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The inferior turbinate: an autonomic organ

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THE INFERIOR TURBINATE: AN AUTONOMIC ORGAN

by

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DEDICATION

I would like to dedicate this work to my wife, Emily, and my son, Clint, for their constant love and support; and to my parents, Brandon and Megan, for always believing in me.
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I would like to express my appreciation to my readers, Dr. Platt and Dr. Brook, for their guidance and insight while writing this thesis. Despite immensely full plates, they provided me with much more time and assistance than I hoped for. In addition, their quick responses and mentorship were especially appreciated. Thank you.

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THE INFERIOR TURBINATE: AN AUTONOMIC ORGAN

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ABSTRACT

The inferior turbinates are important anatomical nasal structures that provide warmth, humidification, and filtration of the inspired air to provide optimal conditioning for lung function. Besides these well-established basic functions, the turbinates are also important in immune function as the interface between the airway and the environment. Proper functioning of the inferior turbinates relies on an intact autonomic system, which maintains homeostasis within the nasal cavity. The autonomic nervous system innervates the submucosal glands and the vasculature within the inferior turbinate, resulting in control of major turbinate functions: nasal secretions, nasal patency, and amount of warmth and humidification provided. This thesis will summarize the normal and abnormal autonomic processes that contribute to the inferior turbinate as an autonomic organ.
TABLE OF CONTENTS

TITLE PAGE ....................................................................................................................... i
COPYRIGHT PAGE .......................................................................................................... ii
READER’S APPROVAL PAGE ...................................................................................... iii
DEDICATION ................................................................................................................... iv
ACKNOWLEDGMENTS ................................................................................................. v
ABSTRACT ....................................................................................................................... vi
TABLE OF CONTENTS .................................................................................................. vii
LIST OF TABLES .............................................................................................................. x
LIST OF FIGURES ......................................................................................................... xi
LIST OF ABBREVIATIONS ........................................................................................... xii
INTRODUCTION .............................................................................................................. 1
The Nasal Cavity ............................................................................................................. 1
Respiration ....................................................................................................................... 4
The Autonomic System ................................................................................................. 6
Specific Aims ................................................................................................................ 10
ANATOMY OF THE INFERIOR TURBINATE ............................................................ 11
Histology ....................................................................................................................... 12
Embryology .................................................................................................................. 14
### LIST OF TABLES

<table>
<thead>
<tr>
<th>Table</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Medications That Affect Turbinate Function</td>
<td>46</td>
</tr>
</tbody>
</table>
# LIST OF FIGURES

<table>
<thead>
<tr>
<th>Figure</th>
<th>Title</th>
<th>Page</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Nasal Cavity</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>Turbinates</td>
<td>4</td>
</tr>
<tr>
<td>3</td>
<td>Pressure Changes in the Lung</td>
<td>5</td>
</tr>
<tr>
<td>4</td>
<td>Human Airways</td>
<td>6</td>
</tr>
<tr>
<td>5</td>
<td>Nervous System Organization</td>
<td>7</td>
</tr>
<tr>
<td>6</td>
<td>Inferior Turbinate with Nasal Lacrimal Duct</td>
<td>12</td>
</tr>
<tr>
<td>7</td>
<td>Mucosal Epithelial Layer</td>
<td>13</td>
</tr>
<tr>
<td>8</td>
<td>Submucosal Layer</td>
<td>14</td>
</tr>
<tr>
<td>9</td>
<td>Arteries of the Inferior Turbinate</td>
<td>18</td>
</tr>
<tr>
<td>10</td>
<td>Stages of Turbinate Hypertrophy</td>
<td>37</td>
</tr>
<tr>
<td>11</td>
<td>Concha Bullosa</td>
<td>38</td>
</tr>
<tr>
<td>Abbreviation</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>--------------</td>
<td>-------------------</td>
<td></td>
</tr>
<tr>
<td>$\alpha$</td>
<td>Alpha</td>
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<td>$\beta$</td>
<td>Beta</td>
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<td>Cm</td>
<td>Centimeter</td>
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<tr>
<td>IgA</td>
<td>Immunoglobulin A</td>
<td></td>
</tr>
<tr>
<td>Kg</td>
<td>Kilogram</td>
<td></td>
</tr>
<tr>
<td>$\mu$m</td>
<td>Micrometer</td>
<td></td>
</tr>
<tr>
<td>Mg</td>
<td>Milligram</td>
<td></td>
</tr>
<tr>
<td>H$_2$O</td>
<td>Water</td>
<td></td>
</tr>
</tbody>
</table>
INTRODUCTION

In the first part of this thesis, the anatomy of the inferior turbinate will be described, including its histology, embryology, blood supply, innervation, and autonomic receptors. Next, normal physiological function of the inferior turbinate under autonomic control will be explained, including nasal patency and the nasal cycle, airway resistance, secretion, and immunity. Environmental changes that occur due to temperature, humidity, exercise, sleep, taste, and the crutch phenomenon will also be detailed. After this, turbinate pathology will be reviewed, including structural abnormalities, infectious disease, allergic rhinitis, sleep apnea, empty nose syndrome, and local drug impacts as well as side effects from other autonomic medicines. Finally, methods of reduction will be described, including medical and surgical.

In the following introduction, background information regarding the basic anatomy and physiology of the nasal cavity will be explored, including its combined role with the lungs in respiration. Background information detailing the autonomic nervous system, including its anatomical origins and physiological functions in the human body, will also be examined.

The Nasal Cavity

The nose is an organ on the anterior section of the head that includes both an external portion and an internal portion. Externally, the nose is pyramidal in shape and is supported by bone and cartilage. The soft tissue is made up of skin, fibroadipose tissue,
and muscles that are mostly located around the nostrils and are controlled by the facial
nerve. Internally, the nose consists of two nasal cavities on both sides of the dividing
nasal septum as well as paranasal sinuses. The nasal cavities (Figure 1) are the proximal
portion of the respiratory passages. They extend from the base of the skull to the superior
roof of the mouth and continue from the face through the nostrils (anterior nares) to the
opening of the superior part of the pharynx (throat), which is known as the nasopharynx.
These cavities are lined with nasal mucosa, which is ciliated. The roof of the cavities,
known as the olfactory cleft, is marked by a horizontal bone called the cribiform plate of
the ethmoid bone. The cribiform plate is perforated with small holes that allow nerve
endings to directly contact the outer surface mucosal membrane. This allows the sense of
smell to function. The floor of the cavities sits on the hard palate above the mouth. The
medial wall, known as the septum, separates the two cavities and is frequently deviated in
adults, possibly because of ossification of the cartilaginous septum that occurs from the
first year of life through the mid-thirties (Gizurarson 2012).
Figure 1. Nasal Cavity. A sagittal section of the nasal cavity demonstrating its lateral wall.

The lateral wall of the nasal cavities consists of superior, middle, and inferior folds known as turbinates or concha. These three folds (and occasionally a fourth, supreme conchae) produce three small passages within their folds called superior, middle and inferior meatuses (Figure 2). The purpose of these turbinates is to increase resistance to the airflow, thereby producing close contact between inspired air and the mucosal surface. The folded structure also greatly expands the surface area of the nasal cavity (Gizurarson 2012).
Figure 2. Turbinates. A horizontal section through the main nasal passage demonstrating the turbinates.

Respiration

The main goal of respiration, or breathing, is to exchanges gasses; oxygen from the atmosphere into the blood and carbon dioxide from the blood into the atmosphere.

