC., 2017). After calibrating and testing each, the previous year's team determined the Rev C was the most feasible. Therefore, the current project team used the same sensor.

## 4.9 LabVIEW Code Methods

The LabVIEW code is a continuation of the code from last year's MQP team. The code incorporates the Bernoulli Equation to demonstrate simulated laminar fluid flow over the sensor. The code includes a conversion equation to change the voltage output from the velocity of the air over the sensor to Volume over time. By graphing the data and plotting it against time, we were able to determine the breathing volume per breathing cycle. This was then compared to previous breaths and standards in the literature to examine any respiratory abnormalities present. The code incorporates a calibration equation to amplify the small voltages, and reduce the signal noise of the sensor. The approach for improving the code are outlined below:

- Change colors from display diagrams to neutral
- Resize text and displays to fit all inputs and graphs on single screen without scrolling
- Remove global variables for improved performance
- Check calibration functions to ensure optimal conversion
- Create case function for calibrating sensor
- Reorganize LabVIEW wiring for cleaner presentation and condensing information
- Export data to Microsoft Excel file at user's specification



## Chapter 5: Design Verification and Results

### 5.1 Material Selection and Decisions

#### 5.1.1 Structural Material Considerations

##### *i) Stainless Steel Considerations*

The first type of material we assessed for the frame was Stainless Steel (SS). As discussed in the previous chapter, SS has a high Young's Modulus, yielding high mechanical strength and minimal bending. However, SS is dense and has a high weight per cubic foot (CES Edupack, 2018). In addition to this, it requires specialized heat treatment and molding to reach the desired shapes. Considering the needs statement from D.VM. Mazan, it was apparent that this material is not suitable for application.

##### *ii) Plastic Considerations*

The second type of material we investigated for the frame was plastic. Plastic copolymers have a range of strengths and flexibility depending on fabrication for application. In addition to its ability to be fabricated to a specific structure and size, it is lightweight and water resistant. However, while researching applications for our final design, creating specific molds for this application were beyond our budget, and requires specific manufacturing at a separate facility. Due to this constraint, this is not a suitable material for our timeline or budget. This is a potential material and application for mass producing the mask design.

##### *iii) 3D Printed ABS Considerations*

The final material consideration was 3D printed ABS. This material is capable of high mechanical shape and formatting to whatever shape is desired within the dimensions of a 3D printer. WPI offers three 3D printers on campus, capable of printing 10" X 10" 3D printed

materials through a Solidworks model. These materials can be infused with Carbon Fiber to increase their mechanical strength. Considering the availability and ability to easily manufacture parts, and maintain structural integrity, 3D Printed ABS is a suitable material for the structure of the mask.

### *5.1.2 Internal Mesh Material Considerations*

#### *i) 3ply Medical Grade Mesh*

Initially, we investigated the properties of 3 ply medical grade respirators used in hospitals around the United States. These are designed with 3 layers of varying mesh thicknesses to filter air intake. This material prevents splatter of blood or water from entering the mask, but does not prevent significant amount of water accumulation. In addition to this limitation, the mesh is not capable of directing airflow due to its primary design purpose of filtering air intake. These limitations remove this as a potential material for the external mesh, however it may be used as an interior lining protecting the sensor.

#### *ii) Neoprene Fabric*

Neoprene fabric is often used in scuba materials due to its water and air resistance. Air is not capable of passing through the material easily, and in addition to this, the material is hydrophobic. Neoprene has high elasticity and tensile strength. These advantages make Neoprene a solid material choice to be added to the internal mesh of the mask design.

### *5.1.3 Final Material Decisions*

Due to limitations on finances and time, in addition to the considerations accounted for in the previous subsections, we made our final material decisions before mechanical testing validation. We selected 3D printed ABS for the external support material and Neoprene fabric to be sewn together for the interior lining. In the neoprene mesh, we sew in Velcro straps to attach

to the bridle for stability. The components of the mask were glued together using an epoxy adhesive, granting solid connection of all pieces.

## 5.2 Material Testing

### 5.2.1 3D Printed Material Testing

3D printed Acrylonitrile Butadiene Styrene (ABS) is tested using an Instron, to report the testing of the forces, yield, and failure of the material under maximum load calculations.

### 5.2.2 Internal Mask Material Testing

The final material selected for the mask internal shielding was Neoprene Heavy Scuba Knit by Mood Fabrics. The material was selected based on its limited permeability and strength, ability to prevent air from escaping, and the protection it would provide the sensor. This material was tested using an Instron, to report the testing of the forces, yield, and failure of the material under maximum load calculations.

#### i) Force Testing

Below are the data for the tensile testing test for the fabric. Figure 5.1 indicates the force vs. displacement graph throughout the entire trial, and Table 5.1 shows all significant data gathered from the test.

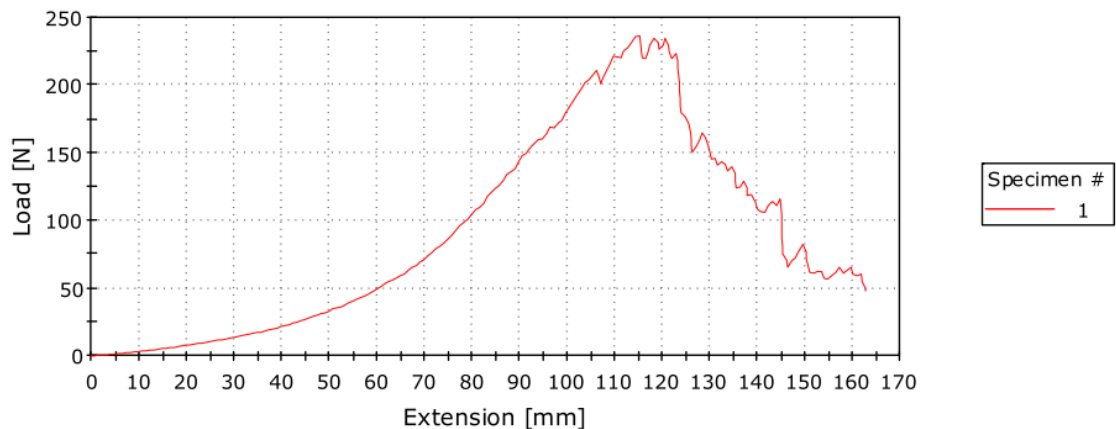


Figure 15: Neoprene Force vs. Displacement

	Area under curve [J]	Energy at Maximum Load [J]	Extension at Maximum Load [mm]	Maximum Load [N]
1	0.00000	8.57003	115.28352	236.34750
	Tensile extension at Maximum Load [mm]	Tensile strain (Extension) at Maximum Load [mm/mm]	Tensile stress at Maximum Load [MPa]	Time at Maximum Load [s]
1	115.28352	1.83719	4.79492	13.83200
	Maximum Slope (Automatic Young's) [mm/mm]	Modulus (Automatic) [MPa]	Tensile strain (Extension) gauge length [mm]	Rate 1 [mm/min]
1	1.00000	4.87883	62.75000	500.00000
	Energy at Yield (Zero slope) [J]	Extension at Yield (Zero slope) [mm]	Load at Yield (Zero slope) [N]	Tensile extension at Yield (Zero slope) [mm]
1	8.57003	115.28352	236.34750	115.28352
	Tensile stress at Yield (Zero slope) [MPa]	Time at Yield (Zero slope) [s]		
1	4.79492	13.83200		

**Table 5:** Neoprene Tensile Test Data

*ii) Hydrophobicity Testing*

The following test was conducted to determine the hydrophobicity and water resistance of the material to prevent spit and phlegm from the horse from accumulating on the inside of the mask. We tied a segment of the Neoprene fabric over an open cup and secure tightly with a rubber band to simulate the sewn final product. A drop of water is placed on the fabric and an external software ImageJ is used to calculate the angle between the base and the edge of the drop. The larger the contact angle, the higher the hydrophobicity. Figure 5.2 below illustrates the image sent in to ImageJ.



**Figure 16:** Neoprene Hydrophobicity Test

Plugging this into ImageJ resulted in a contact angle of 103 degrees, indicating hydrophobicity. This application allows for increased water resistance for the interior of the mask. After the contact angle was calculated for the mask, we tested the effects of water on both sides of the mesh to examine the time dependent properties of water on mesh. We followed the same procedure of the contact angle test, and let a 100 mL sample of water rest for 5 minutes on both the superior and inferior surface of the mesh. Figure 5.3 below shows both sides of the fabric after the 5 minute test.



**Figure 17:** Hydrophobicity Test after 5 Minutes

Notice the right side of the test, holding the material for the interior of the mask. This is significantly more hydrophobic and holds the water without significant absorption. However, the left side of the test shows the internal absorption possible with the flip side of the mask. Due to this difference, we ensure that the design has the hydrophobic side on the interior of the mask for easy cleaning and minimized bias.

### **5.3 Design Optimization**

The design was optimized through the remodeling of mask components to allow for increased strength and structural integrity. Various thicknesses of support brace and connection points are tested between each iteration. To optimize performance and design, we focused on creating a system that met our criteria: lightweight, reproducible, and sturdy. With this in mind, we increased the diameter of the support spans by up to 30%, increasing overall toughness to support 70 lbs of contact force.

### **5.4 Design Modeling**

The design was modeled with the use of various techniques to simulate overall look, function, and attachment locations. We modeled the design in the first iteration with a Kinetics model, then transitioned to a Solidworks model, following the dimensions of a life-sized horse replica. After the first Solidworks model is 3D printed, future iterations were created by altering diameters, component layouts, and shape fitting. The neoprene fabric was traced to surround the interior of the 3D printed mask. The edges were stitched together and Velcro straps were attached to the mesh to bind it to the mask frame.

## **Chapter 6: Discussion**

### **6.1 Results and Objectives**

The result of this project was a functioning respiratory diagnostic system with a form fitting mask. The Rev C sensor is an effective flow monitoring device capable of determining respiratory disorders in horses. Based on improvements to the previous LabVIEW code from last year, and testing with compressed air, we determined that the sensor and system as a whole acts within +/- 6.00% accuracy. The design is lightweight, totalling 0.91 lbs, and costs a fraction of current technologies. Considering that the design can be manufactured with varying component sizes, our design can be made for any breed of horse, with minimal resistance.

There are some limitations present in the design based on the fabrication and testing available. Throughout the testing process, we were not able to test the system on a live horse. Instead, we used simulations based on compressed air and human testing to determine the effectiveness of the sensor and mask. Future testing could determine the comfort of the mask and comparison to the fleisch pneumotachograph. In addition to this limitation, the RIP bands were not operable throughout the year, so they could not be added to the system.

### **6.2 Economics**

The economics of the project are divided into three main categories: Sensor purchasing, Mask design, and Material components, each of which are addressed below.

### *6.2.1 Sensor Purchasing Cost*

As discussed in the Rev C sensor section of this report, the sensor is purchased through Modern Device. The total cost of the sensor is \$17.00 USD before taxes for United States shipment. Any additional costs are determined based on the international export of the sensor.

### *6.2.2 Mask Design Cost*

The mask design, composed of 3D printed ABS is relatively inexpensive, and determined specifically by the size of the overall mask. Based on our trials, we created three different sized mask components, ranging in size to fit numerous horses. The final cost for this design ranges from \$80 to \$120 USD.

### *6.2.3 Material Component Cost*

The final economic consideration for this project is the external materials used for fixation and housing the sensor. The neoprene fabric comes in a large supply through Mood Fabric, costing \$45.00 USD, for each 6 X 6 ft. sheet. This is capable of creating up to two masks with some remainder for error correction. In addition to the neoprene components, we use velcro strips to connect to the halter/bridle for the horse. We purchased velcro strips through AC Moore for \$5.00 USD.

### *6.2.4 Total Cost*

The total cost of the design came from adding all of the components of the previous sections. The total cost is approximately \$150.00 with slight variance due to size for the horse's head.



### *6.2.5 Mass Production Cost*

Mass production reduces the cost significantly per mask when the mask components are molded to fit, and sent through production facilities. Due to the limited scope and application of this project, there currently is no need to mass produce this design. In future iterations and applications of this project, if it is to continue in future years, team members can reach out to facilities to produce the fabric and design much faster and cheaper.

### **6.3 Environmental Impact**

There are minimal environmental impacts concerned with this project due to the relative small scale of application and manufacturing. The components are all purchased through outside vendors, and the main manufacturing piece is 3D printed ABS, which does not produce significant weight for the design.

### **6.4 Societal Influence**

There are no significant societal influences present in this project. Due to the limited scope of the project, there is minimal societal impact of the project. This does not interface with humans, and does not pose as a societal concern.

### **6.5 Political Ramifications**

There are no significant political ramifications present in this research and project. There are no patent disputes discovered, endangerment to animals, or concerns to be discussed on the political aspect.

## **6.6 Ethical Considerations**

There are no significant ethical concerns present in this research and project.

There are no ethical disputes, concerns with impact to animals or humans, environmental concern, etc.

## **6.7 Health and Safety Issue**

Due to the scope of the project, the health and safety issue of this project reflects the interface of the horse. The voltage required to operate the sensor and the DAQ box is minimal, and poses no risk to the animal during testing. The low mask weight reduces risk of injury to the horse as well as people present during testing.

## **6.8 Manufacturability**

This design is manufactured in multiple stages, including the 3D printed exterior, mesh sewing, and attachment. The exterior of the mask is manufactured through three separate Solidworks models printed to one of the specified sizes for the size of the horse. The components are connected together, as described in the User Manual section of the Appendix. Manufacturing was completed on WPI campus using the available 3D printers and a sewing machine. For large scale applications, manufacturing sources may vary to reduce cost and provide sufficient design requirements.

## **6.9 Sustainability**

The project has a sustainable initiative, and does not produce significant waste. The interior mesh is reusable for numerous uses and is hand washable for cleaning. The frame is hand washable in between trials. The sustainability concerns are limited to the excess produced from the Rev C sensor and neoprene fabric companies.

## Chapter 7: Final Design and validation

### 7.1 Final Mask Design

The final mask is composed of an external circular frame to fit around the mouth of different sized horses, along with a bracing support beam on both sides to keep the frame sturdy and fixed throughout the testing process. Two support rods are extended from the base of the mask to connect the mask to the horse's halter. The circular frame, horizontal and vertical side supports and the mask extensions are secured using ABS cement which virtually makes the four parts into one. The four parts in the middle, being the top and bottom supports and the middle supports are inserted in slots or onto cylindrical rods and then zip tied on so that they can be easily removed. The middle parts can be printed in different sizes so that the mask can fit different horses.