Respiration is driven by pressure changes in the lungs and thoracic cavity compared with the atmosphere (Figure 3).
Figure 3. Pressure Changes in the Lung. Air follows the pressure gradients created by inspiratory and expiratory muscles. Pressures, taken from (West 2008), are measured in cm H2O. A) Before inspiration, the pressures in the atmosphere and in the alveoli within the lungs are equal, and breathing momentarily pauses. B) Inspiration begins when the diaphragm muscle below the lungs contracts and moves inferiorly while external intercostal muscles in the chest wall contract to move the ribs superiorly and anteriorly, creating more space in the thoracic cavity for the lungs to expand. The expansion of the lungs decreases the pressure in the alveoli relative to the atmospheric pressure and air enters the lungs. C) Inspiration ends when the alveolar pressure equals the atmospheric pressure again. D) The diaphragm muscle then relaxes back into the thoracic cavity, increasing the relative pressure on the alveoli, forcing air back down the new concentration gradient, this time from the lungs to the nose and mouth until the pressures equalize. The cycle repeats itself.

Air travels down its concentration gradient from the nose and mouth into the pharynx, larynx, trachea, and lungs (Figure 4). Oxygen in the air is taken up by hemoglobin in the blood through capillaries in the alveoli while carbon dioxide is released and exhaled through a similar mechanism. Through this, the body gets needed oxygen to its tissues while ridding itself of unwanted carbon dioxide (Garcia-Diaz 2016).
The Autonomic System

The human nervous system is organized into two divisions (Figure 5), the central nervous system and the peripheral nervous system. The central nervous system includes the brain and spinal cord. The peripheral nervous system includes the somatic division and the visceral or autonomic division. The somatic nervous system consists of nerves that carry sensations from the periphery (sensory neurons) back to the central nervous system as well as nerves from that central nervous system that innervate voluntary muscles (motor neurons). The autonomic or visceral nervous system also has sensory and motor neurons, but is more involuntary. The sensory nerves monitor changes in the internal organs, while the motor nerves innervate involuntary smooth and cardiac muscle
as well as glands. The autonomic motor division is subdivided into sympathetic and parasympathetic sections, which tend to act reciprocally to each other (Drake, Vogl, and Mitchell 2012).

Figure 5. Nervous System Organization. The nervous system contains two main divisions, the central and peripheral nervous systems. Each division has subsets, as shown here.

Anatomically, the sympathetic nervous system consists of preganglionic neurons or fibers, ganglions, and postganglionic neurons. Preganglionic fibers exit the spinal cord at the level at which their cell bodies are located, between T1 and L2. Most of the ganglia lie close to the spinal cord and form the sympathetic trunk (one on each side of the spinal cord). Once in the trunk, preganglionic fibers travel upward or downward for several segments before forming synapses with many postganglionic neurons. The sympathetic system innervates structures in peripheral regions of the body as well as visceral organs
Sympathetic effects are generally referred to as a “fight or flight” response, so called for the need to mobilize energy, and the body in general, rapidly. Effects include an increase in heart rate and contraction, glycogenolysis, lipolysis, bronchial dilation, sweating, and skeletal muscle blood flow. There is a general decrease in gastrointestinal motility (“Autonomic Nervous System” 2016).

The parasympathetic nervous system follows the same anatomical pattern of preganglionic neurons, ganglions, and postganglionic neurons, but differs in axon length. Preganglionic neurons have much longer axons because parasympathetic ganglia lie close to or are actually embedded in visceral target organs. Their preganglionic fibers also have a different exit location, leaving the spinal cord between C1 to C8 and L3 to S5, basically on either side of the sympathetic nerves. The parasympathetic system innervates the visceral organs only (Drake, Vogl, and Mitchell 2012). Parasympathetic effects are referred to as a “rest or digest” response because this state occurs at times when the body is conserving and storing energy. Effects include a decrease in heart rate, heart contractility, and blood flow to skeletal muscles. There is an increase in insulin secretion and blood flow to the gastrointestinal tract (“Autonomic Nervous System” 2016).

The nervous system relays information between the brain and the body thru chemical messengers called neurotransmitters that travel along the neurons. The autonomic nervous system mainly relies on two neurotransmitters, acetylcholine and norepinephrine. Acetylcholine is used in preganglionic neurons of both the sympathetic and parasympathetic divisions as well as the postganglionic neurons of the parasympathetic
division. Norepinephrine is used in postganglionic neurons of the sympathetic division. Neurotransmitter receptors that recognize norepinephrine or epinephrine are termed adrenergic, while those that recognize acetylcholine are termed cholinergic. Cholinergic receptors can be further classified as nicotinic or muscarinic (“Neurotransmitters” 2016).

In the following thesis, the inferior turbinate of the nasal cavity will be explored and its autonomic characteristics will be exhibited.
Specific Aims

Specific aims of the following thesis include:

1. Demonstrate autonomic properties that contribute to the function of the inferior turbinates, including both parasympathetic and sympathetic effects.

2. Comprehensive review of the literature to characterize the anatomy, physiology, pathology, and methods of reduction of the inferior turbinates, as related to the autonomic nervous system.
ANATOMY OF THE INFERIOR TURBINATE

Those who study anatomy are familiar with the phrase “form follows function.” The inferior turbinate is no different; its structural form is intricately linked to its physiological function. Both the inferior turbinate and the inferior meatus are the largest of the group and reach along the entire length of the lateral nasal wall. On the superior recess of the inferior meatus and lateral to the body of the inferior turbinate (Figure 6), there is an opening, known as Hassner’s valve, for the nasolacrimal duct that allows tears from the eye to exit through the nasal cavity (Gizurarson 2012). The inferior turbinate is made up of a bony frame underneath soft tissue, specifically respiratory epithelium. The bone itself is cancellous, consisting of interwoven trabeculae that accommodates the major arterial supply of the turbinate (Sahin-Yilmaz and Naclerio 2011). The inferior turbinate is also the only turbinate that develops as a separate bone; the middle and superior turbinates are part of the ethmoid bone (Măru, Rusu, and Sândulescu 2015).
Figure 6. Inferior Turbinate with Nasolacrimal Duct. Drawing of the anterior nasal cavity, including the inferior turbinates surrounding the inferior meatus and the nasolacrimal ducts that feed into the inferior meatus.

The following sections will detail the histology, embryology (including growth and development), innervation, blood supply, and autonomic receptors of the inferior turbinates.

**Histology**

The lining of the nose has a mucosal epithelial layer on top of a submucosal layer. The mucosa consists of a protective pseudostratified columnar (respiratory) epithelium (Figure 7). Within this epithelium are mostly ciliated (and some non-ciliated) columnar cells, goblet cells, and basal cells. The cilia have a length of about 5 μm and protrude out into the nasal cavity, where they are able to mechanically move mucous particles. The goblet cells produce secretions that add to the mucous film that covers the epithelium.
Basal cells can differentiate if needed (Sahin-Yilmaz and Naclerio 2011). Mast cells, eosinophils, and lymphocytes from the immune system also reside in the mucosa (Jafek 1983). The folded structure of the inferior turbinates can increase the mucosal surface area of the nasal cavity up to 200 cm² (Joseph D Brain et al. 1977).

**Figure 7. Mucosal Epithelial Layer.** A drawing of respiratory epithelium showing ciliated columnar cells, goblet cells, and basal cells.

Immediately following the basement membrane of the epithelial mucosal layer is the submucosa (**Figure 8**). This layer contains glands, nerves, and blood vessels. The three most common types of glands in the submucosa, anterior serous glands, seromucous glands, and Bowman glands, produce the majority of the nasal secretions. Anterior serous glands are generally found close to the nasal vestibule (by the nostril) and assist in moisturizing the mucosa. Seromucous glands are found throughout the cavity but are most commonly located in the anterior section. They secrete either a serous or a mucous
fluid. Bowman glands are located in the olfactory region and aid in the sense of smell. Inflammatory mediators are also found in the submucosa, such as histamine, bradykinin, prostaglandins, and cytokines (Sahin-Yilmaz and Naclerio 2011).

**Figure 8. Submucosal Layer.** A drawing of the exterior layer of the inferior turbinate, featuring respiratory epithelium and a large submucosa with various glands and vasculature.