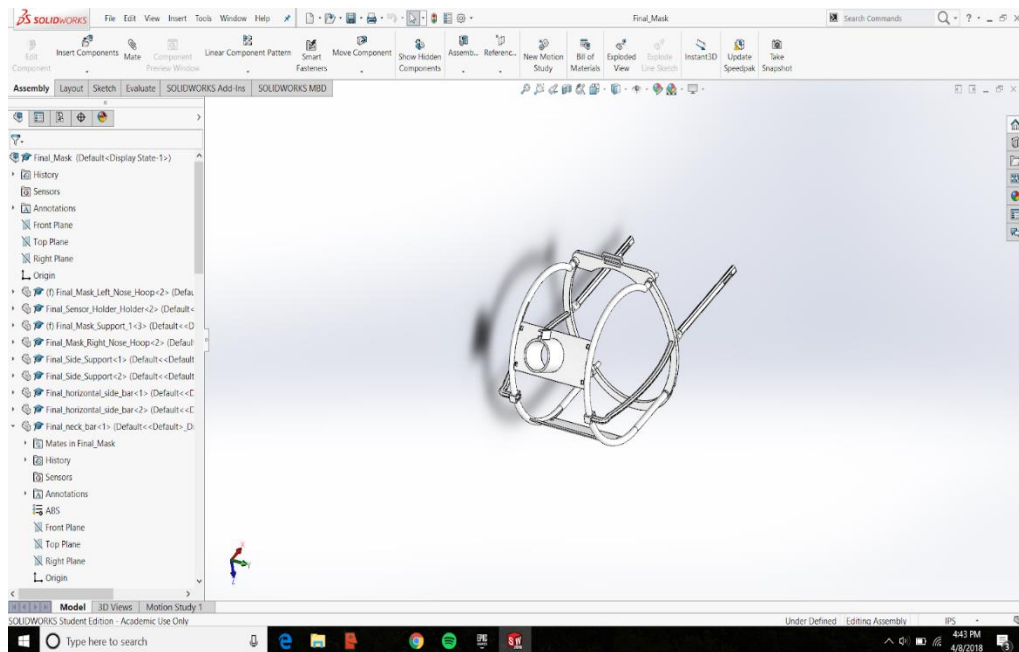


Figure 18: Final mask design



**Figure 19:** Final mask design.

The major difference with the final mask was making the circular frame 0.4 inches in diameter which was an improvement from the previous mask at 0.25 in in diameter. Another change was making the slots in the circular supports .2 in deep so that the support that holds the sensor cannot push through the circular support. The tolerance for the hole that holds the sensor holder is so low that the sensor holder can stay in place while being used but then can also be removed if necessary. The goal with the final mask was to make it rigid around the nostrils of the horse to protect the sensitive areas of the horse, but then also provide some flexibility in case the mask is slammed into any objects by the horse. The flexibility was created with the mask extensions which are angled slightly out so that if they are bumped there is some room to move.

Another perk of the final mask is the slots in the top support incase an extra strap is added. The extra strap would just provide even more support and take weight off of the horse's

nose. The final 3D-printed mask only weighs .67 pounds and with the neoprene liner is still under one pound.

## Chapter 8: Conclusions and Recommendations

### 8.1 Future Recommendations

Our mask design is a viable option for the respiratory testing of horses for diagnostic purposes, due to the testing results of the Rev C sensor and the human trial of the breathing rate. However, there are multiple future considerations for the improvement of this design. These are included below for the benefit of any future iterations or applications of this design.

#### *8.1.1 Component Selection and Mass Production*

The first consideration is changes in material selection for the frame of the mask. While our material choice of 3D printed ABS is structurally sound and capable of being cleaned, this is not the easiest to mass produce or sterilize between trials. During our testing and selection process, we discussed the potential use of stainless steel for its mechanical strength and ease of sterilizability.

Stainless Steel (SS) has a high Young's Modulus, and fracture resistance making it a safe for application to the mask. In addition to its strength and ease of sterilization, it has the capability of being mass produced with high quality as a single component. With all of the components designed together, structural integrity of the mask increases, preventing cracking or potential breaks if expressed to high forces. However, SS is limited due to its weight. The 3D printed ABS we used in the mask has a density of  $1.27\text{g/cm}^3$ , whereas SS has a density of  $8\text{g/cm}^3$ . The total mask weight with components comes to 0.91 lbs. Our sponsor Dr. Mazan impressed the importance of a lightweight design. Due to this, further material selection may be discussed for the continuation of the project to meet clinical and distribution needs if this is to be taken to mass production.

### *8.1.2 Wireless Connectivity*

Wireless connectivity was one consideration for equine respiratory monitoring that we intended to address. Due to the limited timeframe for the project, the function and applications were researched but not implemented in the final product.

To achieve wireless connectivity, we suggest the use of an Arduino UNO due to its analog inputs and data collecting capabilities. In addition to its strength in computing, the Arduino is capable of collecting data wirelessly by using a AA battery attachment and the USB port present on the system. The AA battery attachment allows the Arduino to function without connection for up to 2 hours, significantly longer than any equine respiratory testing requires. The use of a 32Gb or greater USB is capable of gathering more than the 20 minutes required for standard equine respiratory testing. Future iterations of this research and product can use these resources to apply wireless data acquisition.

### *8.1.3 Integration of RIP Bands*

Following the wireless data collection, a future recommendation for this project originally intended for this project was the incorporation of Respiratory Inductance Plethysmography Bands (RIP). Due to system malfunction of the operating RIP bands in the beginning of the year, integrating the RIP bands with the respiratory display was not within the scope of the project. As a potential direction for the future of this project, the following discussion provides the framework for potential inclusion of the RIP bands:

The RIP bands owned by Tufts are connected with AO pins, capable of connecting to an Arduino or other data acquisition method. Combining the wireless connectivity discussed above

with the extra pin of the RIP bands creates another channel for measuring breathing function. As discussed in the Literature Review section, the RIP bands measure the voltage displacement of the bands, and relate that to volume displacement of the diaphragm. Professionals are then able to compare these flow loop graphs with standard values for healthy individuals, whether animal or human.

#### *8.1.4 Display Software and Operation*

The software utilized for data collection and analysis for this project was LabVIEW. The output of this software presents the operator with a live feed of breathing rate vs. time. Within the LabVIEW code is calibration equations that convert the voltage displacement from the Rev C sensor to approximate breathing rate. All of the data is exported to an excel file to be analyzed individually if the operator desires. Future iterations of this project can output the Excel (.csv) file to Matlab for a simple function presenting the full respiratory test with overlaid graphs, minimum and maximum levels of breathing rate, etc. With this, veterinarians and individuals will only have to run the function once per trial after all the data is collected. The drawback of this method is that the Matlab software is costly for individuals to purchase. As a clinical method, this may be beneficial, as there is minimal debugging required if a well-written, commented code is presented.



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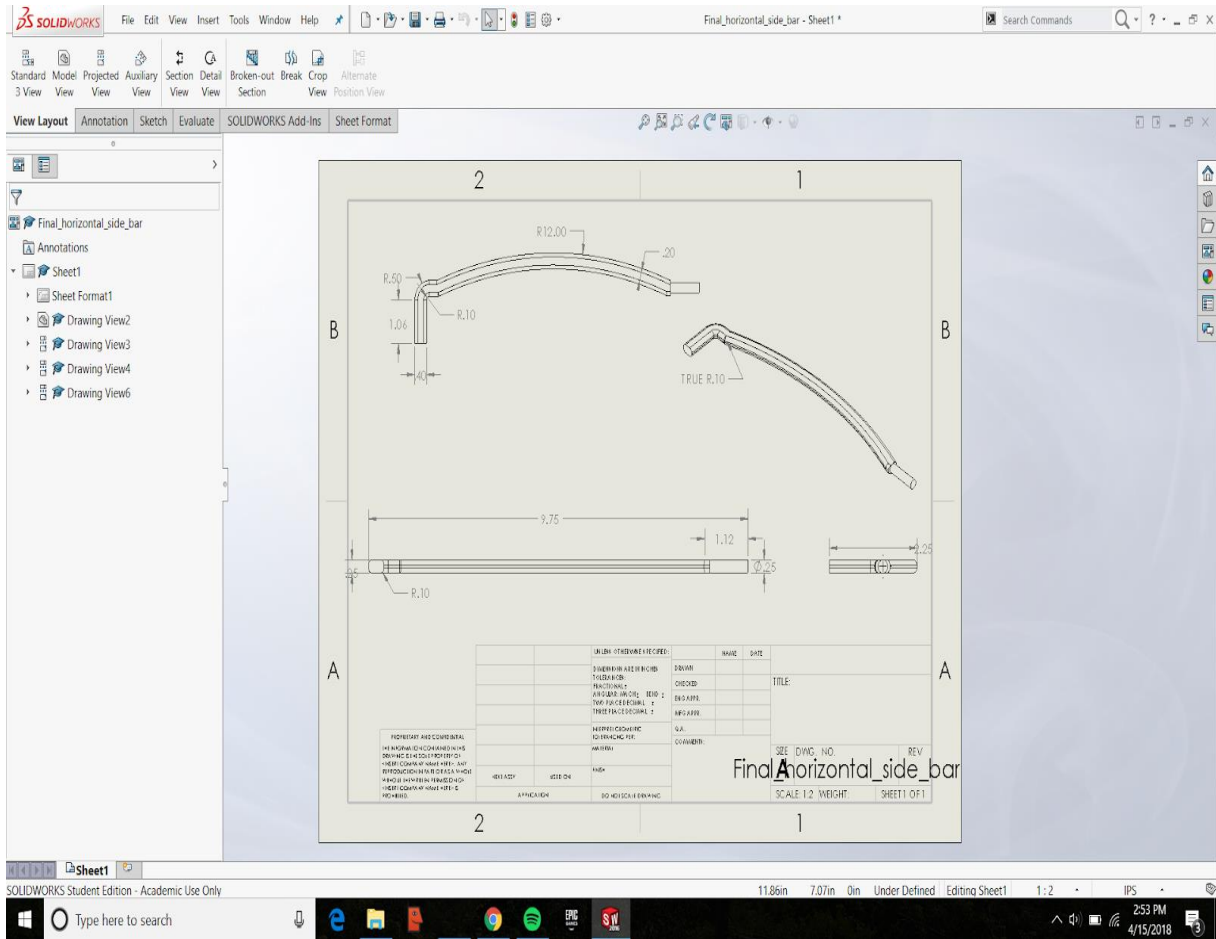
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**Figure 21:** Drawing of final horizontal support. Used on each side of the horses muzzle as horizontal supports.

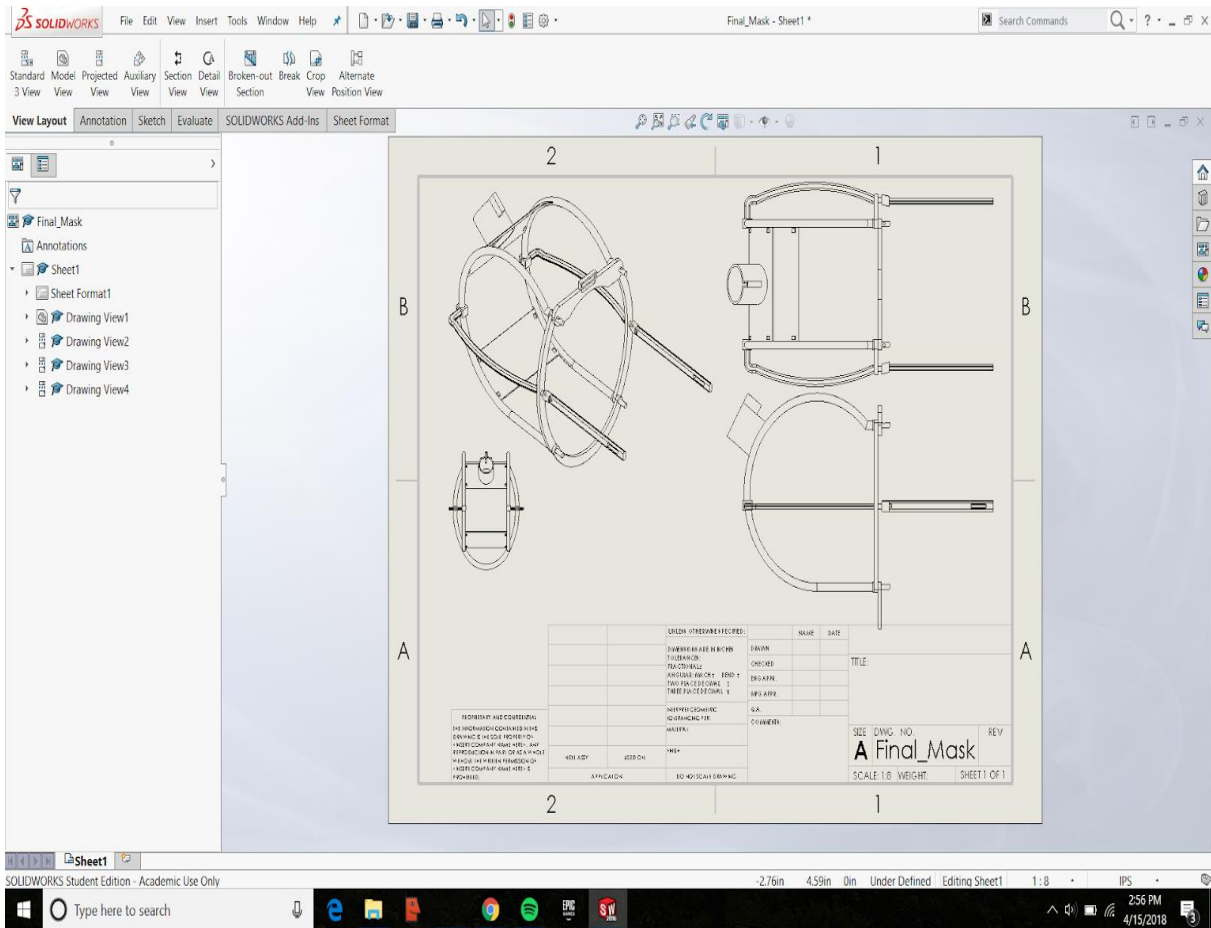
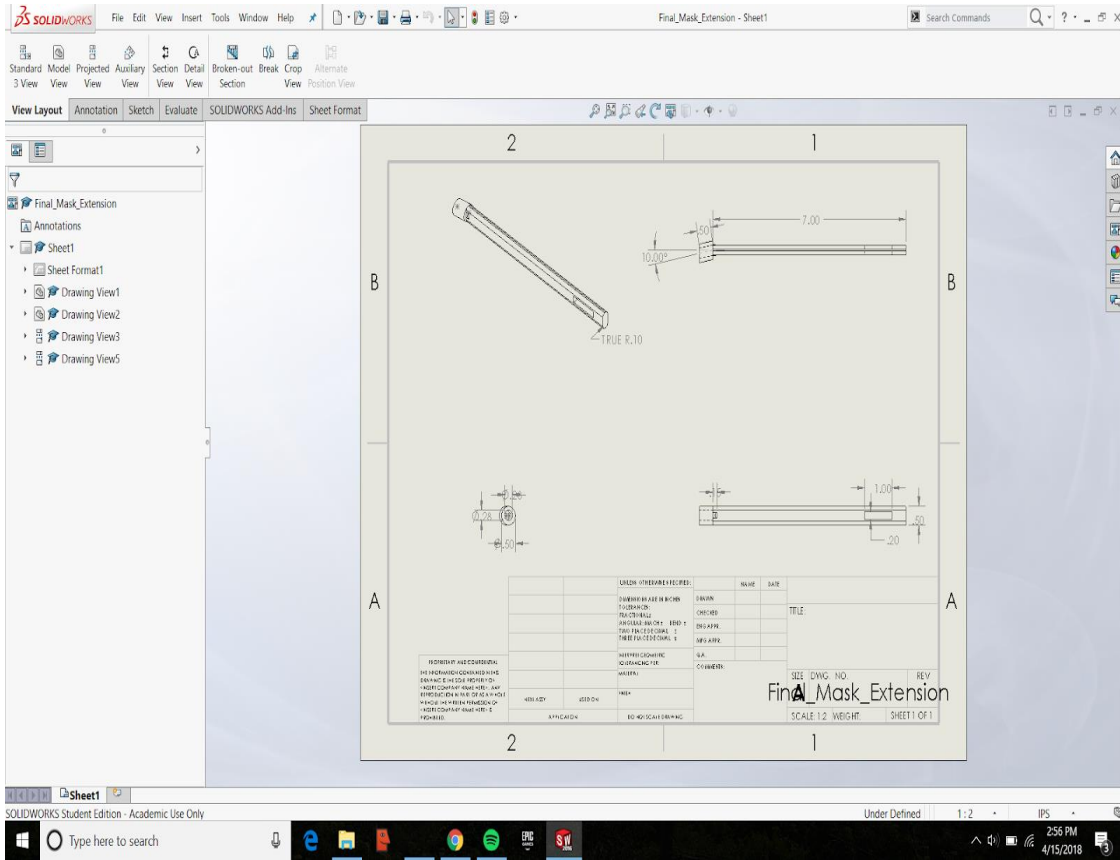
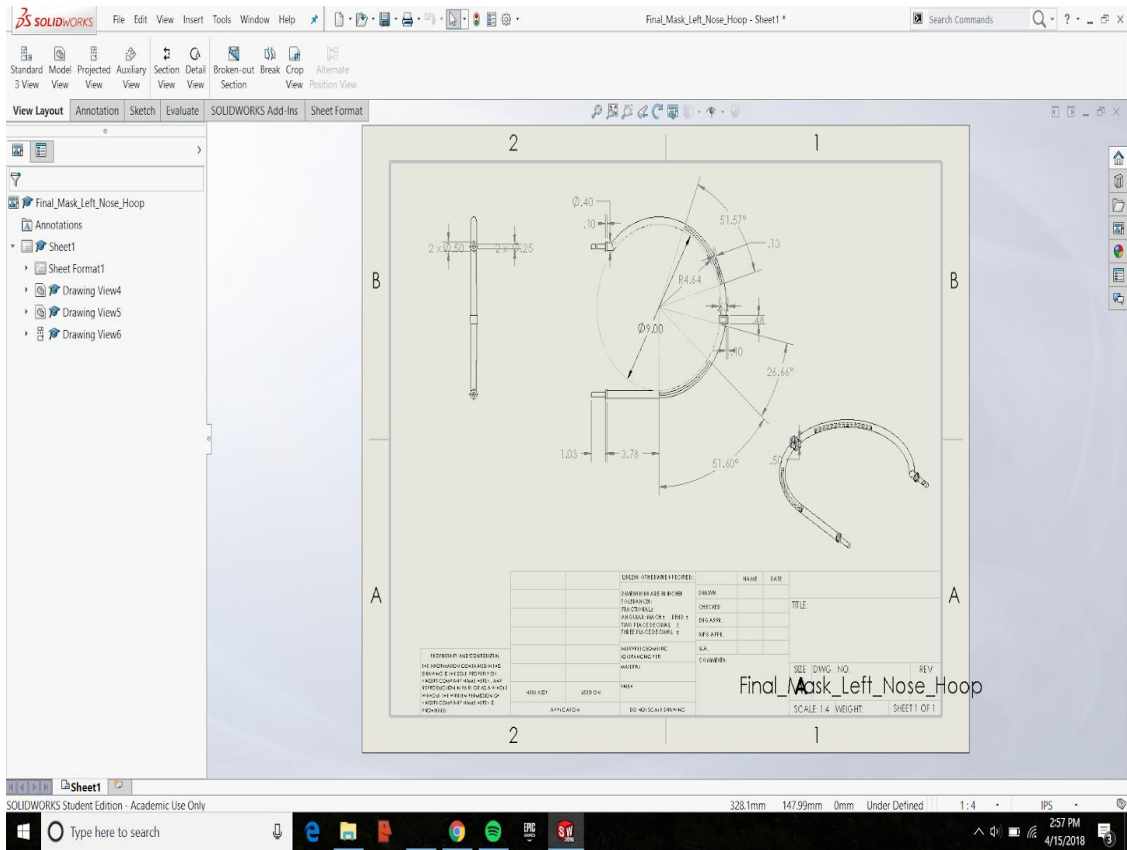


Figure 22: Final Mask Views



**Figure 23:** Drawing of Mask Extension. Used to connect the mask to the halter.

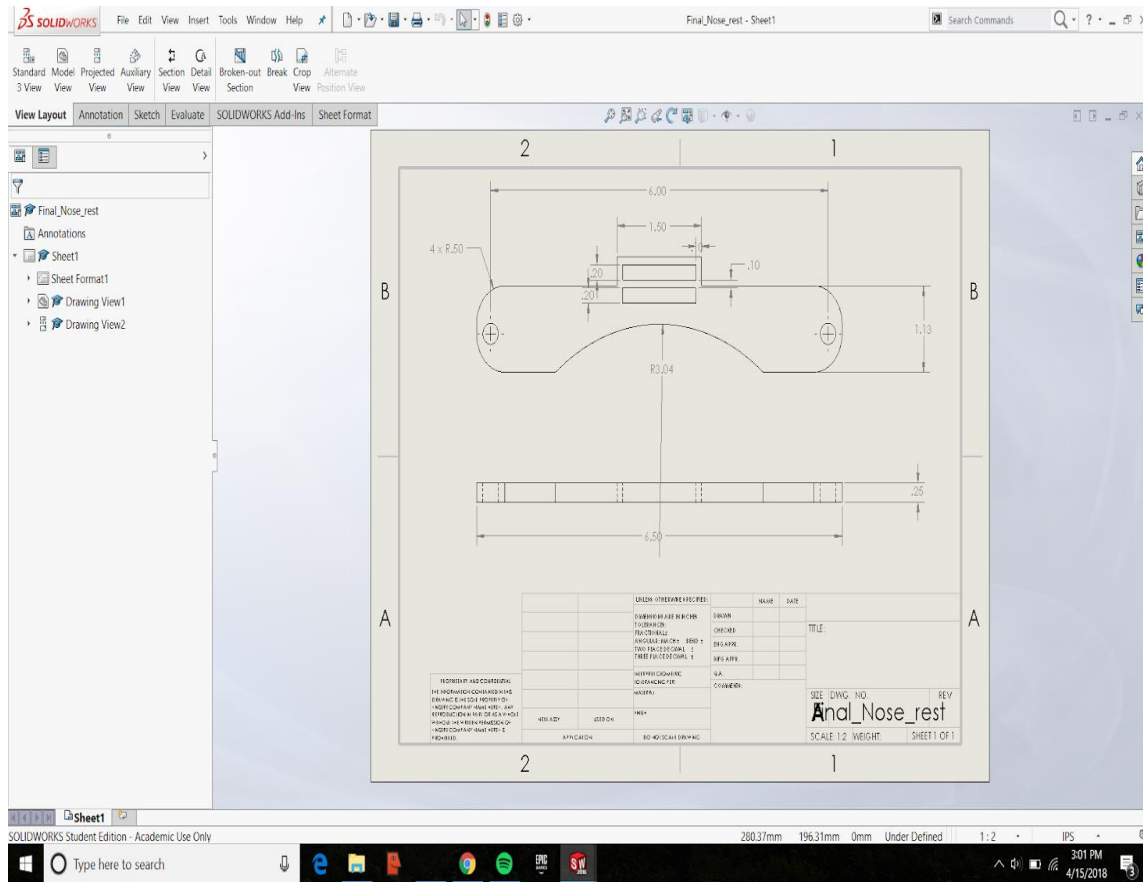


**Figure 24:** Drawing of Left Nose Hoop. One of the two main supports for the mask.





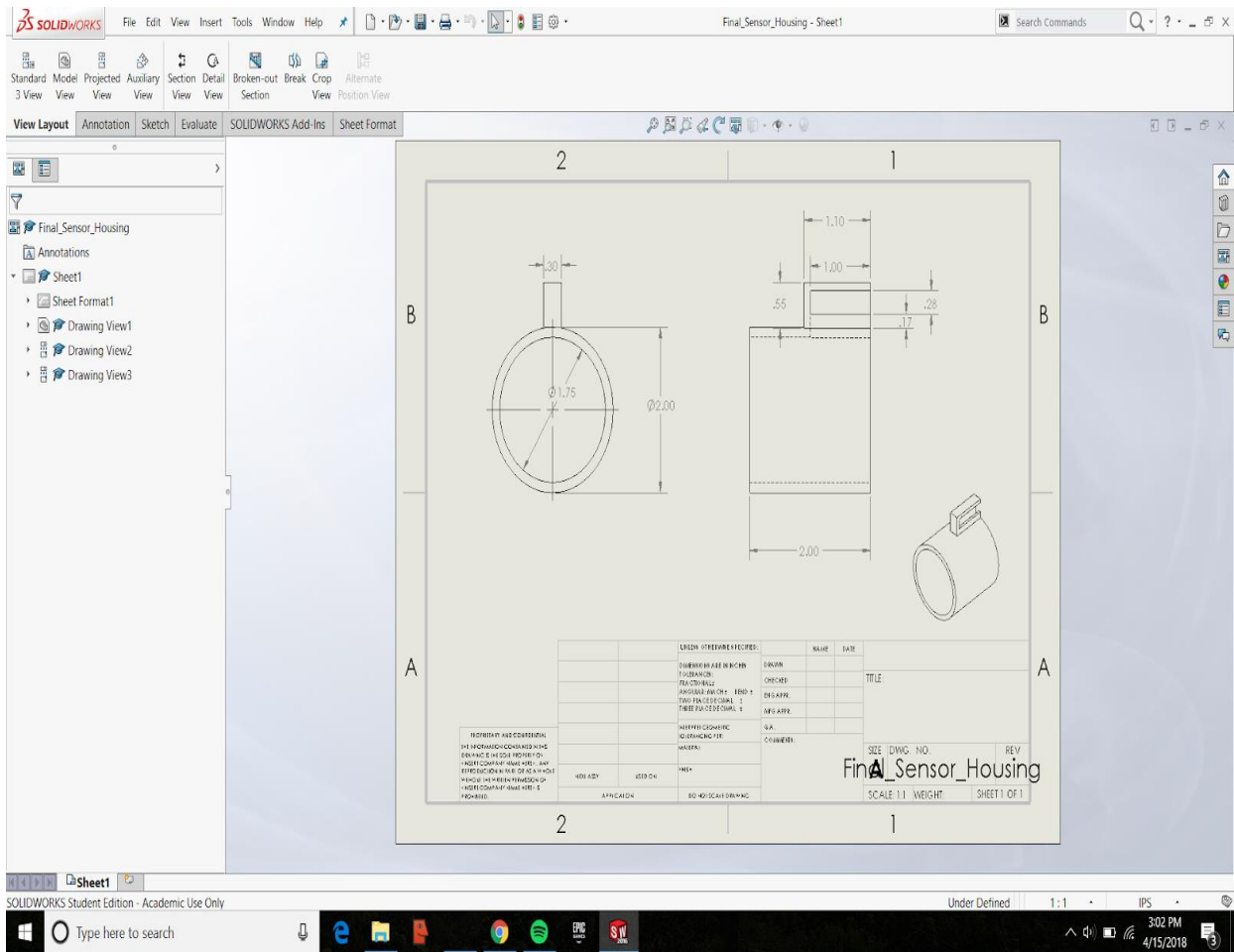




**Figure 28:** Drawing of the nose rest. The nose rest is the major weight bearing part for the mask. The radius of the part is former to fit a typical horse.

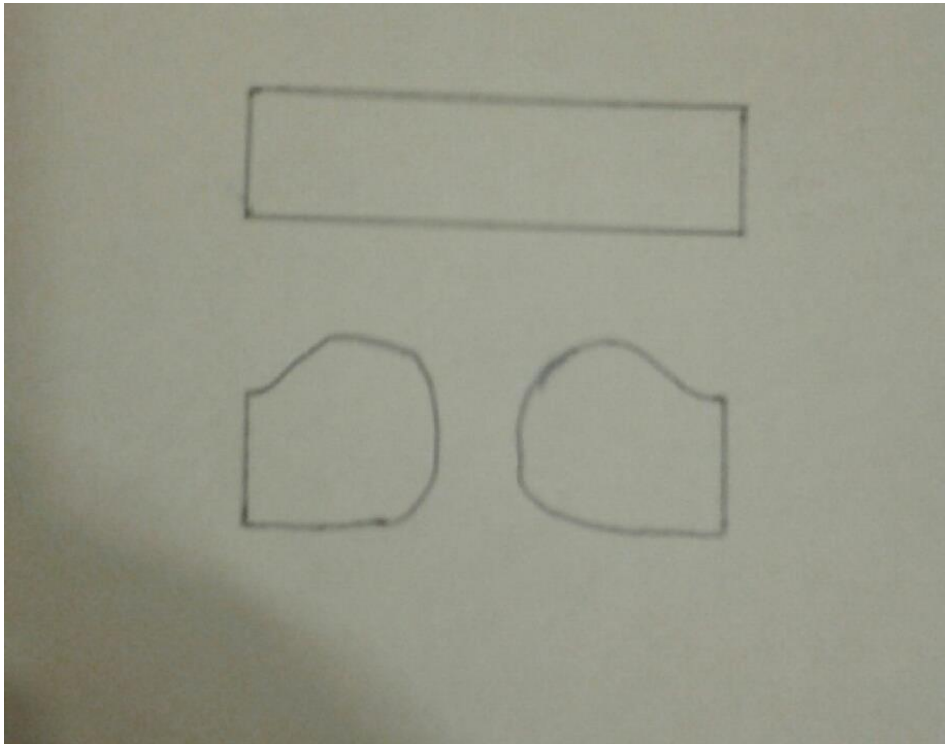






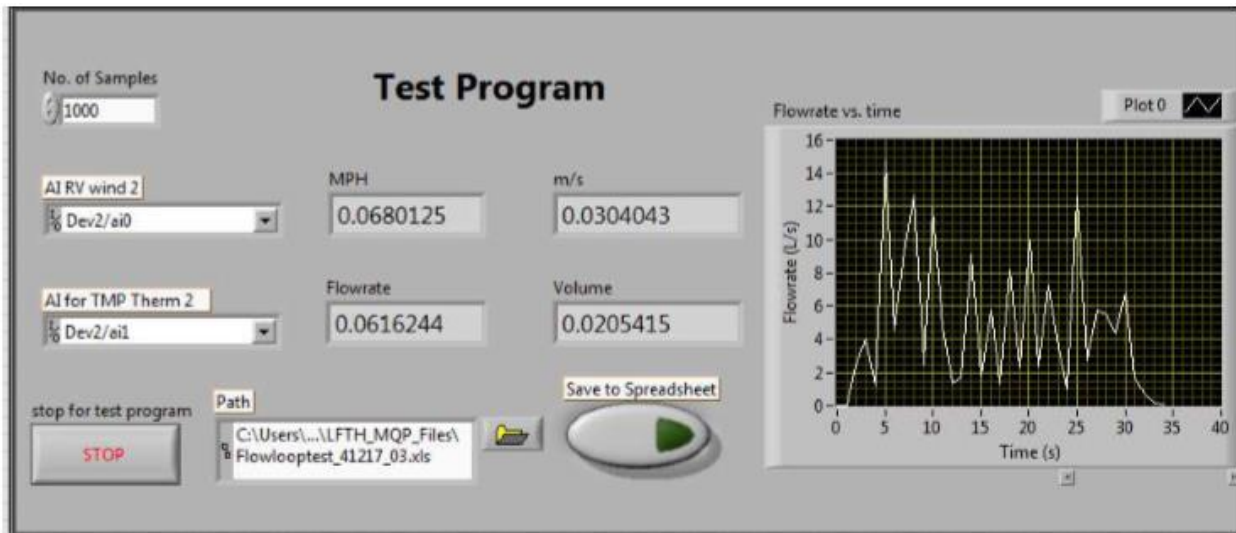
**Figure 30:** Drawing of the Sensor Housing. This part holds the sensor in place and also funnels the breaths from the horse towards the sensor.