**Embryology**

The major development of the face occurs between the 4th and 8th weeks of gestation. The development includes contributions from the head ectoderm, which creates the face, oral cavity, and mucosal lining, and the neural crest mesenchyme, which assists in the formation of the initial cartilaginous framework that later ossifies into bone of the inferior turbinate (Platt, Devaiah, and Marple 2014). The neural crest mesenchyme is derived
from the neural crest and prechordal plate. The developing frontonasal area has mesenchyme from two origins of neural crest cells, the midbrain neural crest cells, which result in the lateral nasal process that includes the inferior turbinate, and the forebrain neural crest cells, which form the medial nasal processes (Som and Naidich 2013).

The inferior turbinate arises from two origins, the maxilla and the lateral cartilaginous capsule. At 8 weeks, three soft tissue preturbinates can be identified within the nasal cavity, which is surrounded by a cartilaginous nasal capsule. By week 10, this capsule develops into two cartilaginous plates that invade the soft tissue of the inferior and middle turbinate (Bingham et al. 1991). By week 14, the maxilla expands and forms the lateral wall of the inferior meatus (Som and Naidich 2013). By 16 weeks, the inferior turbinates, as well as the middle and superior, are well shaped. By 18 weeks, inferior turbinate ossification of its cartilaginous precursor occurs. Development of the lateral nasal wall is generally complete by 24 weeks (Bingham et al. 1991).

The maturation of the mucosal and submucosal surfaces follows a similar timeframe. Ciliated epithelium appears at week 9, as does vascularization. The glandular acini and the goblet cells start to develop around the 11th week. Mucosal and submucosal development continues and differentiation is also completed around the 24th week (Watelet and Van Cauwenberge 1999).
Innervation

Nerves in the nasal cavity are considerably involved with the local regulation of airflow, blood flow, secretion from glands, and the sense of smell. Accordingly, the nasal cavity contains a complex neuronal system that includes sensory, parasympathetic, and sympathetic nerves (Sarin et al. 2006). This thesis will focus on the parasympathetic and sympathetic nervous systems within the nasal cavity.

The parasympathetic neurons arise in the superior salivary nucleus of the midbrain and then journey with the neurons of cranial nerve seven, the facial nerve. At the geniculate ganglion in the temporal bone, these neurons separate and compose the greater superficial petrosal nerve. These neurons travel along the base of the anterior cranial fossa and the pterygomaxillary space and synapse in the sphenopalatine ganglion. Parasympathetic postganglionic neurons then enter the nose through the sphenopalatine foramina. From here, parasympathetic postganglionic fibers are distributed to the mucosa and submucosa by branches from the sphenopalatine ganglion (Sahin-Yilmaz and Naclerio 2011). Postganglionic fibers contain the expected acetylcholine as well as neuropeptides, such as vasoactive intestinal peptide and secretoneurin (Korsgren et al. 2005). Stimulation of these parasympathetic fibers results in glandular secretions and some vasodilatation of blood vessels (Borum 1979).

The sympathetic neurons arise in the hypothalamus. These neurons exit the central nervous system in the cervical spine, synapse in the superior cervical chain ganglion (from this point on the fibers are considered postganglionic), and then journey with the
carotid plexus until the pterygoid canal, where they combine with the parasympathetic neurons from the facial nerve to create the vidian nerve. The sympathetic neurons do not synapse in the sphenopalatine ganglion, as the parasympathetic ones do, but go on to innervate the mucosa and submucosa (Sahin-Yilmaz and Naclerio 2011). Sympathetic fibers contain norepinephrine and Neuropeptide Y. Sympathetic effects occur when neurotransmitters stimulate adrenoceptors, which results in vasoconstriction, decreasing airway resistance (Baraniuk et al. 1990).

**Blood Supply**

The inferior turbinate receives blood mainly from branches of the external and internal carotid arteries, with some possible contributions from the facial artery (Figure 9). The external carotid branches into the internal maxillary, which branches into the terminal sphenopalatine artery. The sphenopalatine artery enters the nasal cavity through the sphenopalatine foramen on the posterior lateral inferior wall (Dawes and Prichard 1953). The internal carotid artery branches into the ophthalmic artery, which branches into the anterior ethmoidal artery. The anterior ethmoidal artery enters the nasal cavity through the orbit and the lamina papyracea. Branches of the anterior ethmoidal artery anastomose with branches of the sphenopalatine artery in the area of the inferior turbinate, giving the turbinate a robust blood supply (Sahin-Yilmaz and Naclerio 2011). Nutrient-rich blood reaches its destination through the smallest vessels of this area, the subepithelial, glandular, and periosteal capillaries. Nutrient-depleted blood then leaves the nasal cavity through veins that mainly follow adjacent to the arteries. The ethmoidal veins pass
through the cribriform plate and eventually reach the sagittal sinus. The sphenopalatine veins are continuous with the venous plexuses of the palate and nasopharynx and also pour into the infraorbital vein (Dawes and Prichard 1953).

Figure 9. Arteries of the Inferior Turbinate. Anastomoses between branches of the sphenopalatine and anterior ethmoidal (not labeled; top-left artery shown) arteries supply the inferior turbinate.
**Autonomic Receptors**

Adrenergic and muscarinic receptors, belonging to the sympathetic and parasympathetic systems, respectively, are commonly found on the inferior turbinate and play a vital role in the innervation of the local submucosal glands and vasculature.

Adrenergic receptors are G-protein coupled cell membrane receptors. They receive the sympathetic neurotransmitter norepinephrine and respond by activating second messengers or ion channels. Adrenergic subtypes include three α1 subtypes: α1A, α1B and α1D; three α2 subtypes: α2A, α2B and α2 C; and three β subtypes: β1, β2 and β3 (Kirstein and Insel 2004). Immunohistochemical analysis was carried out using anti-human adrenergic subtype-specific protein antibodies (α1A-, α1D-, α2C- and β2-adrenergic receptors). The immunostaining displayed that submucosal glands contain a high amount of α1D- and β2-adrenergic receptors while smooth muscle surrounding the vasculature contains a high amount of α1A- and α2C-adrenergic receptors (Shirasaki, Kanaizumi, and Himi 2016).

Muscarinic receptors are also G-protein coupled cell membrane receptors. They receive the parasympathetic neurotransmitter acetylcholine and respond similarly to adrenergic receptors. Muscarinic subtypes include m1, m2, m3, m4, and m5. In an experiment similar to the one above, immunostaining revealed m1 and m2 receptors are commonly distributed on glands, arteries, veins, and epithelia. M3 receptors are extensively dispersed on glands, arteries, and veins. Receptors of type m4 were identified in arteries. M5 receptors were found sparingly on glands and arteries. M3 receptors appear to
dominate in number and are likely the most important muscarinic receptor to the physiology of the inferior turbinate (Nakaya, Yuasa, and Usui 2002).
NORMAL PHYSIOLOGICAL FUNCTION OF THE INFERIOR TURBINATE

The turbinates serve to warm, humidify, and filter inspired air, with the inferior turbinate being chief among the others in fulfilling these functions. To fully comprehend its normal physiological function, as well as the later discussed environmental changes and pathology, an understanding of nasal patency and the nasal cycle must be reached. These topics will be discussed first and will then be followed by airway resistance, secretion, and immunity.

Nasal Patency

Nasal patency is defined as being a measurement of the openness of the nose. However, it is not necessarily equivalent to airflow or its resistance, although patency does effect airflow and resistance. When used correctly, nasal patency should refer to a cross-sectional area or volume of the nasal cavity (Malm 1997). Unlike most physiological domains, it has proved difficult to set normal values for nasal patency. This is due to wide variations in the nasal cycle, external environment, congestion, age, height, weight, race, sex, and of course, nasal shape and size (Moore and Eccles 2012).

Nasal patency can be determined through methods of computed tomography, magnetic resonance imaging, volumetry (both the closed cavity method and intranasal balloons), rhinostereometry, and acoustic rhinometry. Some authors also include expiratory or inspiratory peak nasal flow to calculate patency, although this method more accurately measures airflow (Malm 1997). Currently, acoustic rhinometry is the newest and
arguably the most promising method because it can be done quickly and non-invasively.

Sound waves are emitted into the cavity and measurement equipment analyzes the intensity and arrival time of the echo. Using this data, the known distances can be converted into useful cross-sectional area measurements for topographical maps of the nasal and nasopharyngeal airways, generating a better understanding of the openness of the nasal cavity (Melo et al. 2015).

**Nasal Cycle**

The nasal cycle refers to the asymmetrical, spontaneous changes in congestion or vasodilation and decongestion or vasoconstriction of nasal mucosal large veins. As the left inferior turbinate becomes more congested with blood, airflow through the left nasal cavity decreases. Meanwhile, the right inferior turbinate decongests and airflow increases through the right nasal cavity. Between 50 minutes and 4 hours, the congestion and decongestion reverse in at least 80 percent of the population and the cycle continues (Hasegawa and Kern 1977). A normal individual is generally unaware of the nasal cycle, since total nasal airflow remains constant (Sahin-Yilmaz and Naclerio 2011).

While precise research is still lacking, the “pacemaker” that generates and controls the nasal cycle is believed to be located within the suprachiasmatic nucleus of the hypothalamus in the brain (Mirza, Kroger, and Doty 1997). From the hypothalamus, the cycle is believed to be controlled by the sympathetic nervous system through the previously mentioned sympathetic fiber pathway to the inferior turbinate because the
cycling can be terminated by a sympathetic cervical ganglion blockade (Rooker and Jackson 1969).

**Airway Resistance**

Airway resistance can be defined as “the opposition to flow caused by the forces of friction” (“Airway Resistance” 2016). Resistance within the nasal airway is responsible for more than 50 percent of total airway resistance. The nasal valve, of which the inferior turbinate makes up the lateral border while the septum makes up the medial border, is the area of the nose with the highest airway resistance. Air must flow through this valve in each direction (Bailey 1998).

Resistance plays an important role in the normal physiology of respiration. During inspiration, the friction added by the inferior turbinate slows the laminar flow of air and allows it to spend more time in the nasal cavity, interacting with the warm epithelial mucosa as turbulent flow. These precious extra moments of interaction with the mucosa allow the air to be warmed, humidified, and filtered. It has been shown that air can be warmed up to 34 degrees Celsius and humidified up to 80 percent relative humidity before reaching the pharynx (Lindemann et al. 2004). Hence, a healthy nose can provide approximately 90 percent of the heat and moisture needed to prepare inspired air to alveolar conditions. The inferior turbinate by itself contributes to about 16 percent of conditioning, which is the largest contribution by any one structure in the airways. These nasal figures greatly outperform the capacities of the mouth, which is why it is better to
breathe thru the nose for proper conditioning and improved lung function (Naftali et al. 2005).

During expiration, nasal airway resistance is needed to keep air in the lungs for a certain period. Because a positive pressure difference exists between the lungs and the atmosphere, air wants to flow down its gradient: from the lungs, out through the nose, and into the atmosphere. Nasal resistance keeps air from exiting so easily. Hence, the nasal valve functions as a respiratory brake, allowing sufficient time for gas exchange within the alveoli in the lungs (Hairfield et al. 1987).

As evident in the nasal cycle, the size of the turbinates is one of the major factors in determining nasal airway resistance. The larger the inferior turbinate, the more resistance, the less air flows through the nasal cavity. Since the cycle is controlled by the sympathetic nervous system, drugs that affect this system can be applied to create desired airflow effects. One example is an α-adrenergic receptor agonist drug that mimics sympathetic agents to increase airflow. They function by binding to adrenergic receptors, which starts a excitatory cascade that results in decreased volume of the nasal mucosa, which decreases resistance and increases airflow (Shirasaki, Kanaizumi, and Himi 2016). Other agonists would have similar effects, while antagonists could reverse the process. It is important to note that parasympathetic innervation can also affect the size of the turbinates, since all subtypes of parasympathetic muscarinic receptors are found on the arterioles and venules of the submucosa.
The size of the inferior turbinate, specifically its mucosa, can also be changed by other factors including exercise, emotions, hormones, and environment (Ohki et al. 1987). Many of these topics will be explored in a later section.

**Secretion**

Filtration is the other vital responsibility of the nose. Inspired air contains a high concentration of particles, which would end up in the alveoli of the lungs if they were not filtered. This can result in damage to these fragile structures. To keep particles out of the lungs, they are trapped in the watery mucous film covering the nasal epithelium. The film, or blanket, is 10 to 15 μm deep and is made up of glandular secretions from goblet cells and other submucosal glands. The blanket covers the entire nasal cavity, including the inferior turbinate (Wilson and Allansmith 1976). It is estimated that goblet cells and other submucosal glands produce between 0.1 to 0.3 mg/kg of mucus per day. Large particles (greater than 3 μm) are generally filtered in the nasal valve, while smaller particles (between 3 and .5 μm) are trapped by the mucosa (Sahin-Yilmaz and Naclerio 2011). Because of its location as part of the nasal valve and its histological structure that includes the nasal mucosa, the inferior turbinate plays a role in filtering a large range of particles. After particles are trapped in the mucus, the epithelial cilia beat in a fixed direction to move the mucous blanket towards the nasopharynx and into the oropharynx, where they can be swallowed and then neutralized by acid within the stomach. In addition to filtration, the secreted mucus also helps to warm and humidify the air. The watery secretions tend to be warmer than the inspired air, since they come from the
interior of the body. As in humidification, the mouth does not filter as well as the nose, which also indicates the importance of nasal breathing versus oral breathing (Watelet and Van Cauwenberge 1999).

The parasympathetic nervous system mainly controls glandular secretion in the nasal mucosa, especially in the inferior turbinate (Eccles and Wilson 1973). As previously mentioned, parasympathetic cholinergic receptors, specifically the muscarinic subtypes m1, m2, m3, and m5, are found on the glands of the inferior turbinate mucosa (Nakaya, Yuasa, and Usui 2002). Cholinergic agonist drugs such as methacholine result in hypersecretion (Brofeldt et al. 1986), while anticholinergic antagonist drugs including atropine and ipratropium decrease secretion (Borum, Larsen, and Mygind 1979).

**Immunity**

The nose also participates in providing defensive immunity to the body. In addition to the trapping and subsequent neutralization of dangerous particles, it is also a first line of defense against bacteria and viruses. Immunoglobulin A (IgA), an antibody known to play a vital role in mucous membranes throughout the body, is produced in the submucosa of the nasal cavity, including the inferior turbinate. IgA is the major immunoglobulin found in nasal secretions and it can bind dangerous pathogens from the air that have become trapped in the mucous blanket before they can penetrate into the nasal mucosa and effectively access the blood stream or lymph (Bellanti, Artenstein, and Buescher 1965).
Mast cells, eosinophils, and lymphocytes are also present in the mucosa to provide immunity (Jafek 1983). Specifically, T-helper cells, T-cytotoxic cells, B cells, Natural Killer cells, neutrophil granulocytes, eosinophil granulocytes, and macrophages have been located in the inferior turbinate. In patients with chronic sinusitis, T-helper cells, T-cytotoxic cells, and B cells significantly increase in number compared to patients without sinusitis (Grevers et al. 2000). Additionally, lactoferrin, lysozyme and kallikrein, antimicrobial enzymes capable of breaking down pathogens, are synthesized in the cells of the respiratory epithelium are found in glandular secretions of the submucosa (Watelet and Van Cauwenberge 1999). Other helpful antimicrobial agents found in the epithelial secretions include glycosaminoglycans, antioxidants and antibacterial substances (Jeffery 1983).

Although the parasympathetic system is generally activated for secretion, there is evidence that the sympathetic nervous system can be utilized as well. For example, it has been shown that sympathetic innervation by both types of adrenergic receptors is needed for the secretion of IgA from the nasal mucosa during acute stress (Jarillo-Luna et al. 2015). This is made possible by the α1D- and β2-adrenergic receptors that are found on the submucosal glands.