## Appendix B: Bag Drawing



**Figure 31:** Final Bag Drawing

## Appendix C: LabVIEW Front Panel



**Figure 32:** Front Panel of the LabVIEW Program.

**Appendix D: Human Mask**



**Figure 33:** View of the Human mask used for testing.





**Figure 34:** View of the Human mask used for testing.



**Figure 35:** View of the Human mask used for testing.

## Appendix E: Mask Instructions

- 1.) Apply ABS Cement to L shaped end of Final\_Horizontal\_Side\_Bar and insert into rectangular slot of Final\_Mask\_Left\_Nose\_Hoop
- 2.) Before previous step dries, apply ABS cement to the 3 holes of the Final\_Side-Support and attach to the ends of the Final\_Mask\_Left\_Nose\_Hoop and to the cylindrical end of the Final\_Mask\_Side\_Bar
- 3.) Repeat first two steps for the Final\_Mask\_Right\_Nose\_Hoop
- 4.) Let dry for 15 minutes or until completely dry
- 5.) Insert Final\_Mask\_Support\_1 into bottom slot of Final\_Mask\_Left\_Nose\_Hoop
- 6.) Insert Final\_Sensor\_Holder\_Holder into top slot of Final\_Mask\_Left\_Nose\_Hoop
- 7.) Press Final\_Mask\_Right\_Nose\_Hoop onto the Final\_Mask\_Support\_1 and Final\_Sensor\_Holder\_Holder
- 8.) Firmly press mask together
- 9.) Slide Final\_Nose\_Rest onto the the top cylindrical ends of the Final\_Mask\_Left\_Nose\_Hoop and Final\_Mask\_Right\_Nose\_Hoop
- 10.) Slide Final\_Neck\_Bar onto the bottom cylindrical ends of the Final\_Mask\_Left\_Nose\_Hoop and Final\_Mask\_Right\_Nose\_Hoop
- 11.) Zip-tie tightly the Final\_Mask\_Support\_1, Final\_Sensor\_Holder\_Holder, Final\_Nose\_Rest, and Final\_Neck\_Bar onto the Final\_Mask\_Left\_Nose\_Hoop and Final\_Mask\_Right\_Nose\_Hoop using the appropriate slots provided
- 12.) Insert Final\_Sensor\_Housing into Final\_Sensor\_Holder\_Holder as far as allowable
- 13.) Using the ABS cement attach Final\_Mask\_Extension to the cylindrical end of the Final\_Horizontal\_Side\_Bar making sure the extensions are angled out and parallel to the Final\_Horizontal\_Side\_Bar
- 14.) Let mask dry
- 15.) Apply half of a velcro strip to the outside of the Final\_Sensor\_Housing protruding into the mask
- 16.) Insert Neoprene lining into the completed mask and attach with the velcro loops

### Attaching to the bridle

1. Slide the mask of the muzzle of the horse  
Final\_Nose\_Rest should side above the nostrils and Final\_Mask\_Extensions should be connected to the bridle using velcro



## Appendix F: Low flow wind tunnel SOP

1. Connect cemented reducers to reducing coupling at end of wind tunnel



A. B.

**Figure 36:** A) reducers attached; **Figure 37:** B) Reducers unattached from reducing coupling

2. Use a threaded nipple to connect the reducers to the top of the rotameter
3. Connect an airline hose to the bottom of the rotameter



**Figure 38:** threaded nipple and airline hose attached to rotameter

4. Connect the ball valve to the rotameter with the hose



**Figure 39:** Ball valve attached to rotameter via airline hose

5. Use another airline hose to connect the ball valve to the regulator



**Figure 40:** Ball valve connected to regulator via airline hose

6. Ensure the regulator is closed and the ball valve is closed



A.B.

**Figure 41:** A) Regulator in closed position; **Figure 42:** B) Ball valve in closed position

7. Use the quick disconnect to connect the airline to the regulator



**Figure 43:** Male quick disconnect of regulator that interfaces with compressed airline

8. Use electrical tape to secure the sensor at the end of the wind tunnel with the sensing element in the center of flow



**Figure 44:** Rev C sensor secured at end of wind tunnel

9. Connect the sensors wires to the correct ports of the DAQ box (see Appendix L for detailed instructions)
10. Hold the hot wire probe or Hold Peak handheld anemometer in the center of flow (see Appendices I and J for instructions on use)
11. Start running the software programs to collect data as described in (Appendix L and J)
12. Open the regulator completely by turning the cap on the top
13. Regulate the flow by slowly opening the ball valve until desired pressure and thus flow rate is reached



**Figure 45:** Ball valve completely open

14. Stop the flow by returning the ball valve back to the closed position
15. Disassemble the wind tunnel by following these steps in reverse

## Appendix G: SOP for single calibration LabVIEW program

**Policy:** This SOP will comply with veterinary standards and guidelines for external device sterilization and equine testing.

**Purpose:** The purpose of this SOP is to ensure safe and proper setup of the wind sensor lung function testing device for reliable and repeatable results.

**Scope:** This procedure is for veterinarians using the wind sensor lung function testing device to diagnose pulmonary disorders.

### Prerequisites:

- Wind sensor system
  - Including: Rev C sensor with 4 wires attached and a 5V wall wart connected to the sensor and a ground wire
- USB-6000 DAQ box
- 1.5 in. rubber connector (housing)
- Plastic face mask for the horse
- 2.4 mm flat head screwdriver
- Electrical tape
- Scissors
- Paper towels or rag
- 70% ethanol for disinfecting the housing
- Computer with LabVIEW 2015 software (or newer) and USB port
- Electrical outlet

### Procedure:

#### System setup

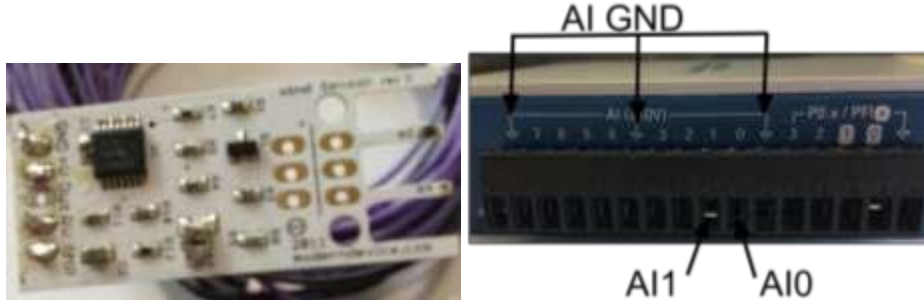
1. Connect wires to DAQ box using the following steps (a-d)



**Figure 46:** DAQ box used with the system; wires insert into the side below screws

- a. Ground (GND) of the sensor (1st pin) should be in one of the ports marked by an arrow (AI GND)

- b. The ground (V+ GND) of the power supply should be in another port marked by an arrow (Ai-GND)
- c. The RV pin on the sensor (4th pin) should be connected to port Ai0 on the DAQ box
- d. The TMP pin on the sensor (5th pin) should be connected to port Ai1 on the DAQ box



A. B.



C.

**Figure 47:** A) Sensor with pins on left; **Figure 48:** B) DAQ box ports with labels; **Figure 49:** C) Schematic of Rev C sensor with labeled pins to corresponding DAQ box ports

- i. All pins are connected by inserting the exposed end of the wire into the respective port and then tightening the port (clockwise) using the 2.4 mm flat head screwdriver
  - ii. The wires can typically be left attached, so check if they are secure with a soft pull on each
    - 1. If it comes out: loosen screw (counterclockwise) with 2.4 mm flat head screwdriver, insert the wire, and re-tighten the screw
2. Insert housing in face mask
- a. Locate the rectangular slot on the rubber connection
  - b. Orient this slot so that it will point up when attached to the mask on the horse
  - c. Insert the rubber connector (duct taped side) into the PVC portion of the mask ensuring the slot is closest to you when you slide it on
    - i. Lightly tug the device or shake the horse face mask to ensure the housing is securely attached

3. Insert wind sensor in housing
  - a. Slide wind sensor into slot in housing until the wires on the wind sensor rest on the stop (extended piece of rubber on the housing)



**Figure 50:** Sensor in housing in mask



- b. Using scissors cut a piece of electrical tape 1 inch in length
  - c. With the piece of electrical tape, tape the four wires from the wind sensor to the stop
3. Plug 5 V wall wart into an electrical outlet



**Figure 51:** Wall wart plugged into electrical outlet

5. Plug USB cable from DAQ box into computer's USB-port



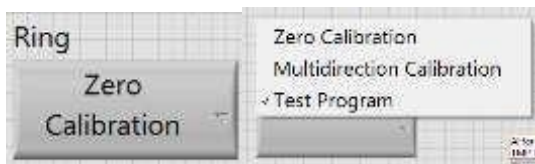
**Figure 52:** DAQ box connected to computer via USB

#### LabVIEW Setup

1. Power on computer with LabVIEW
2. Open LabVIEW 2015 or newer
3. In LabVIEW: File -> open -> Final\_RevC\_2.vi
4. Check to make sure the DAQ box is connected properly and turned on (should see blue light on the side of the DAQ box)

#### Calibrating the device to the room

1. Use the down arrow on the ringer (labelled ring) to choose the zero-calibration program



A. B.

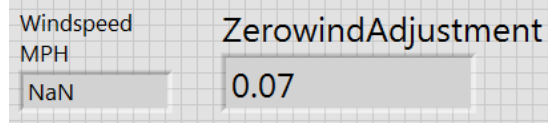
**Figure 53:** A) Ringer used to choose which program is running; **Figure 54:** B) Programs that can be chosen

2. Click the run arrow (highlighted in image below with a red box) in the upper left hand corner right below edit on the toolbar



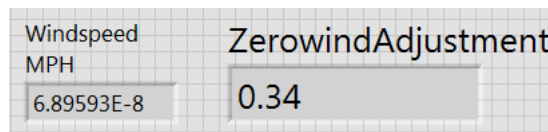
**Figure 55:** Run arrow on upper left of screen when in LabVIEW

3. The windspeed MPH should be displaying NAN when the program when started



**Figure 56:** Desired start conditions for the zero-calibration program

- a. If it is not reading NAN click the stop button and ensure everything is connected properly before rerunning the program
4. The program will stop on its own once reaching a wind speed less than 0.0005 MPH



**Figure 57:** Desired end condition (zerowindadjustment factor will vary with test environment)

- a. Note: For a 5 V wall wart, the adjustment factor should be approximately 0.30- 0.40
- i. If the program does not stop and the windspeed is reading higher than 0.0005 stop the program using the stop button
- ii. Check the setup and rerun the program
5. Once the program stops running keep the LabVIEW Final\_RevC\_2.vi open

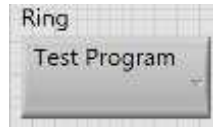
#### Horse setup

1. Put the mask on the horse's muzzle by holding the black rubber cover back and sliding it on
2. Release the rubber seal and allow it to fit tightly to the horse's muzzle
3. Attach the blue Velcro strap over the horse's head to keep the mask on

#### Testing the horse

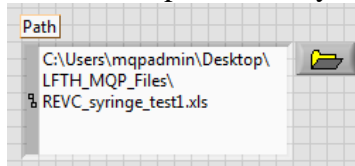
1. Check that Final\_RevC\_2.vi is still open in LabVIEW
- a. If not, go back to "Calibrating the device to the room" and follow steps again
2. Use the arrow on the ringer (labeled ring) to select the test program





**Figure 58:** Ringer setting for testing

3. Set file name by editing existing or browsing for a file using the folder button
  - a. The file type must be .xls
  - b. Program will produce an error if file is open when trying to run the program



**Figure 59:** Define file path or choose a file by browsing

4. Click the run arrow in the upper left hand corner as done before
  - a. Note: data does not automatically begin saving
5. Click the save button to begin recording data



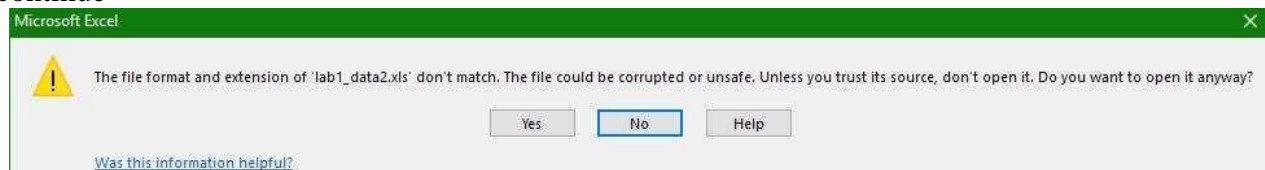
**Figure 60:** Click this button to stop or start saving (currently not saving, light changes to brighter green when saving)

6. To stop saving click the save button again
7. If finished testing stop the program using the stop button



**Figure 61:** Use this button to stop the test program; it will not stop on its own

8. Your file will be saved in the location specified with the defined filename
9. Open the file and save as an .xlsx file before analyzing
  - a. When opening an .xls file, Excel will produce a warning message. Select “Yes” to continue



**Figure 62:** Excel warning message

### System disassembly

1. Unplug 5 V wall wart from electrical outlet
2. Horse face mask disassembly
  - a. Detach blue Velcro strap from horse's head
  - b. Slide face mask off of horse's muzzle
3. Wind sensor housing disassembly
  - . Take off electrical tape from wind sensor wires
  - a. Slide wind sensor out of the slot
  - b. Slide housing (rubber connector) off of horse face mask
4. Close LabVIEW
5. Unplug DAQ box USB cable from computer USB port
6. Optional: Wire removal from DAQ box
  - . Unscrew each DAQ box screw (4 total) with a wire attached (2 GND, Ai0, Ai1) using the 2.4 mm flat head screwdriver (counter clockwise)

### Cleaning system after testing

1. Spray 70% ethanol disinfectant onto paper towel (or rag)
2. Wipe down housing (rubber connector)
3. Set housing down to dry
  
4. Spray 70% ethanol disinfectant onto a new paper towel (or rag)
5. Wipe down horse face mask
6. Set horse face mask down to dry

## Appendix H: Cost Breakdown and Budget

<b>Table of Costs</b>	
Rev C Sensor	\$ 17.00
Neoprene Fabric	\$ 47.84
3D Print of Mask (Prototypes)	\$ 245.00
3D Print of Mask (Final)	\$ 100.00
Horse Head Model	\$ 97.00
<b>Total Cost:</b>	\$ 506.84
<b>Total Budget:</b>	\$ 750.00
<b>Remainder:</b>	\$ 243.16

**Table 6:** Cost Breakdown and Budget

## *Preface*

The following paper is in fulfillment of the Professional Writing degree requirements for David Frederick. This paper will examine human lung function and the symptoms, detection methods, treatment, and epidemiology of three human respiratory diseases: Asthma, Chronic Obstructive Pulmonary Disease, and Pneumonia, as well as emerging respiratory health concerns.

## *Anatomy*

The human respiratory system is composed of the nose and nasal cavity, pharynx, epiglottis, larynx, and the lungs. The pharynx is the membrane lined cavity behind the nose and mouth, and directly below it is the epiglottis, a cartilage flap that covers the opening to the trachea. The larynx, also known as the “voice box”, is a hollow muscular organ that contains the vocal cords. Air passes through the larynx to the trachea and lungs. The trachea is a cartilaginous tube that's primary function is to transport air to the lungs. Within the lungs are a network of bronchi,

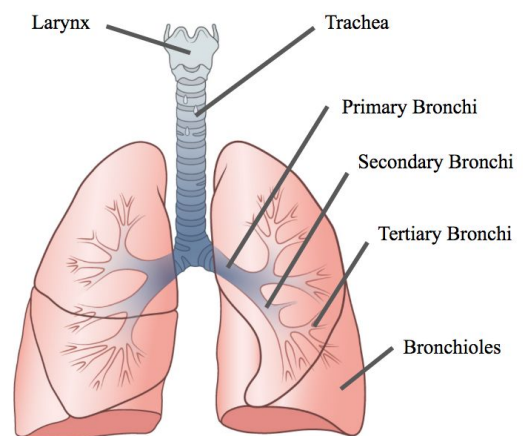


Figure 1, basic anatomy of the lungs [1]

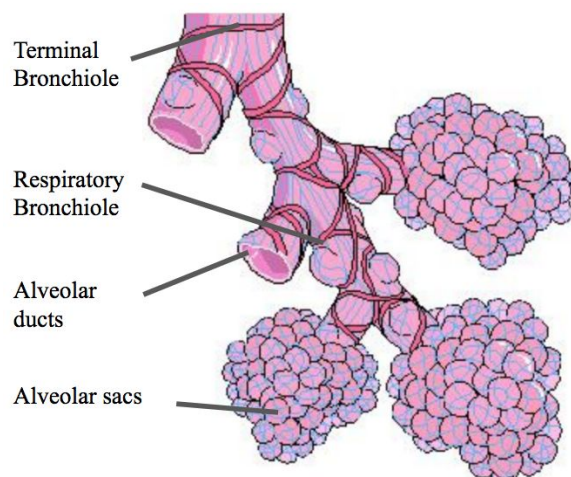


Figure 2, Bronchioles [2]

arranged in a root-like system. The bronchi transport air within the lungs to the bronchioles.

The bronchioles are the end terminuses of the bronchi, and lead to the alveolar sacs. The alveolar sacs are tiny balloons that inflate and deflate simultaneously during gas exchange. The walls of the alveolar sacs are coated with capillaries, and they facilitate the transfer of CO<sub>2</sub> out of the blood, and O<sub>2</sub> into the blood.

### *Mechanics of Breathing*

The most important muscle of inspiration is the diaphragm, as seen in Figure 3. It is a thin dome-shaped sheet of muscle which is inserted into the lower ribs. When it contracts, the abdominal contents are forced downwards and forwards, which creates a negative pressure within the chest cavity, causing the alveolar sacs to inflate. During passive expiration, the diaphragm relaxes which causes a positive pressure in the chest cavity, and drives the air out of the alveolar sacs. Forced expiration, as in coughing or sneezing, utilizes the rectus abdominis, internal and external obliques, and transversus abdominis muscles to force the diaphragm upwards and create a larger positive pressure in the chest cavity, (West, pg. 89-91).

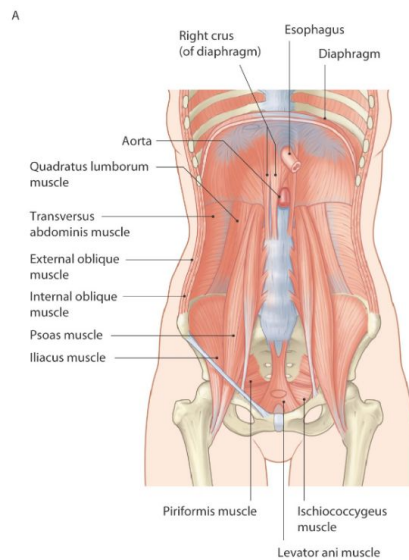


Figure 3, muscles of the abdomen, [3]

## Gas Exchange and Respiration

The capillaries of the alveolar sacs are the location where gas exchange takes place. CO<sub>2</sub> is removed from the blood and O<sub>2</sub> is moved into the blood. The movement of gases across the capillary walls is called diffusion, and in this case is passive diffusion. O<sub>2</sub> and CO<sub>2</sub> flow from areas of high concentration to low. The rate at which the gases diffuse is a function of cross sectional area, wall thickness, partial pressures, gas solubility, and the gas constant, as explained in Figure 4, (West, pg. 22).

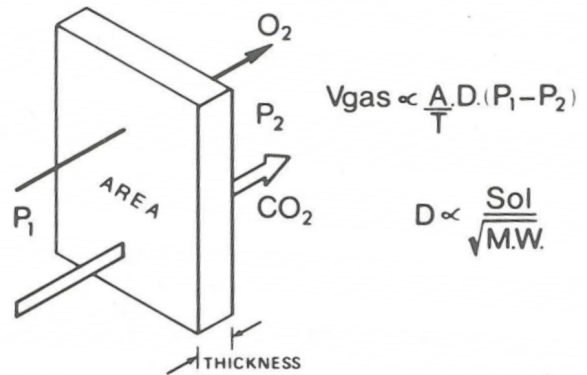


Figure 4, gas diffusion relationships across capillary walls. Transferred gas is proportional to the area (A), a diffusion constant (D), the differences in partial pressure, and is inversely proportional to capillary thickness (T). The diffusion constant is proportional to the gas solubility (Sol), and inversely proportional to the square root of molecular weight (M.W.) [4]

The movement of O<sub>2</sub> and CO<sub>2</sub> into and out of the blood is essential for the process of cellular respiration. Cellular respiration is the process in which cells break down sugars to create energy in the form of Adenosine Triphosphate, (ATP). There are two modes in which cells can make ATP. The first is glycolysis, which is the splitting of glucose molecules for a low yield of 2 ATP and it does not require O<sub>2</sub>. This process also produces pyruvate, which is used in the citric acid cycle. In the second process, the citric acid cycle, O<sub>2</sub> is used as an electron acceptor for pyruvate, and makes H<sup>+</sup> ions which are used to create a chemical gradient across the membranes of the mitochondria. When this gradient is released it creates enough energy to make 34 ATP. When O<sub>2</sub> is not present, the cells cannot conduct the citric acid cycle, and must dispose of the

pyruvate by other means. During lactic acid fermentation, the pyruvate is fermented, and turned into lactic acid, which can then be deposited into the blood as a waste product.

*The Nervous System and Respiratory Controls*

The sympathetic and parasympathetic nervous systems govern the body’s reaction to the environment. The sympathetic nervous system prepares the body for intense physical activity, and is also known as the fight or flight reaction. The sympathetic nervous system stimulates several bodily systems, as seen in figure 5. The

key factor that effects the lungs is the release of epinephrine into the blood from the adrenal glands. This triggers the beta 1 receptors within the heart, causing the heart to beat faster.

Additionally, the epinephrine triggers the beta 2 receptors within the bronchioles, causing them to dilate in order to keep up with the increased demand for O<sub>2</sub>, which is the result of the faster

heart beat. The parasympathetic nervous system prepares the body for rest and recovery. It effects several bodily features as seen in figure 5, including the constriction of the bronchioles.

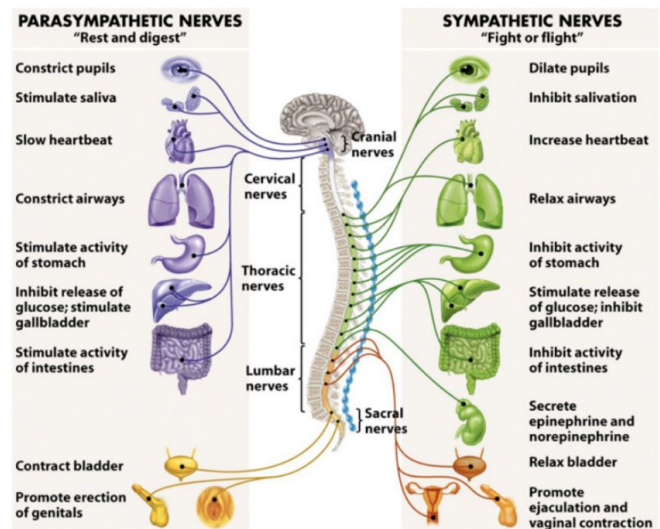


Figure 5, sympathetic and parasympathetic nervous system [5]

## I. Background

Asthma is a chronic inflammatory disorder of the airways. The word asthma is derived from the ancient Greek word for “panting”, which highlights the key feature of this disorder. Patients who suffer from asthma will undergo episodes, known as “asthma attacks”, which are characterized by labored, rapid breathing. Asthma is classified as an air trapping disorder, and during these asthma attacks, a patient will struggle to remove air from their lungs. Asthma prevalence has increased dramatically over the past 35 years and has become a significant public health concern due to the pervasiveness of the disorder and the environmental factors that contribute to it, (Broaddus, pg. 1168).

Chronic asthma is characterized by inflammation of the airway walls, with abnormal accumulation of eosinophils, lymphocytes, mast cells, macrophages, dendritic cells, and myofibroblasts. Inflammatory mediators and proteins secreted by these cells contribute to lasting changes to airway epithelial tissue. These changes result in goblet cell metaplasia and subepithelial fibrosis. Due to these changes, an asthmatic’s airway epithelial tissue stores more mucus, which can cause obstructions in the form of mucus plugs, and constricts the path to the bronchioles and alveolar sacs, (Broaddus, pg. 1176) An asthmatic reaction is a severe constriction of the bronchioles, but the reason for this constriction is debated.

The traditional line of thinking is that the reason an asthmatic’s bronchioles will constrict is due to an oversensitivity to mild irritants, (Broaddus, pg. 1169). However, the alternate view is



that an asthmatic is less capable of filtering these irritants before they enter the bronchioles due to defects in airway epithelial tissue, (Holgate et al. 2009). The airway epithelial tissue is the mucus lined coating of the inner airways, and is responsible for trapping both physical and chemical irritants before they can enter the bronchioles. Despite the source of the inflammation being disputed, it is widely agreed that inflammation and constriction of the bronchioles causes the symptoms of asthma.

Asthmatic airway inflammation begins with an inhaled allergen being processed by antigen presenting cells such as dendritic cells or macrophages. These cells present the antigen to T cells for secretion of cytokines. The type of cytokine produced will determine the magnitude of the inflammatory response, and in asthmatic individuals, inhaled environmental triggers will cause the production of Th2 cytokines, rather than Th1 which produce mild inflammatory reactions. The presence of Th2 cytokines triggers the production of eosinophils, mast cells, and B cells, (Broaddus, pg. 1178).

## II. Symptoms and Risk factors

The symptoms of asthma include coughing, wheezing, shortness of breath, difficulty breathing, and chest tightness, (Broaddus pg. 1168). These symptoms are a result of inflammation in the bronchioles tubes. This inflammation significantly constricts the path from the alveoli and requires the individual to work much harder to deflate their lungs. Furthermore, during an asthma attack, a patient may become panicked, increasing their heart rate. Increased heart rate and decreased air passage frequently leads the patient to become light headed. In some

cases this can cause the patient to become unconscious, and can even lead to death if untreated. Because of this, asthma is widely recognized as a major cause of disability, medical expense, and preventable death, (Broaddus, pg. 1168).

Chronic asthma creates lasting changes to the structure and function of the airways. Frequent damage to airway epithelial tissue, (caused by coughing and wheezing episodes), leads to a threefold increase in the amount of mucin stored in the airways, which can cause further issues of airway obstruction. Furthermore, the structure of mucus changes in an asthmatic's lungs. Gel-forming mucins become highly expressed, leading to a thicker consistency. This thicker mucus is the leading cause of fatal asthma via asphyxiation. This is due to mucus clots that become lodged in an airway, also known as mucus plugging, (Broaddus, pg. 1176-1177).

Individuals with asthma are more prone to environmental factors than non-asthmatics. Due to chronic inflammation and damage accrued to the epithelial tissues of the lungs during coughing fits, an asthmatic is more susceptible to viral infections. Viruses such as the Human Rhinovirus (HRV) are known to worsen an asthmatic's condition, particularly in the autumn and winter months, (Holgate et al. 2009). Other environmental factors will exacerbate the symptoms, to include second hand smoke, air pollutants, dust mites, and pet ownership, (Broaddus, pg. 1170). These environmental factors may cause asthma attacks and increase the frequency of attacks. Lifestyle choices can have an effect on the severity of asthma symptoms. These choices can include smoking, high intake of salt, and obesity, (Broaddus, pg. 1170). Additionally, exercise can cause or exacerbate an asthma attack, and for some, is the most frequent cause of attacks. These cases are known as exercise-induced asthma. Furthermore, asthma can be allergy

induced, where inflammation, coughing and sneezing, or other symptoms of an allergic reaction can trigger an asthma attack.

Asthma is classified in four general categories based on the frequency and severity of symptoms, mild intermittent, mild persistent, moderate persistent, and severe persistent. Mild persistent involves mild symptoms up to two days a week and two nights a month, while mild persistent is more than twice a week, but not more than once per day. Moderate persistent involves daily symptoms and multiple instances at nighttime, and severe persistent is multiple occurrences daily and frequently at night, (Asthma, 2016).

### III. Detection

There are several methods used to diagnose asthma. One type is lung function testing, which is the most simple test, as it involves blowing several breaths into a tube. It measures the volume produced and the speed with which air leaves the lungs. A score is assigned based on this data, and from the score it can be estimated how constricted the bronchioles are and how likely it is that the patient has asthma, (Asthma and Lung Function Tests, n.d.).

The other diagnostic tools include challenges and tests that screen for the subtle differences between a normal lung and that of an asthmatic. One such test is the nitric oxide test, which analyzes levels of nitric oxide present in a patient's breath. Higher levels of nitric oxide indicates airway inflammation, a sign of asthma. X-ray scans and CT scans of the lungs and nasal cavities can also be used to identify structural abnormalities or infections that are causing

breathing issues. Analysis of cough saliva can be used, as patients with asthma will have higher concentrations of white blood cells in their saliva, (Asthma, 2016).

There are also a series of provocative tests that aim to trigger a mild asthmatic reaction. One such test is the methacholine test, which requires the patient to inhale a small amount of methacholine, a chemical known to trigger asthma. Another form is allergy testing, in which allergens are introduced via skin or blood in order to trigger a reaction. Additionally, there are provocative tests for exercise and cold, in which a doctor will measure lung function before and after vigorous exercise or after several breaths of cold air, (Asthma, 2016).

#### IV. Treatment

##### *A. Medications*

There are two types of pharmacological treatment, short term relievers, and long term relievers. Short term relievers are beta<sub>2</sub> adrenergic agonists and are best delivered by aerosol, which maximizes delivery to the airway and minimizes systemic absorption. These beta<sub>2</sub> agonists block beta<sub>2</sub> receptors in the lungs, reducing the body's parasympathetic reaction of constricting airways. Ipratropium bromide is a fast acting bronchodilator, that relaxes the smooth muscle walls of the lungs and submucosal glands by blocking the actions of acetylcholine released from the motor branches of the vagus nerve. Ipratropium is delivered via aerosol, usually through the use of a rescue inhaler. Ipratropium action peaks within 30 minutes, and its effects last for 4-6 hours, (Broaddus, pg. 1195). A newer beta<sub>2</sub> agonist is tiotropium, and it functions using the same

mechanisms as Ipratropium, but with the advantage of a 24 hour duration. Additionally, it does not inhibit M-2 receptor-mediated inhibition of acetylcholine release from parasympathetic nerve endings, (Broaddus, pg. 1195).

Long term controllers are typically inhaled corticosteroids, that inhibit the production of pro-inflammatory cytokines. They also may stimulate the production of anti-inflammatory proteins to reduce and prevent inflammation. These are typically delivered in a rescue inhaler, but can also be delivered orally on a daily basis to prevent flare ups. Also available are long acting beta<sub>2</sub> agonists such as salmeterol and formoterol, which provide bronchodilation over longer periods of time, (Broaddus, pg. 1194).