Sneezing may also be included in this category, since its purpose is to expel mucus-trapped foreign particles or irritants from the nasal cavity. Sneezing is an autonomic response with both respiratory and nasal phases. An irritant is first presented within the nasal mucosa. Trigeminal nerve endings are activated and signals are sent afferently to
the brain, where the respiratory phase begins (Songu and Cingi 2009). While the sneezing control center has been found in the brainstem of the cat (Nonaka et al. 1990), its location has yet to be confirmed in humans (Seijo-Martínez et al. 2006). From this central area in the brain, efferent signals leave to activate abdominal, intercostal, and pharyngeal muscles, resulting in the sneezing mechanism to clear potentially immuno-compromising irritants from the nasal cavity (Brubaker 1919). It has also been hypothesized that the nasal phase, which results in nasal secretions that dilute and remove irritants in the nose to prevent it from entering the lungs is the true purpose of the sneeze (Burke 2012). These signals travel along the parasympathetic nerves of the sphenopalatine ganglion (Brubaker 1919). It is likely that both phases play a necessary role in the function of nasal immunity.
ENVIRONMENTAL PHYSIOLOGY OF THE INFERIOR TURBINATE

Certain environmental situations result in necessary adaptations within the nasal cavity to maintain homeostasis. Such circumstances include an increase or decrease in temperature and/or humidity, exercise, sleep, taste sensation or gustatory rhinitis, and pressure on a specific body part such as the crutch phenomenon. These situations, and the autonomic contributions, will be explored below. Much of the research presented does not focus solely on the inferior turbinate, but on the nasal cavity as a whole. Still, with the importance of the inferior turbinate within the cavity clearly evident (as previously described above), it can be understood that it continues to play a large part in homeostasis due to its role in airway resistance, secretion, etc.

**Temperature**

In cold weather, there tends to be an increase in nasal secretions. When cold air is inhaled and comes in contact with the nasal mucosa, the glands secrete extra water and mucus. This extra addition to the mucous blanket is needed to assist in warming and humidifying the air for preparation of entry into the alveoli. The colder the air is, the greater quantity of water and mucus that need to be produced (Shmerling 2011). It has been shown that, when exposed to cold air, nasal airflow slightly increases on average (Pirilä, Kiukaanniemi, and Jokinen 2000), or may slightly decrease (Proctor, Andersen, and Lundqvist 1977). As such, it seems there is not much of a change in nasal resistance in cold weather. This finding marks an interesting insight into turbinate physiology. Cold weather should induce vasoconstriction of surface vasculature, as it does in other
locations, to keep heat in the body. This should result in shrinkage of the turbinate mucosa, since they would receive less blood. However, the need to warm the incoming cold air must take physiological precedence, as nasal resistance hardly changes, indicating conserved blood flow to the turbinates. It is important to note that some otolaryngologists believe cold air within the nose may increase blood flow. These physicians may rely on an irrigation technique using hot water to decrease blood flow during posterior nasal epistaxis, and this technique has proven to be as effective as more conventional methods (Schlegel-Wagner, Siekmann, and Linder 2006).

Conversely, a hotter climate tends to decrease the need for nasal secretions. Since the air is already warm, secretion is not as relied upon as a method of heating (Shmerling 2011). Resistance decreases in warm air, since there is not as much need for air to stick around longer in the mucosa to heat up (Proctor, Andersen, and Lundqvist 1977).

**Humidity**

The perceived effects of humidity on the inferior turbinate are similar to those of temperature. The drier the air, the more need for secretion. The wetter, or more humid the air, the less a need for secretion exists (Shmerling 2011). However, it has been shown that there is no significant change in nasal mucus flow, or secretion, between 10 and 70 percent relative humidity, if the temperature is kept constant at 23 degrees Celsius (Andersen, Lundqvist, and Proctor 1972). The difference in perception and experimental results may be due to the fact that cold air tends to be drier, so the increased secretion may be caused solely by the cold temperature. It is possible that experimental results
could become significant at more extreme relative humidity values, such as 0 or 90 to 100 percent. The same study also revealed that there is no change in nasal airflow resistance between 10 and 70 percent relative humidity (Andersen, Lundqvist, and Proctor 1972). It can be assumed that the mucosal changes that do occur do so under the direction of the innervating autonomic nervous system.

**Exercise**

At rest, the nose is capable of taking in 20 to 30 liters of air per minute (Sahin-Yilmaz and Naclerio 2011). During exercise, metabolic use of oxygen by muscle and other organs increases. As such, an uptake in oxygen is required and respiration must increase. More air must flow thru the nasal cavity, and mouth-breathing, though not as efficient at conditioning inspired air, may also be required depending on the body’s primary need for oxygen. To accommodate this, the size of the turbinates decreases, allowing for a greater nasal cavity volume and decreased resistance. Nasal airflow resistance as measured by rhinomanometry decreases by approximately 70 percent during exercise (Sozansky and Houser 2014). The duration of exercise has also been shown to decrease resistance more than the intensity (Fonseca, Voegels, and Pinto 2006).

The autonomic system controls the reduction in size of the inferior turbinate during exercise. Specifically, the sympathetic portion, which tends to control other “fight or flight” actions including as exercise, is responsible. Sympathetic fibers induce active vasoconstriction in the nasal mucosa (Fonseca et al. 2006). This is likely accomplished by activating $\alpha_{1A}$- and $\alpha_{2C}$-adrenergic receptors within the smooth muscle of mucosal
vasculature. This action would have a dual purpose in the body’s exercise physiology; not only does the decreased blood flow to the inferior turbinate result in decreased turbinate size and thus decreased resistance, but the blood is made available to transport oxygen to other parts of the body that require greater uptake during exercise.

Exercise also impact the ability of the mucosa to condition. It has been shown that even at a moderate level of exertion in a comfortable environment, the air conditioning capacity of the nasal cavity was reduced by up to 11 percent (Naftali et al. 2005). This is likely due to the fact that, with the decreased resistance, inspired air is spending less time interacting with the warm and humid mucosa. As exercise intensity and duration maximize, the efficiency of the mucosa to condition would be expected to substantially decrease to a currently unknown level.

While air may not be sufficiently conditioned during exercise, the autonomic system works tirelessly to ameliorate this anomaly by stimulating additional submucosal secretions, especially in cold weather. Mucus flow and volume both increase significantly during exercise in colder temperatures (Pirilä, Kiukaanniemi, and Jokinen 2000).

Sleep

During sleep, the metabolic demand for oxygen is suppressed. As such, respiration slows compared to normal basal levels. Breathing is also completely controlled by the autonomic system during sleep. Most humans tend to sleep in a recumbent position (Pevernage, De Meyer, and Claeys 2005). In this position, nasal resistance increases.
This is likely due to gravitational effects that disrupt emptying of vessels in a supine position versus an upright position. Capacitance venules and veins in the mucosa fill and don’t drain easily, leading to a swollen turbinate (Cole and Haight 1986). Oddly enough, the supine position decreases the ability of the nasal mucosa to condition air. Experimentation has shown nasal mucosal temperatures to drop more significantly in a supine position compared to an upright position. The mechanism that explains this decrease is unknown, but theories have been presented that focus on a decrease in blood flow to the nasal mucosa because of a decreased pulse during sleep (Assanasen et al. 2001). This would decrease the blood’s ability to warm the mucosa, limiting the warming interaction between the mucosa and the inspired air. Still, blood should access the mucosa easier in the supine position due to the decreased gravitational pull and turbinate filling compared to the upright position, although the decreased draining of capacitance vessels may result in backflow of blood into resistance vessels. Obviously, there is still work to be done in this area.

In addition to a supine position, other typical sleep positions include left lateral and right lateral recumbent postures. It is evident that sleep position has a great effect on the nasal cycle. The average duration of the cycle when supine almost doubles during sleep, from a measured value of 91.1 minutes to 178 minutes. Its amplitude increases as well (Rohrmeier et al. 2014). A positional shift during sleep also tends to alter the cycle. Lateral recumbency results in an increase in nasal resistance on the inferior side and a decrease in nasal resistance on the superior side. The increase in nasal resistance one the
inferior side while lying laterally is even greater than that of a simple supine position (Hasegawa 1982). Interestingly, a reversal of congestion in one side of the inferior turbinates does not appear to cause one to alter his or her sleeping position (Rohrmeier et al. 2014).

A major sleep pathology that affects millions around the world, sleep apnea, will be discussed later.

**Gustatory Rhinitis**

Individuals often find that eating spicy foods results in a runny nose. This strange physiological action is known as gustatory rhinitis. Gustatory rhinitis is characterized by watery rhinorrhea, or mucus, seeping out of one or both sides of the nasal cavity after ingestion of unusually hot and spicy foods (Jovancevic et al. 2010). Evidence has shown this to be an autonomic reflex; sensory nerves in the olfactory portion of the cavity are stimulated and travel to the brain, where efferent signals are sent parasympathetically to the nasal mucosa, which are received by muscarinic receptors and result in secretion from the turbinate. The first step of treatment is avoidance of stimulatory foods, but there are other options if this is not possible. Application of an intranasal anticholinergic agent, like atropine, blocks the muscarinic receptors on submucosal glands and stops over-secretion (Raphael, Raphael, and Kaliner 1989). Similar applications include ipratropium bromide and intranasal capsaicin. If these treatments aren’t effective, a surgical technique called a vidian neurectomy can be used to interrupt the parasympathetic supply to the nasal cavity (Georgalas and Jovancevic 2012). This technique is morbid and can lead to
chronic nasal and eye dryness, so it is generally performed as a technique of last resort (Jovancevic et al. 2010).

**Crutch Phenomenon**

Pressure applied to some body surfaces including the shoulders, arms, axilla, thorax, and pelvis can alter the nasal cycle (Haight and Cole 1984). An example of this, known as the “crutch phenomenon,” was first studied in 1970, although the idea has been around for much longer; yogis in India used it to correct left or right nasal airflow (S. Kuvalayanada and S. L. Vinekar 1963). When a crutch is placed under the arm of a sitting patient, the nasal cycle shifts so that the ipsilateral turbinate congests, increasing nasal resistance, while the contralateral side decongests, decreasing resistance. It is generally believed that autonomic reflexes near the shoulder or arm result in this ipsilateral congestion. There are two possible mechanisms that have been presented. First, pressuring the brachial plexus of this region may initiate a reflex that ascends to the brain, from which efferent impulses descent to the nasal mucosa of the turbinate by way of parasympathetic fibers, resulting in vasodilation. Second, the walls of the brachial and axillary arteries of this region may contain sympathetic nerve fibers that are irritated by the crutch. This could result in signals traveling antidromically to the superior cervical ganglion and then being sent efferently to the nasal mucosa, vasodilating its vasculature (Rao and Potdar 1970). A more recent study believes the second option, innervation by the sympathetic system, to be more likely (Davies and Eccles 1985).
PATHOLOGY OF THE INFERIOR TURBINATE

Many pathological issues can arise within the inferior turbinate. Such issues include structural abnormalities such as concha bullosa, infectious diseases including tuberculosis and more, both allergic and non-allergic rhinitis, sleep apnea, and empty nose syndrome. These problems will be discussed here. In addition, inferior turbinate pharmacology and drug effects on the autonomic system will be detailed.

**Structural Abnormalities**

The most common structural abnormality found in the inferior turbinate is hypertrophy of the mucosa. A hypertrophied inferior turbinate (Figure 10) can be unilateral or bilateral, which may create asymmetric nasal cavities. This often results in partial or total obstruction of the nasal airways. Symptoms can include an inability to breathe through the nose, nasal congestion, mid-facial pain or pressure, and rhinorrhea. Allergies may contribute to the hypertrophy. Medical reduction through medication or surgery is often required to relieve congestion and facilitate nasal breathing and will be discussed in detail later (Hernandez 2016).
Figure 10. Stages of Turbinate Hypertrophy. Hypertrophy of the inferior turbinate can increase until it obstructs the nasal cavity, severely limiting the flow of air.

A rarer structural abnormality of the inferior turbinate is turbinate pneumatization, also known as concha bullosa (Figure 11). A pneumatization is an air-filled cavity or pocket within the turbinate. This is more common in the middle and superior turbinates, but cases have also been seen in the inferior turbinate. Concha bullosa is likely due to an embryological error. Like hypertrophy, it may also result in enlargement that becomes obstructive, and may require surgical reduction (Pittore, Al Safi, and Jarvis 2011).
Infectious Disease

Infectious diseases that affect the nasal cavity include, but are not limited to, tuberculosis, rhinosporidiosis, rhinoscleroma, leprosy, syphilis, histoplasmosis, leishmaniasis, and sarcoidosis (Zargari and Elpern 2009). A few of the more prominent diseases that especially disrupt the inferior turbinate will be explored here.

Tuberculosis is caused by a bacterium called mycobacterium tuberculosis. While it mainly affects the lungs, it can also invade the interior of the nose, especially the anterior part of the inferior turbinate and the nasal septum. It results in secretion from the mucosa, pain, and even possible perforation of the nasal septum (Zargari and Elpern 2009). Treatment for tuberculosis involves a variety of antibiotics (CDC 2016).
Rhinosporidiosis is a fungal disease caused by Rhinosporidium seeberi, which mainly affects the nasopharynx but can be present in other parts of the body. Fungal spores breathed in through the nose result in a reddish-pink mass on the nasal mucosa of the inferior turbinate. Surgery is usually required for removal (Aquino et al. 2016).

Rhinoscleroma is a bacterial disease caused by Klebsiella rhinoscleromatis. It localizes in the upper airways, especially in the nasal mucosa of the inferior turbinate, after being inhaled through infected droplets (Shoeib 2010). Rhinoscleroma results in hypertrophy of the turbinate and has even been seen to infiltrate the tissue completely, separating the inferior turbinate from the lateral wall of the nasal cavity (Yassin, Badrawy, and Mokhtar 1971). Antibiotics and surgical reduction are recommended (Mukara et al. 2013).

**Rhinitis**

Rhinitis is generally described as an irritation of the nasal mucosa that often results in swelling, congestion, and a runny nose. There are two categories of rhinitis, allergic rhinitis and non-allergic rhinitis. Allergic rhinitis is due to an overreaction of the immune system following the introduction of an allergen into the mucosa. The allergen is most often pollen carried in the air. Common treatments include avoidance, nasal steroids, antihistamines, and allergy shots. Non-allergic rhinitis is not a result of an over-active immune system. Instead, it can develop from exposure to odors, pollution, changes in the weather, or overuse of nasal decongestants. In addition, non-allergic rhinitis symptoms can be caused by medications, including blood pressure medicines, oral contraceptives, or medications used for erectile dysfunction. Nasal sprays including corticosteroids,
antihistamine, and Ipratropium are commonly used to treat non-allergic symptoms. Surgery may also be required (“Rhinitis” 2016).

Research has shown that, within the inferior turbinate, nerve fibers in patients with allergic rhinitis were significantly increased within the epithelium, subepithelium, and glandular and vascular regions of the submucosa. A neurotransmitter for sympathetic nerve fibers, neuropeptide tyrosine, was also found in higher amounts in subepithelium and submucosal regions. Neuropeptide tyrosine is generally involved in vasoconstriction and decongestion of the mucosa (O’Hanlon et al. 2007). This increased concentration may indicate the need for excess innervation to alleviate the common allergic rhinitis symptom of congestion. It also provides a clear example of the importance of the autonomic system in the regulation of pathologic homeostasis within the inferior turbinate.