Because many asthmatics also suffer from other allergies which create symptoms such as sneezing, itchy nose, clear mucus, and nasal congestion, leukotriene modifiers may be used as a treatment option. This is not typically the first mode of treating asthma, but it provides an effective solution for some. Leukotrienes are the inflammatory chemical the body produces when it comes in contact with allergens or irritants, and the subsequently trigger inflammation of the bronchioles of an asthmatic during an attack. A leukotriene blocker is a daily ingested medication that prevents leukotrienes from activating and causing airway inflammation, and is typically used as a treatment option for exercise-induced asthma. In comparison to inhaled corticosteroids, however, leukotriene blockers were found to be less effective in clinical trials, (Leukotriene Modifiers and Allergies, n.d.).

## *B. Immunotherapy*

For some patients with severe allergy-induced asthma that is not controlled by rescue inhalers, immunotherapy is a treatment option. Immunotherapy is a reconditioning of an immune system that is sensitive to certain allergens. Patients with allergies in addition to asthma may choose immunotherapy to prevent the attacks caused by their allergies.

Allergy shots are one form of immunotherapy, and are usually administered once a week for a couple months, and then once a month for 3-5 years. They contain doses of the allergen and increase in dosage over time. The result is an eventual buildup of tolerance to the allergen. For patients whose asthma attacks are triggered by an allergic reaction, this can reduce the frequency of the attacks, and eliminate some environmental triggers, (Allergy Shots, n.d.).

Omalizumab is another treatment option, and is an injected medication, administered every 2-4 weeks, (Asthma, 2016). Omalizumab is a monoclonal anti-immunoglobulin antibody, and it prevents allergic reactions by influencing the immune system to create anti-immunoglobulins that bind pathogens and preventing them from entering the system and causing an allergic reaction. This treatment option has shown to significantly reduce asthma exacerbations as a result of allergic reactions, (Willsie, 2006).

## *C. Other Treatments*

For cases that medication and other treatment options do not effectively control a patient's asthma, bronchial thermoplasty may be an option. This procedure is not widely

available, and is not suitable for every case. It heats the inner airways using the thermal energy from radio frequencies to reduce the mass of the smooth muscle tissue within the lungs, (Laxmanan et al, 2015). This thinning of the interior bronchiole walls significantly reduces the symptoms of an asthma attack by reducing the amount the airway constricts. While the mechanisms of this treatment are not well understood, it is emerging as a viable treatment method for some cases of asthma.

#### *D. Lifestyle Changes*

Aside from proper medication and treatment, there are various lifestyle adjustments that can be made by a person with asthma to reduce the frequency and severity of their attacks. Avoiding triggers can play a huge role in a patient's quality of life. For patients whose asthma is triggered by pet dander or dust mites and mold, cleanliness can have a large impact. Cleaning or removing carpeting, cleaning areas such as the kitchen and bathrooms, and frequently replacing bedding can reduce the amount of airborne irritants. Additionally, the use of air conditioners around the house can improve air quality and prevent attacks from occurring, (Asthma, 2016). For some patients, air humidity and temperature can cause asthma attacks. Using humidifiers to maintain proper humidity and wearing a face mask outside when it is cold can help prevent attacks.

Personal health also has an impact on the symptoms of asthma. Regular exercise has shown to reduce the frequency and severity of asthma attacks by increasing the strength of the respiratory system. Maintaining a healthy weight also affects the symptoms of asthma by

reducing the heart rate and therefore reducing the oxygen demand the lungs must fulfill. Additionally, patients can use breathing exercises to strengthen their lungs and reduce the amount of medication necessary to control their asthma, (Asthma, 2016).

## V. Epidemiology

### A. Worldwide prevalence

The International Study of Asthma and Allergies in Childhood examined the prevalence of asthma in over 56 countries worldwide in the 1990s, and determined that asthma mortality had increased tenfold in the previous three decades.

Over that time period asthma related hospitalizations increased by over 200% in children, and 50% in adults. It also found that asthma's prevalence grew exponentially among many European countries, (Broaddus, pg. 1170). Further research and surveying in the past two decades has shown, (figure 6.1), that rates of asthma are continuing to rise, especially in developed countries.

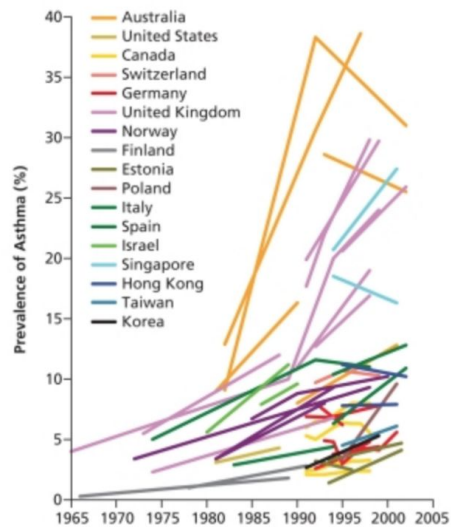


Figure 1.1, Increase in asthma prevalence [6]



## *B. Genetics*

There are genetic risk factors that affect the prevalence of asthma. Genome studies have isolated 18 genomic regions and over 100 genes that are associated with allergies and asthma, in particular, certain areas of the long arms of chromosomes 2, 5, 6, 12 and 13. Specifically, one gene, ORMDL3, has been highly correlated with asthma. Mutations in this gene were determined to be a cause for the development of childhood asthma, (Subbarao, 2009).

## *C. Prenatal risk factors*

There are several prenatal factors that can influence the development of early childhood asthma. Prenatal smoking has consistently been linked with asthma, as well as food allergies and a number of other health issues. Diet and nutrition can play a role in the development of respiratory disorders. Prenatal consumption of omega-3 fatty acids and high levels of vitamin E have both been correlated with a lower risk of development of wheeze before age 6. Additionally, prenatal use of antibiotics can have a negative impact on a child's health, as there is a high correlation between antibiotic use and early development of wheeze, (Subbarao, 2009).

## *D. Childhood risk factors*

There are many environmental and social factors that can contribute to early childhood development of asthma. In fact, many studies point to the idea that environmental factors are the

most critical in the development of asthma. There are mixed results as to the effects of breastfeeding, as some studies have seen a correlation between breastfeeding and asthma development, while others have shown the opposite, that breastfeeding is correlated with lower rates of asthma. However, a meta analysis of these studies has led to the conclusion that exclusively breastfeeding for 3 months leads to reduced rates of asthma in children between the ages of 2 and 5. Additionally, postnatal exposure to tobacco smoke is consistently associated with early childhood development of asthma, as well as the exacerbation of asthma symptoms, (Subbarao, 2009).

An emerging theory on the environmental and cultural causes of asthma is the “hygiene hypothesis”. This theory states that the rise in asthma prevalence is an unintended consequence of the success of domestic hygiene in reducing infection rates in early childhood, (Broaddus, pg. 1172). This theory was first formulated through an analysis of rates of asthma in East and West Germany during the cold war. It was found that despite higher rates of pollution and overall poorer air quality, rates of asthma were lower in East Germany. This phenomenon stemmed research into how cultural trends affect the prevalence of asthma. The findings showed that western cultural trends were highly correlated with childhood development of asthma, (Broaddus, pg. 1172).

One particular cultural trend is family size, and exposure to other children. Eastern cultures tend to have larger families, and are generally more communal. While germs and disease spread more easily in this setting, it leads to an higher tolerance of microbes and bacteria, and as such, rates of asthma are significantly lower in more “eastern” cultures. On a similar note, the tendency to over prescribe antibiotics has not only led to the propagation of new strains of

bacteria that are resistant to these antibiotics, but it has also shown a correlation to asthma prevalence. Another western cultural trend is living alongside pets. While it has been found that children exposed to farm animals have lower rates of asthma overall, children exposed to house pets, and especially cats, are more susceptible to asthma. This is largely due to the increased presence of dust mites and pet dander, (Broaddus, pg. 1172).

*E. Adult onset asthma*

Asthma in adults is typically a continuation of childhood asthma or a relapse of childhood asthma, but occasionally an adult with no history of asthma will experience symptoms known as adult onset asthma. A typical cause of adult onset asthma is a person's occupational environment. Airborne irritants that lead to airway inflammation in a normal respiratory system can lead to the development of asthma in some individuals. Occupations that have a higher rate of adult onset asthma include painters, hairdressers, domestic and commercial cleaners, healthcare professionals, and bakers, among others. Smoking tobacco or marijuana can also lead to adult onset asthma as well as more serious respiratory issues, (Subbarao, 2009).

I. Introduction

Chronic Obstructive Pulmonary Disease, (COPD), is a heterogeneous collection of conditions characterized by persistent expiratory airflow limitation, (Broaddus, pg. 1116). It can be the result of several etiologies, but the most common cigarette smoke. COPD is non-reversible, in contrast with asthma, which is a reversible air trapping disorder. COPD is typically a combination of diseases, asthma, chronic bronchitis, and emphysema, as seen in figure 2.1. Individuals in subsets 6 and 7 have partially reversible COPD. Most patients that require medical care for their disease fall into subsets 5 and 8, (Broaddus, pg 1116).

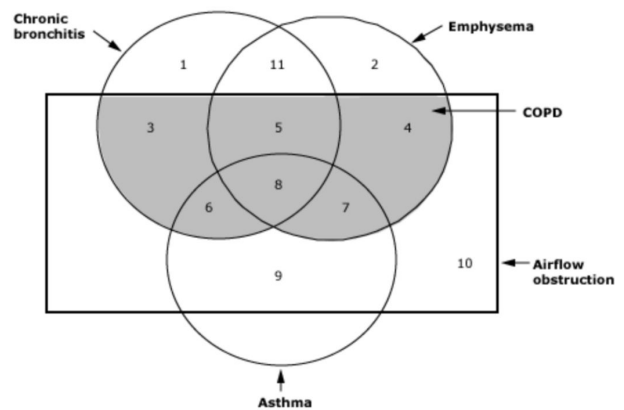


Figure 2.1, venn diagram of respiratory disorders. Shaded grey areas denote individuals with COPD [7]

Chronic Bronchitis is the presence of a productive cough for 3 months during each of two successive years. Patients with other sources of chronic cough such as mycobacterium tuberculosis, carcinoma of the lung, bronchiectasis, cystic fibrosis, and chronic congestive heart failure have been excluded from chronic bronchitis. It is characterized by a chronic cough that is unrelated to other respiratory issues, (Broaddus, pg. 1116). Emphysema is a abnormal permanent enlargement of the air spaces in the respiratory bronchioles accompanied by destruction of their walls and without obvious fibrosis. This destruction is nonuniformity in the appearance of the

acinus and its components within the alveolar walls, and reduces the alveoli ability to facilitate gas diffusion, (Broaddus, pg. 1117).

A triad of overinflation, oligemia, and bullae are the major contributing factors to the symptoms and associated diseases of COPD. Overinflation of the lungs is the phenomenon where air becomes trapped in the alveolar sacs because of obstructions in the bronchioles. Oligemia is a decrease in volume of blood plasma, and is a result of decreased amounts of salt and ions in the blood. Bullae are blister like sacs of fluids, frequently caused by burns to the epithelial tissue resulting from inhaling smoke. These bullae further obstruct the path to and from the alveoli. These three conditions cause the symptoms of COPD by obstructing the path to the alveoli and reducing the body's ability to exchange gases. Trapped air becomes more acidic as CO<sub>2</sub> builds, which reduces the chemical gradient necessary for gas exchange, and reduced blood volume reduces the solubility of gases in the blood, (Broaddus, pg. 1118).

## II. Signs and Symptoms

The most obvious signs of COPD include coughing, breathlessness, and wheezing. Typically a patient with COPD will exhibit coarse crackling during air intake. These symptoms will worsen and cause other issues as the disease progresses. There are four stages of the disease. Patients with stage 1 COPD (mild) experience coughing, slight airflow limitations, and sometimes an increase in mucus production, but generally no other symptoms. Stage 2 (moderate) patients will experience decreased airflow, breathlessness, coughing, wheezing, and sputum production. Stage 3 (severe) patients will see an increase in these symptoms, particularly

breathlessness and exhaustion, and likely will require intermittent hospitalization. Stage 4 (end stage) patients experience an increase of breathlessness and exhaustion. COPD flare ups for stage 4 patients can be potentially life threatening, and require hospitalization, (Is COPD a Progressive Disease, 2017).

Sputum production is altered in individuals with COPD. In reaction to tissue damage cause by emphysema or accumulation of bullae in the bronchioles and alveoli, the lungs will overproduce mucus. When coughed up, sputum will be purulent, which is composed of white blood cells, cellular debris, and serous fluids, and is typically yellow or green. Additionally, Hemoptysis can occur, which is blood in the sputum, and is a result of epithelial tears, most frequently from coughing fits, (Broaddus, pg. 1120)

Damage caused by emphysema reduces the body's ability to transfer gas into and out of the blood. This leads to conditions such as hypoxemia, which is an abnormally low concentration of  $O_2$  in the blood, or hypercapnia, an abnormally high concentration of  $CO_2$  in the blood. These conditions are problematic for cellular respiration as cells need  $O_2$  to process glucose. Furthermore, they need a chemical gradient in order to deposit waste  $CO_2$  into the blood, which is more difficult with already high levels of  $CO_2$ , (Broaddus, pg. 1120).

Low levels of  $O_2$  and high levels of  $CO_2$  in the blood can lead to metabolic acidosis, which is the decrease in blood pH, and is more common in late stage COPD. It is frequently the result of increased amounts of lactic acid fermentation in the cells from anaerobic respiration. The waste product, lactic acid is deposited in the blood, leading to an overall lower pH, (Metabolic Acidosis, 2017). Many patients with COPD develop pulmonary artery hypertension,

which is high blood pressure of the pulmonary artery. It is caused by reductions in capillary compliance and blockages, caused by emphysema damage, (Broaddus, pg. 1119).

COPD also leaves patients highly susceptible to other illnesses. COPD is considered to be an important predisposing condition for pneumonia. Furthermore, symptoms of pneumonia can be difficult to distinguish from acute exacerbations of COPD, which increases the risk of mortality, (Broaddus, pg. 1121). Additionally, due to hypertension, patients with COPD are at significant risk of developing cardiac disease and other heart related issues, mainly due to systemic inflammation, (Broaddus, pg. 1123).

### III. Detection and Diagnosis

#### A) *Spirometry and disease tracking*

The most typical diagnosis of COPD is conducted with spirometry, which is the measurement of the ratio of forced expiratory volume in one second ( $FEV_1$ ) over forced vital capacity (FVC). The results of this test are applied to the GOLD staging system, which is used to track the progression of the disease. Stage 1 is categorized by an  $FEV_1$  of 80% or higher while stage 2 individuals will have an  $FEV_1$  of 50-79%. Stage 3 is 30-49%, and stage 4 is less than 30%  $FEV_1$ , (Johns et al. 2014). Periodically, individuals with COPD will have spirometry tests conducted to re-assess the progress of their disease.

*B) Arterial blood gas analysis*

Arterial blood gas analysis (ABG) provide estimates of the acuteness and severity of disease exacerbation. As the disease worsens, a patient's hypoxemia worsens. During acute exacerbations, gas exchange and lung mechanisms worsen, and the blood becomes more acidic because of increased levels of CO<sub>2</sub>. ABG measures the acidity of the blood, and a pH of 7.3 or lower is considered to be a sign of acute respiratory compromise, (Chronic Obstructive Pulmonary Disease (COPD) Workup, 2017).

*C) Chest radiographs*

Chest radiographs can be used to reveal the presence of pulmonary artery hypertension in patients with emphysema. From front and lateral scans, physicians will be able to note several features, to include flattening of the diaphragm, increased retrosternal airspace, a long narrow heart shadow, rapidly tapering vascular shadows and hyperlucency of the lungs. Patients with COPD tend to show increased bronchovascular markings and cardiomegaly, (Barker, 2006).

*D) High resolution CT scans*

CT scans may be used to determine if surgical intervention is necessary, but can also be used to diagnose various forms of COPD, as well as determining causes of the symptoms of the



disease. CT scans have a greater sensitivity than standard radiographs, and as so have a higher specificity for diagnosing emphysema, (Imaging, n.d.).

*E) Other tests*

Other tests can be conducted to determine the extent of the disease, as well as many other factors. Hematocrit tests assess the ratio of red blood cells to total blood volume, and a ratio of .52 for men or .47 for women indicates that the patient should be screened for hypoxemia. Serum potassium tests measure levels of potassium in the blood, which is an indicator of metabolic rates and can be used to diagnose metabolic acidosis. Sputum evaluations are used to show a transformation from mucoid, which is typical of stable COPD, to purulent, which indicates high levels of white blood cells. Pulse oximetry is used to determine O<sub>2</sub> levels in the blood, which is indicative of the progression of the disease. Electrocardiography is used to rule out the heart as the cause of respiratory issues, as it will rule out cardiac ischemia, which can be caused by hypoxia. Additionally, two dimensional echocardiography may be used to screen for pulmonary hypertension, and right sided heart catheterization is used to confirm pulmonary hypertension and gauge the patient's response to vasodilators, (Chronic Obstructive Pulmonary Disease (COPD), 2017).

#### IV. Treatment

COPD is a progressive disease, and currently there is no cure. However, there are several treatment methods that can be used to manage the disease at its various stages. The number one therapeutic intervention is smoking cessation. There are also a series of medications and therapies available to treat this disease.

##### *A) Medications*

Current symptom-based therapies are primarily directed at reducing airway smooth muscle tone or at reducing inflammation, (Broaddus, pg. 1143). In cases where bronchospasms are present, bronchodilators can be used to improve airflow. However, even in cases that bronchospasms are not present, it is still recommended that bronchodilators are used. Patients with COPD will see modest to large improvements in airflow after use, and as such patients with COPD are always given a clinical trial of bronchodilators. Patients are typically prescribed long acting beta<sub>2</sub> agonists such as salmeterol and formoterol, which provide bronchodilation over longer periods of time, and are administered daily orally, (Broaddus, pg. 1144). A patient with COPD typically will be prescribed a rescue inhaler with fast acting beta<sub>2</sub> agonists and glucocorticoids. The fast acting agonists reopen airways, and corticosteroids reduce the inflammation, (Broaddus, pg. 1145).

*B) Pulmonary Rehabilitation*

Pulmonary rehabilitation attempts to return patients to their highest possible lung functional capacity. The benefits include increased independence and quality of life, decreased hospitalization, and improved exercise capacity. Exercise conditioning is the single most important aspect of rehabilitation. Improving cardiovascular endurance helps to maximize a patient's lung capacity at various stages of the disease. Additionally, muscle strengthening using light weights, specifically upper extremity exercises, has shown to be beneficial as it reduces the effort needed to perform day to day tasks, (Broaddus, pg. 1149).

Respiratory muscle training is controversial, but some methods have proved to be beneficial. The most reliable method is a pressure-threshold breathing device, that involves producing an inspiratory pressure of at least 30% of the patients maximum inspiratory pressure. The goal is to spend 30 minutes a day using this device. Additional exercises include pursed lip breathing, which involves standing in a bent position with arms outstretched against a wall. This exercise decreases air trapping and improves diaphragm function, but also has benefits in controlling resting dyspnea, anxiety, and panic attacks, (Broaddus, pg. 1149).

*C) Surgical intervention*

There are few surgical options to treat COPD, but the most successful is single lung transplantation. This is preferable over double lung transplantation, which requires cardiac bypass, and has a higher rate of complications. Furthermore, one donor may supply two patients

with a new lung. Lung transplant still remains one of the most difficult transplants in comparison to other solid organs such as the heart or kidneys, and has a high rate of complication and rejection. Another surgical procedure is surgery for bullous lung disease, which involves the surgical removal of giant bullae. This procedure may significantly improve a patient's lung capacity depending on size and location of the bullae, as well as capacity of non-bullous lung tissue. This procedure is not used in most cases of COPD.

## V. Epidemiology

### A) *Worldwide prevalence*

The prevalence of COPD varies from country to country in adults age 40 and older. This is because of a wide range of environmental and cultural factors. An Australian study placed COPD prevalence at 7.5% overall, but with greater rates for those aged over 75, for which the rate was 29.2%. A more recent study conducted worldwide among smokers estimated that for those age 30-69, rates of COPD were 54% for males and 24% for females, (Johns et al. 2014). In America, COPD was the third leading cause of death in 2014, affecting almost 15.7 million Americans, primarily those aged 65-74, (Chronic Obstructive Pulmonary Disease (COPD), 2017).

B) *Gender and socioeconomic status*

Most population studies have reported that men have a higher prevalence of respiratory symptoms than women, even when the studies are controlled for smokers. However, recent data suggests that female may be at an increased risk for developing COPD, with more women in the United States dying from the disease than men. Furthermore, rates of morbidity and mortality are inversely proportional to socioeconomic status, measured in income and level of education. Generally, COPD is more prevalent among “blue collar” workers than “white collar”, (Broaddus, pg. 1126)

C) *Exposure to toxic fumes and gases*

Cigarette smoking is the most important exposure risk factor for COPD. Smoking affects rates of COPD in a dose dependant manner, as seen in figure 2.2. Tobacco smoking accounts for 80% to 90% of risk of developing COPD in the United States. Other environmental factors affect the diseases prevalence. Occupational exposure to chemicals and pollutants are associated with accelerated loss of lung function. Farming or working in dusty occupations increases the risk of developing chronic bronchitis two-threefold. In the developing world, exposure to smoke generated from the burning of

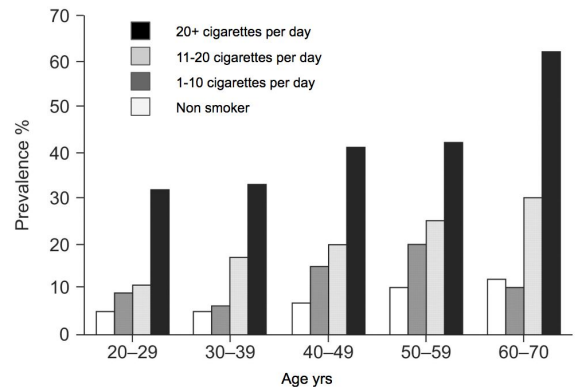


Figure 2.2, Chronic Bronchitis prevalence per dose [8]

biomass fuels are a comparable risk of developing COPD as is smoking cigarettes, (Broaddus pg. 1126-1127).

*D) Non-environmentally acquired COPD*

The “Dutch hypothesis”, is that an “asthmatic constitution”, influences the development of chronic airflow limitations. This hypothesis states - in some cases - that chronic asthma can lead to fixed airflow obstruction. The “British hypothesis” states that innate development of COPD is a result of mucus hypersecretion that causes a more rapid decline of lung function with age. Additionally, the deficiency of the homozygous alpha<sub>1</sub>-protease inhibitor is a significant risk factor for the development of COPD, (Broaddus, pg. 1126-1127). In any case, the presence of respiratory issues of any sort in early life have shown to have a great impact on later life prevalence of COPD.

*E) Perinatal and childhood effects*

Maternal smoking has shown to lead to childhood respiratory illnesses and low birth weight. Both low birth weight and childhood respiratory infections and diseases are positively correlated with the development of COPD in later life, (Broaddus, pg. 1127).

*F) early onset COPD from marijuana abuse*

Use of marijuana has been linked to symptoms of COPD and is now included as a differential diagnosis in bullous emphysema. Marijuana abuse has become a growing trend worldwide in the past decade, and while there have been few population studies as to these trends and the resulting effects on respiratory health, multiple case studies have been conducted that demonstrate the damaging effects of frequent use. On average, smoking marijuana involves a two-thirds larger puff volume, a one-third greater depth of inhalation, and a four-times longer breath holding time than that of cigarette smoking. For these reasons, it has been estimated that three to four “joints” of marijuana has an equivalent effect on the lungs as smoking an average of 24 cigarettes a day, (Golwala, 2012).

## I. Introduction

Pneumonia is an infection in the lower respiratory tract, (LRT), which entails the trachea, bronchioles and alveoli. It causes inflammation of the alveoli, and a buildup of pus and fluids in the alveolar sacs, which leads to the signs and symptoms of pneumonia. This fluid buildup can become solid, and can be fatal if untreated. Pneumonia is curable, with many treatment options for its various types. Nonetheless, pneumonia is a common cause of death worldwide, and as such requires proper treatment and early detection to prevent mortality.

The microorganisms that infect the LRT may reach the lungs by four routes, direct extension from the mediastinum or subphrenic space, hematogenous seeding from an extrapulmonary focus, inhalation of microorganisms, and aspiration of oropharyngeal contents. The latter two routes are the most common modes of infection, (Broaddus, pg. 921). Typically inhaled particles expand upon entering the trachea due to humidity, and as such do not pass through the terminal bronchioles. Only fine particles (less than 5  $\mu\text{m}$  in size) are able to enter the alveoli. Because of this only small bacteria are able to enter the alveoli and potentially cause an infection. Additionally, a penetrating bacteria must also evade the host defences. However, as is the case with aspiration pneumonia, larger bacteria may penetrate the lungs when a large particle becomes lodged in the bronchioles during the daytime, and eventually moves to the alveoli during sleep when the airway walls relax and expand, (Broaddus, pg. 921).



Whether or not a microorganism can take hold and cause an infection is a result of the three major components of lung defence, mechanical defences such as cough and mucus entrapment, humoral immune factors in respiratory secretions such as lysozyme or immunoglobulins, and cellular components of immunity such as alveolar macrophages. Complex interactions between the virulence and quantity of inhaled or aspirated microorganisms that contaminate the LRT determine whether pneumonia develops, (Broaddus, pg. 921).

## II. Signs and Symptoms

Typical symptoms of an LRT include coughing, chest pain, shortness of breath, wheezing, sore throat, and other symptoms of infection. Due to an increased amount of fluids in the alveolar sacs, the patient will cough to try to rid their lungs of the fluid. Sore throat usually develops as a result of the cough. Furthermore, the buildup of fluids combined with inflammation of the alveoli and bronchioles reduces the lungs ability to intake air and exchange gas, leading to shortness of breath. Reduced gas exchange can lead to other symptoms such as fatigue and blue lips or fingers. Chest pain is due in part to inflammation of the alveoli and bronchioles, but also is a result of inflammation of the pleura, also known as pleuritis, (Broaddus, pg. 941).

Additionally, a patient will experience symptoms of infection that are a result of the body fighting the infection. These include nausea, chills, fever, swollen lymph nodes, and abnormal sputum production. Swollen lymph nodes are an indication that the nodes are filtering lymph

fluid, and producing large amounts of lymphocytes in order to kill microorganisms. As dead white blood cells and microorganisms accumulate, sputum will become purulent.

### III. Detection and Diagnosis

When an LRT is suspected, a laboratory evaluation is conducted to determine factors such as blood cell counts, serum glucose and electrolyte measurements, and pulse oximetry or arterial blood gas assays, (Broaddus, pg. 926). Additionally, a radiographic evaluation is done to establish the presence of pneumonia. Finding the etiology of the infection is key in determining the treatment method. There are several microbiologic evaluation tools used for this task.

Microscopic examination of sputum is the easiest and most available method to determine the etiology of a case of pneumonia. Approximately 40% of pneumonia cases can be positively diagnosed using this method. Typically fluorescent antibodies are used to evaluate the sputum sample and determine the type of microorganism that is causing the infection, (Broaddus, pg. 928). Blood and pleural cultures can also be used to definitively determine the etiology, although blood cultures are only able to pinpoint the bacterial source in roughly 20% of cases, (Broaddus, pg. 929). Often the most practical means to establish a microbiological diagnosis is serologic techniques. This is typically used when the pathogen cannot be readily cultured as is the case in *M. pneumoniae*, *C. pneumoniae*, and *L. pneumophila*, (Broaddus, pg. 929).

Because of issues with contamination of expired sputum samples, invasive diagnostic techniques may also be used to determine the etiology of pneumonia. Bronchoscopic samples can be taken during a bronchoscopic procedure and then analyzed with the same techniques used

in sputum evaluations. Transthoracic lung aspiration obtains specimens suitable for microbiological and cytologic examinations directly from lung parenchyma, but it tends to be more successful in diagnosing malignant pulmonary lesions than infectious diseases. Lung biopsy is another option, but it is rarely used because less invasive methods are usually able to diagnose the etiology of pneumonia, (Broaddus, pg. 931).

#### IV. Treatment

Because pneumonia is a bacterial infection of the lungs, once the strain is determined, the appropriate antibiotic must be administered. So long as the antibiotic is administered early enough and no complications occur, the patient will recover. Antibiotics are typically a fungi such as penicillin, but other lipid forms and antimicrobial peptides are available. Antibiotics selectively target specific characteristics of different bacteria, such as the presence of a cell wall, and kill the bacterial cells. Different etiologies of pneumonia require different antibiotic treatments. Table 3.1 summarizes the agents used to target the many etiologies of pneumonia.

**Table 3.1** agents for specific therapy of selected respiratory pathogens,  
(Broaddus, pg. 937)

Type of Infection	Preferred Agent(s)	Alternative Agent(s)
<b>Community-Acquired Pneumonia</b>		
<i>Streptococcus pneumoniae</i> PCN-susceptible (MIC < 2.0 µg/ml) PCN-resistant (MIC ≥ 2.0 µg/ml)	Penicillin G, amoxicillin	Cephalosporin, macrolide,* clindamycin, fluoroquinolone, <sup>†</sup> doxycycline, telithromycin Telithromycin
<i>Mycoplasma</i> <i>Chlamydia pneumoniae</i> <i>Legionella</i>	Agents identified using in vitro susceptibility tests, including cefotaxime, ceftriaxone, vancomycin, and fluoroquinolone <sup>†</sup> Doxycycline, macrolide Doxycycline, macrolide Azithromycin, fluoroquinolone (including ciprofloxacin), <sup>†</sup> erythromycin (± rifampin)	Fluoroquinolone <sup>†</sup> , telithromycin Fluoroquinolone <sup>†</sup> , telithromycin Doxycycline ± rifampin
<i>Haemophilus influenzae</i>	Second- or third-generation cephalosporin, doxycycline, beta-lactam/beta-lactamase inhibitor, azithromycin	Fluoroquinolone, <sup>†</sup> clarithromycin, trimethoprim/sulfamethoxazole, telithromycin
<i>Moraxella catarrhalis</i>	Second- or third-generation cephalosporin, trimethoprim/sulfamethoxazole, macrolide doxycycline, beta-lactam/beta-lactamase inhibitor	Fluoroquinolone <sup>†</sup>
<i>Neisseria meningitidis</i>	Penicillin	Ceftriaxone, cefotaxime, cefuroxime, chloramphenicol, fluoroquinolone <sup>†</sup>
Streptococci (other than <i>S. pneumoniae</i> ) Anaerobes	Penicillin, first-generation cephalosporin Clindamycin, beta-lactam/beta-lactamase inhibitor, beta-lactam plus metronidazole	Clindamycin (susceptibility should be confirmed), vancomycin Carbapenem
<i>Staphylococcus aureus</i> Methicillin-susceptible Methicillin-resistant	Oxacillin, nafcillin, cefazolin; all ± rifampin or gentamicin <sup>‡</sup> Vancomycin ± rifampin or gentamicin <sup>‡</sup>	Cefuroxime, cefotaxime, ceftriaxone, fluoroquinolones, <sup>†</sup> clindamycin, vancomycin Linezolid, quinupristin-dalfopristin; trimethoprim/sulfamethoxazole, fluoroquinolones, <sup>†</sup> and tetracyclines may also show activity (in vitro testing required)
<i>Klebsiella pneumoniae</i> and other Enterobacteriaceae (excluding <i>Enterobacter</i> spp.)	Third-generation cephalosporin or cefepime (all ± aminoglycoside), carbapenem	Aztreonam, beta-lactam/beta-lactamase inhibitor, <sup>§</sup> fluoroquinolone <sup>†</sup>
<b>Hospital-Acquired Infections</b>		
<i>Enterobacter</i> spp.	Carbapenem, beta-lactam/beta-lactamase inhibitor, <sup>§</sup> cefepime, fluoroquinolone; all + aminoglycoside in seriously ill patients	Third-generation cephalosporin + aminoglycoside
<i>P. aeruginosa</i>	Anti-pseudomonal beta-lactam <sup>†</sup> + aminoglycoside, carbapenem + aminoglycoside	Ciprofloxacin + aminoglycoside, ciprofloxacin + antipseudomonal beta-lactam <sup>†</sup>
<i>Acinetobacter</i>	Aminoglycoside + piperacillin or a carbapenem	Doxycycline, ampicillin-sulbactam, colistin
<b>Less Common Pathogens</b>		
<i>Nocardia</i>	Trimethoprim/sulfamethoxazole	Imipenem ± amikacin, doxycycline or minocycline, sulfonamide ± minocycline or amikacin
<i>Coxiella burnetii</i> (Q fever) <i>Chlamydia psittaci</i> (psittacosis) <i>Eikenella corrodens</i>	Doxycycline Doxycycline Penicillin	Fluoroquinolone Erythromycin, chloramphenicol Tetracyclines, beta-lactam/beta-lactamase inhibitor, second- and third-generation cephalosporins, fluoroquinolones