**Sleep Apnea**

Sleep apnea is a common chronic disorder in which the patient pauses in breathing for a few seconds up to minutes during sleep. It can happen over 30 times an hour and is obviously very disruptive to the sleep cycle, leading to daytime drowsiness. Obstructive sleep apnea is the most common type and results in the airway collapsing or being blocked during sleep, causing breathing to pause. In most cases, this is more due to a narrowing of the throat than the nasal cavity. Large tonsils, redundant pharyngeal tissue in overweight individuals, and over-relaxation of throat muscles are often to blame (“What Is Sleep Apnea?” 2012). Still, is it believed that the nose plays a role in sleep
apnea (Valipour 2014). This is due to nasal obstruction, including enlarged inferior turbinates, that would result in increased nasal resistance.

Currently, clinical guidelines for the evaluation, management, and long-term care of obstructive sleep apnea in adults focuses on mainly pharyngeal procedures to eliminate obstructive sleep apnea. A few nasal surgical procedures, including inferior turbinate reduction, are discussed. However, the current belief is that such surgeries are rarely curative for obstructive sleep apnea, although they can improve clinical outcomes such as mortality, cardiovascular risk, function, quality of life, and symptoms (Epstein et al. 2009). Some nasal surgeries may help patients manage their sleep apnea. One such surgery involves improving compliance with Continuous Positive Airway Pressure, which is the first line treatment for obstructive sleep apnea. A combination of septoplasty and inferior turbinoplasty have been shown to improve Continuous Positive Airway Pressure in patients with sleep apnea and nasal obstruction (Poirier, George, and Rotenberg 2014). A second compound nasal surgery consisting of septoplasty, submucosal inferior turbinectomy, and posterior nasal neurectomy significantly improved (but did not cure) obstructive sleep apnea without any pharyngeal procedures. Such procedures should be considered if high nasal resistance is present in sleep apnea patients (Hisamatsu, Kudo, and Makiyama 2015).

**Empty Nose Syndrome**

Empty nose syndrome is considered a rare iatrogenic complication of turbinate reduction surgery, mostly commonly following reduction of the inferior turbinate. Interestingly, it
tends to manifest itself years later. Symptoms include nasal obstruction (despite a lack of tissue that would be more likely to result in less obstruction and less nasal resistance), mucosal dryness and crusting, and a constant feeling of dyspnea. It is theorized that empty nose syndrome is caused by alterations to the local environment, lack of mucosal cooling, and derangement of neurosensory mechanisms (Kuan, Suh, and Wang 2015). The disruption of neurosensory mechanisms is especially harsh for patients, as it leads them to feel as though they are not able to respire sufficiently; a lack of sensitivity in the nose results in a persistent sensation of shortness of breath. Unfortunately, these symptoms can lead to anxiety and depression, including suicidal thoughts (“Empty Nose Syndrome” 2016). Medical and surgical therapies are available, including turbinate reconstruction using implants. These implants appear to be safe and quite effective, decreasing empty nose symptoms significantly (Houser 2007). Still, prevention of empty nose syndrome should be a focus of otolaryngologists. A surgeon can always remove more tissue if necessary and should err on the side of caution to avoid over-resection complications. It is important to note, however, that some physicians question whether symptoms of empty nose syndrome are actually caused by a lack of turbinate tissue (Das, Patel, and Poetker 2016).

Pharmacology

Multiple medical therapies to correct inferior turbinate dysfunction by influencing the autonomic system are available. Decongestants that generally reduce turbinate size and nasal resistance by vasoconstriction include oxymetazoline, pseudoephedrine, and
phenylephrine. Cocaine is also known to be a powerful and highly regulated decongestant. Table 1 summarizes medications and their effect on inferior turbinate function.

Oxymetazoline, commonly marketed under the brand name Afrin, is a full α1 receptor agonist and a partial α2 receptor agonist. When oxymetazoline binds the alpha receptors found on the inferior turbinate vasculature, vasoconstriction occurs, the turbinate decongests, and nasal resistance decreases (Gómez-Hervás et al. 2015). Oxymetazoline has been shown to be arguably the strongest decongestant, achieving the most rapid onset, longest duration of action, and greatest improvement in airway patency when compared with pseudoephedrine, the next strongest decongestant (Connell and Linzmayer 1987).

Pseudoephedrine, commonly marketed under the brand name Sudafed, is an indirect α agonist. It induces the vascular smooth muscle in the turbinate mucosa to vasoconstrict by releasing stored norepinephrine from sympathetic fibers within the vascular smooth muscle (Wang, Kao, and Chu 2006). This is the mechanism leading to inferior turbinate decongestion, and is quite effective. Because pseudoephedrine can be converted into a dangerous methamphetamine drug, the U.S. Senate passed a bill that restricts its sale (“What’s the Difference between Pseudoephedrine and Phenylephrine?” 2016).

Phenylephrine, commonly marketed under the brand name Sudafed PE, is another α agonist decongestant. Unfortunately, it does not seem to be more effective than a placebo.
when taken orally, perhaps because it is not absorbed well (Horak et al. 2009). As such, it is also marketed as a local nasal spray, which is likely to be significantly more effective than the oral pill.

Other medications to manage inferior turbinate dysfunction exist. Oral or intranasal spray antihistamines block histamine effects, such as vasodilation, at H1 receptor sites and are especially useful when combined with decongestants. Intranasal corticosteroid sprays improve rhinitis and also contain general anti-inflammatory properties, reducing turbinate size. While the exact mode of action of intranasal corticosteroid sprays is unknown, it is believed that the steroid penetrates and acts locally in the nasal mucosa. It may also target inflammatory cells and their chemical mediators such as epithelial cells, lymphocytes, basophils, mast cells, and Langerhans cells (Mygind et al. 2001). A leukotriene receptor antagonist, montelukast, is also used to alleviate rhinitis and has shown to reverse nasal congestion (Archer 2016).

Cocaine is a powerful drug that is often illicitly made into a powder form and snorted through the nose. In addition to a host of other effects, it functions as a local vasoconstrictor and decongestant within the nasal cavity and is used in surgical practices. Long-term abuse, however, can lead to inferior turbinate hypertrophy (Hamilton 2016). Yet in some individuals, long-term use has resulted in erosion of the turbinates and nasal septum, eventually causing complete collapse of the nose (Villa 1999).
Drugs not intended to affect the nose may still have side effects there. Alpha blockers such as silodosin, a treatment for benign prostatic hyperplasia, can vasodilate the vessels of the inferior turbinate, congesting the nose (Fonseca and Da Silva 2015). Theoretically, beta blockers such as β2-adrenergic receptor antagonists could decrease submucosal secretions, limiting the effectiveness of the turbinate to condition inhaled air. In addition, some non-specific beta blockers can have alpha blocker activity that may lead to nasal congestion (Rosendorff 1993). Sildenafil, commonly marketed as Viagra, increases the effect of the vasodilator nitric oxide, and has been shown to result in nasal congestion (Kiroglu et al. 2006). Xanax, an anticholinergic medication for depression, carries a less common but known side effect of nasal congestion (“Xanax Side Effects in Detail” 2016). Xanax likely causes vasodilation through at least the m3 receptor in submucosal vasculature.
Table 1. Medications That Affect Turbinate Function

<table>
<thead>
<tr>
<th>Medications</th>
<th>Effect</th>
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<tbody>
<tr>
<td>Oxymetazoline (Afrin)</td>
<td>Decongestant</td>
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<tr>
<td>Pseudoephedrine (Sudafed)</td>
<td>Decongestant</td>
</tr>
<tr>
<td>Phenylephrine (Sudafed PE)</td>
<td>Decongestant</td>
</tr>
<tr>
<td>Cocaine</td>
<td>Decongestant</td>
</tr>
<tr>
<td>Loratadine (Claritin)</td>
<td>Antihistamine</td>
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<tr>
<td>Loratadine + Pseudoephedrine (Claritin D)</td>
<td>Antihistamine, decongestant</td>
</tr>
<tr>
<td>Silodosin (Rapaflo)</td>
<td>Congestant</td>
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<tr>
<td>Sildenafil (Viagra)</td>
<td>Congestant</td>
</tr>
<tr>
<td>Xanax</td>
<td>Congestant</td>
</tr>
<tr>
<td>Montelukast</td>
<td>Anti-inflammatory, decongestant</td>
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<tr>
<td>Corticosteroid Sprays (Nasacort, Rhinocort)</td>
<td>Decongestant, decrease mucus secretion</td>
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<tr>
<td>Antihistamine Sprays</td>
<td>Antihistamine</td>
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</table>
REDUCTION OF THE INFERIOR TURBINATE

Inferior turbinate hypertrophy that results in nasal obstruction can occasionally be managed by medications such as intranasal steroidal sprays and typical allergy drugs. Unfortunately, this is often not sufficient. Depending on the individual’s nasal anatomy, office-based or maximal operating room surgery may be recommended. Medical and surgical turbinate reductions will be detailed here, as well as their autonomic impact.