## V. Epidemiology

### A) *Worldwide prevalence*

Globally, pneumonia is a serious health concern. Despite advances in antimicrobial therapies, diagnosis and prevention, pneumonia remains the leading cause of death from infectious disease worldwide, (Cilloniz et. al, 2016). In 2014, the eighth cause of mortality in the United States was Influenza and pneumonia combined, and it is estimated that there are 4 million cases of community acquired pneumonia, (CAP), annually in the United States. The mortality of CAP in hospitalized patients is 14%, but this number jumps to 20-50% in patients requiring intensive care, (Broaddus, pg. 920). Pneumonia is also the single largest infectious cause of death in children worldwide; in 2015, 920,136 children under the age of 5 perished from the disease, which accounts for 15% of childhood mortality, (Cilloniz et. al, 2016).

The most common cause of CAP is streptococcus pneumoniae, (pneumococcus). Pneumococcus was recognized by the World Health Organization in 2014 as one of the 9 bacteria of international concern. However a wide range of pathogens are responsible for nosocomial pneumonia, (Cilloniz et. al, 2016).

### B) *Community acquired pneumonia*

Age, social habits, comorbidities, geographic setting, time of year, recent travel, and occupational or other unusual exposures change the risk of different respiratory tract infections,

(Broaddus, pg. 926). Table 3.2 summarizes the prevalence of different forms of pneumonia based on underlying disease or setting.

**Table 3.2** Organisms prevalent in bacterial pneumonia according to disease or setting, (Broaddus, pg. 926).

<b>Alcoholism</b> Streptococcus pneumoniae, Haemophilus influenzae, Anaerobes, Klebsiella pneumoniae
<b>Risk of Aspiration</b> Anaerobes, Staphylococcus aureus, Gram-negative bacilli
<b>Chronic Obstructive Pulmonary Disease</b> S. pneumoniae, Moraxella catarrhalis, H. influenzae
<b>Intravenous Drug Use</b> S. aureus
<b>Neutropenia</b> Pseudomonas aeruginosa, Enteric gram-negative bacilli, S. aureus
<b>Cell-Mediated Immunodeficiency</b> Legionella, Nocardia
<b>Human Immunodeficiency Virus (HIV)</b> S. pneumoniae, H. influenzae, S. aureus, Rhodococcus equi
<b>Cystic Fibrosis</b> P. aeruginosa, S. aureus, Burkholderia cepacia
<b>Airway Obstruction</b> S. pneumoniae, H. influenzae, S. aureus, Anaerobes
<b>Pulmonary Alveolar Proteinosis</b> Nocardia

As mentioned in previous chapters, existing respiratory disorders frequently lead to further respiratory infections and diseases. When the respiratory system is weakened by one disease and another associated disease takes hold and causes mortality, it is referred to as a

comorbidity. Due to the severity of pneumonia, and the prevalence of the disease, pneumonia is a common comorbidity of several respiratory and non-respiratory disease, to include asthma, COPD, cystic fibrosis, HIV, diabetes, and several others, (Segal et. al, 2018).

Table 3.2 displays this phenomenon and the associated bacteria that a patient will be more likely to contract. Figure 3.1 displays the overall prevalence of each strain of bacteria. Pneumococcus is widely accepted as the most common causative microorganism in Community Acquired Pneumonia, (CAP), (Cilloniz et. al, 2016).

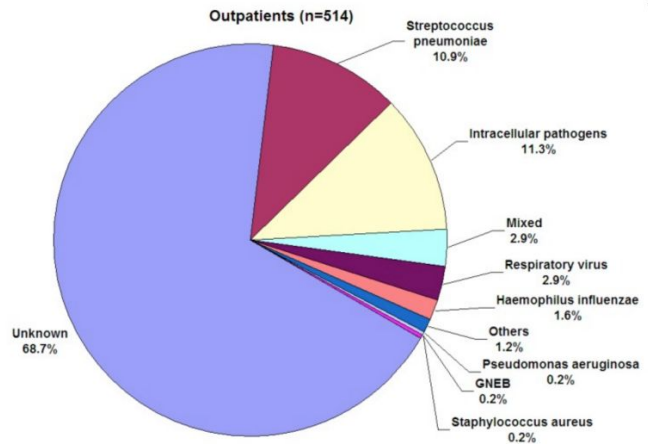


Figure 3.1, prevalence rates of CAP [9]

In CAP, roughly 6% of the cases involve Multidrug-Resistant pathogens, (MDR). Community-Acquired Methicillin-Resistant S. Aureus, (CA-MRSA), is the most common MDR and has become a growing health concern due to its resistance to current treatments. Due to this, early detection and diagnosis is key in reducing mortality rates of this pathogen, (Cilloniz et. al, 2016).

C) *Nosocomial pneumonia*

Nosocomial pneumonia is pneumonia not contracted through interactions with people. The most common type of this pneumonia, Hospital Acquired Pneumonia, (HAP), is defined as pneumonia not incubating at the time of hospital admission and occurring 48 h or more after

admission, (Cilloniz et. al, 2016). Another type of nosocomial pneumonia is Ventilator-Associated Pneumonia, (VAP), which is defined as a pneumonia occurring >48 h after endotracheal intubation, (Cilloniz et. al, 2016). HAP is the second most frequent nosocomial infection, but is considered to be the

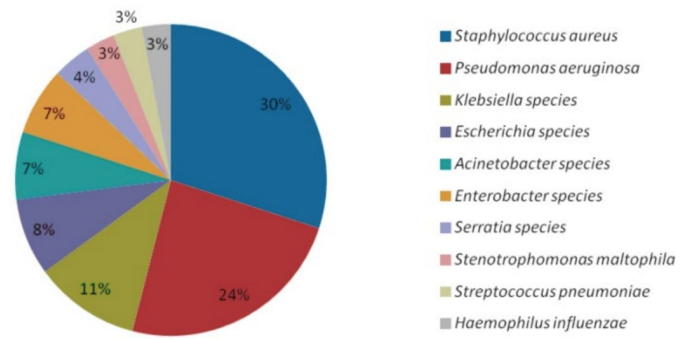


Figure 3.2, Prevalence rates of bacteria strains in nosocomial pneumonia [9]

leading cause of death in nosocomial infections. VAP accounts for 70-80% of HAP cases acquired in intensive care units, (Cilloniz et. al, 2016). As was the case with instances of CAP, the origin of nosocomial pneumonia can be traced back to one of many bacteria strains, as seen in Figure 3.2.



## *Chapter 4 emerging concerns in respiratory health*

### I. Introduction

This chapter examines emerging concerns in respiratory health in America as a result of changes in public opinion and popular culture. Additionally this chapter examines ever present respiratory health concerns associated with weapons of mass destruction.

### II. Cannabis COPD and Lung Cancer

Cases of lung injury due to smoking marijuana have been a growing trend in America. The legal use of cannabis for medical purposes began in 1996 with California's approval of proposition 215. Since then the majority of states in the U.S. have made the medical use of cannabis legal for the treatment of several diseases, for example Cancer, HIV, Glaucoma, seizures, migraines, and arthritis. In 2012, marijuana became legal for recreational use in both Colorado and Washington, and has since become legal in a hand full of other states. While there are few population studies on the effects to respiratory health, many case studies have emerged of individuals with a history of frequent cannabis use with severe cases of lung injury.

Smoking marijuana has been linked to rates of lung cancer. One population study determined that smoking one joint per day for a year, (1 joint-yr), led to a 8% increase in risk of developing lung cancer. This rate is comparable to that of smoking one pack of cigarettes (20

cigarettes) for one year, at rate of 7%. The risk of developing lung cancer has a linear association to joint-yrs, with a patient who smokes 3-4 joints per day for a year to have a 24-32% risk of developing lung cancer, (Tanoue, 2010).

One study examined a patient with severe bullous emphysema. The patient in this case study had a history of a few years of marijuana abuse, which entailed 3-4 joints of marijuana per day for 8 years. The severity of the patient's bullous emphysema was determined to be the cause of the patient's marijuana abuse, as all other potential causes were eliminated. From this study, it was estimated that 3-4 joints per day gives as many symptoms as smoking 24 cigarettes daily. The reason that cannabis is more potent in terms of lung health is that on average, smoking marijuana involves a two thirds larger puff volume, a one third greater depth of inhalation, and a four times longer breath holding time than that of cigarette smoking, (Golwala, 2012).

From this estimation, it can be expected that individuals that smoke cannabis at a rate of 3-4 joints daily will have the same risk of developing other respiratory disorders as that of an individual who smokes over 20 cigarettes per day. For example, a young individual who smokes cannabis at these rates has a 30% risk of developing COPD from ages 20-29, and a 60% risk of developing COPD between ages 60-70. The phenomenons of early onset COPD as a result of smoking marijuana and marijuana induced lung cancer are under-studied and will likely become a significant public health concern in the timeframe of 20-30 years after the legalization of recreational marijuana.

### III. Electronic Cigarette Associated Illness

Popcorn lung, formally known as hypersensitivity pneumonitis, is an inflammatory syndrome of the lung caused by repetitive inhalation of antigenic agents in a susceptible host. There are three antigens that cause this allergic reaction, microbes, animal proteins, and low molecular weight chemicals, (Hypersensitivity pneumonitis,

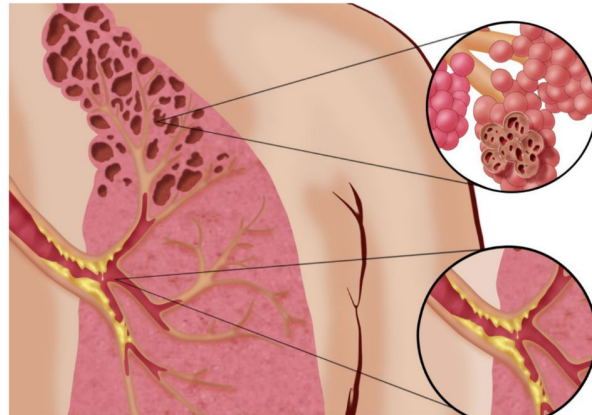


Figure 4.1, Popcorn lung [10]

2017). Popcorn Lung was first recognized in popcorn factories, where workers would contract symptoms similar to COPD. These symptoms were due to scarring of the alveolar and bronchiole walls which causes obstruction of the airways. It was eventually discovered that this condition was caused by airborne diacetyl, the chemical used to create a buttery flavor. Subsequently, popcorn companies removed diacetyl from their products. Hypersensitivity pneumonitis is once again becoming prevalent however, due to the popularity of e-cigarettes, also known as vaping.

Vaping is widely considered to be a “safe” alternative to smoking, as it delivers nicotine to the user via water vapor. Vaping does not present the negative health effects associated with smoking or the use of chewing tobacco, but there are still negative health implications associated with vaping. Aside from nicotine poisoning, which accounts for about 44% of vaping related injuries, there are several systemic injuries that can be acquired from e-cigarette use.

Cardiovascular and gastrointestinal effects are among these, but the most prevalent are respiratory illnesses, (Hua, 2016). Popcorn lung is an associated illness of vaping, as flavor mixes have diacetyl, which causes inflammation and scarring of the airway walls.

Other issues with vaping include the efficiency of the vaporizing system. Several case reports have led to the discovery that poor efficiency of vaporizing systems can lead to overheating of the vape mix which can have negative respiratory impacts. One such impact is the overheating of propylene glycol, an agent used to extract cannabis oil for vape mix. While propylene glycol is classified as safe for consumption by the FDA, it has the potential to transform into carbonyls such as formaldehyde, which is carcinogenic and a respiratory irritant, (He et. al, 2017).

#### IV. Inhaled Insulin and Asthma

Diabetes is a widespread disease that effects the body's ability to produce insulin, and leads to abnormal metabolism of carbohydrates and elevated blood glucose levels. It can be caused by a genetic deficiency that impairs the body's ability to produce insulin, but the disease can also develop over time as a result of the body resisting insulin, or not being able to produce enough insulin. Current treatments include diet and exercise, as well as insulin therapy. One form is inhaled insulin, which delivers a powdered form of insulin directly to the blood via the lungs. This method acts faster than other subcutaneous methods, and is minimally invasive. There are however slight concerns to respiratory health associated with inhaled insulin.

A person with asthma in addition to diabetes is at risk of exacerbating their asthma by using inhaled insulin. Furthermore, during an asthma exacerbation, a person with asthma will not be able to pass as much insulin to their blood via inhalation, and as a result will need to inhale more insulin, (Mastrandrea, 2006).

## V. WMDs

Chemical warfare or weapons of mass destruction pose an ever-present risk for respiratory illness. Major conflicts such as World War I left many with illnesses associated with chemical warfare. Chemical warfare typically is airborne and delivers a chemical agent to the

body, the most common being vesicants (blister or mustard agents), nerve agents, and blood agents.

Vesicants pose the greatest risk to the respiratory system. Vesicants, such as mustard gas, cause severe burns to the skin, eyes, and respiratory tract as seen in Figure 4.2. They result in large yellow blisters that cover affected areas, and can lead to



Figure 4.2, Mustard gas burns, [11]

immediate formation of bullae within the lung tissue, which will prevent the person from passing air. Even with proper treatment readily available, contact with mustard gas frequently leads to death. Survivors of mustard gas inhalation are at an increased risk of developing lung cancer and chronic bronchitis. Immediate decontamination and treatment are essential to minimize the effects, (Gosden et. al, 2006).

Chemical warfare was banned in 1925 by the Chemical Weapons Convention, and made it illegal to use or possess chemical weapons. Nonetheless, chemical warfare and the associated illnesses have still been an issue. One such occasion was the Iraq-Iran war of 1980-1988, which saw the use of mustard gas among other chemical weapons. Out of the 34,000 Iranians affected by mustard exposure, the most prevalent health issue after 13-20 years were respiratory issues in the form of lesions, at 42.5%, (Khateri, 2003). Chemical warfare remains an important public health concern, and requires a state of constant readiness to treat victims of these attacks, respiratory and otherwise.

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