Medical Reduction

Although transient reduction in turbinate size can be achieved with many of the medications outlined in the pharmacology section, durable reduction and symptom improvement from medical therapy is generally achievable only with topical sprays that target autonomic controls. Nasal corticosteroid sprays such as Nasacort or Rhinocort reduce general swelling due to congestion and mucus secretion from the turbinates. Topical nasal antihistamine sprays are also effective at reducing nasal congestion. Prolonged use of these sprays does not appear to cause ineffectiveness. Other previously mentioned decongestants such as Afrin (which is a spray) and Sudafed also reduce the size of the inferior turbinate (Archer 2016). A typical allergy medication such as Claritin-D, a combination of the antihistamine loratadine and decongestant pseudoephedrine, reduces turbinate hypertrophy by relieving nasal congestion (McFadden et al. 2000). Unfortunately, prolonged use of decongestants may reduce effectiveness (Archer 2016).

Surgical Reduction
Surgical therapy may be necessary for patients in whom medical management of inferior turbinate hypertrophy is no longer responsive. Because of the important function of the turbinates in respiration, conditioning, and immunity, and the possible side effect of empty nose syndrome, special care must be taken to avoid excessive resection. The surgeon should focus on addressing the obstructive problem while maintaining function of the autonomic features.

Minimal surgical reduction of the inferior turbinate may be done in the office of an otolaryngologist. Office-based therapies include radiofrequency and electrocautery. The first technique uses radiofrequency to place lesions within the submucosa of the turbinate, which reduces tissue volume while minimizing impact to other surrounding structures. It has proven to be a safe and effective therapy to reduce obstruction without actually altering the outer mucosa (Coste et al. 2001). Ciliary motility may take up to 3 months to fully recover, although this doesn’t significantly affect function (Rosato et al. 2016). Saccharin transit time, a method of measuring turbinate function by calculating mucociliary flow rate, was not significantly altered (Rhee et al. 2001). Coblation is a popular subtype of radiofrequency therapy that can be used to remove additional tissue. A small applicator is threaded under the mucosa through a small incision, and then directs coblation waves that slowly melt the bone and soft tissue (Isaac Namdar 2016). It is also generally effective, though rare individuals may have vascular damage that leads to epithelial shedding and hinders function (Berger et al. 2008). While radiofrequency therapy generally has minimal post-op complications and pain, its efficacy tends to
decrease after 3 years (Passali et al. 2016). Electrocautery is similar to radiofrequency, but uses electrical current instead. It has been shown to be just as safe and effective as radiofrequency, with the same limited complications (Uluyol et al. 2016). With each of these techniques proven safe and effective, the choice is left to the discretion of the surgeon.

Maximal surgical reduction is generally performed in the operating room of a hospital. The type of surgery is chosen after determining whether the cause of inferior turbinate hypertrophy is soft tissue in nature, bony, or a combination of both. If excess soft tissue in the cause, a submucosal resection is often performed. The surgeon removes portions of the submucosa layer in order to shrink the overall volume of tissue. By removing portions of the submucosa only, receptors on the external layer of the mucosa are not affected (Bhandarkar and Smith 2010). The recent use of a microdebrider tool in this surgery, which permits continuous suctioning of blood from the area while quickly removing the tissue, has made this surgery even more effective and popular (Brunworth, Holmes, and Sindwani 2013). Despite the expected loss of turbinate function because of the vital role of the submucosa, it appears that mucus and IgA secretion are eventually restored to functional levels (Leong and Eccles 2010). If the cause of hypertrophy is bony or a combination of bony and soft tissue, partial turbinectomy is usually performed. Portions of the bone and/or submucosa may be removed during this surgery. Complications are minimal, but partial turbinectomy may negatively impact intranasal air heating, although it does not seem to affect humidification (Tsakiropoulou et al. 2015). Still, the relief of
nasal obstruction would likely outweigh these considerations. Full turbinectomy was a popular choice of surgeons until empty nose syndrome was discovered. Now, it has fallen out of favor due to the high rate of complications (Brunworth, Holmes, and Sindwani 2013). Again, with most of these techniques proven safe and effective, the choice of surgery is left to the otolaryngologist. A study comparing radiofrequency therapy, submucosal resection with the microdebrider, and partial resection found no significant differences in major complications, patient satisfaction, improvement of nasal patency, and recurrence of nasal obstruction (Arganbright et al. 2015). The anatomical needs of the patient and comfortability level of the surgeon would likely be the key determinants when planning a course of action.
CONCLUSION

The inferior turbinates perform a highly valuable role in respiration and immunity. Their anatomy and histology allow air entering the nose to be warmed, humidified, and filtered before moving on to the lungs for optimal oxygen extraction. Additionally, size of the inferior turbinate due to blood flow drives nasal patency as mandated by the nasal cycle. The autonomic nervous system regulates these activities. Without the autonomic inferior turbinate, air would not be as well conditioned, breathing would be more difficult, and one would contract illnesses more readily.

The inferior turbinate contains sympathetic adrenergic receptors within the glands and vasculature of the submucosa. Parasympathetic muscarinic receptors are found within the glands and vasculature of the submucosa, as well as on the epithelia of the inferior turbinate. Autonomic innervation that controls vasoconstriction and vasodilation of the vasculature in the submucosa administers the nasal cycle. As vessels enlarge and more blood is present in the inferior turbinate, nasal patency decreases and nasal resistance increases. As vessels constrict, a reversal takes place. The blood flow also contributes to the warming and humidifying capacity of the turbinate. The autonomic system also controls secretion rates, which add to the humidification and immunological functions. Many medications used to alleviate inferior turbinate dysfunction operate by interacting with autonomic fibers and receptors. While surgery to reduce inferior turbinate hypertrophy has not been shown to significantly alter function despite often removing vital tissue, this may be due to the fact that surgeons aim to only remove the extra tissue
that is initially present. The remaining tissue, when healed, is able to resume normal function.

The inferior turbinate is composed of its own bone, is enclosed by specific soft tissue that contains parasympathetic and sympathetic receptors that receive innervation from the autonomic nervous system, and functions according to the input from those autonomic fibers. As such, it should be considered an autonomic organ.
FUTURE DIRECTIONS

While much of the inferior turbinate and its autonomic properties have been thoroughly researched, potential topics still exist. A considerable amount of work needs to be done in the realm of surgery and its impact on the autonomic system. While some functional effects of various surgeries are somewhat known, additional research focusing on the surgical disruption of autonomic fibers and neurotransmitters is needed. It would also be pertinent to research whether autonomies lose control for some time following turbinoplasty and turbinectomy surgeries, and if that control is regained, or whether the remaining tissue is truly sufficient for function and never loses autonomic control.
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CURRICULUM VITAE

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Education

Boston University, School of Medicine, Boston, MA
M.S., Master of Medical Sciences
August, 2016

Brigham Young University, Provo, UT
B.S., Exercise Science; minors in Spanish and History
April, 2015

Centennial High School, Las Vegas, NV
Class Valedictorian
June, 2008

Experience

Laborer—Craft Supplies USA, Provo, UT
June – Aug., 2015

Research Assistant—Brigham Young University, Provo, UT
June, 2012 – May, 2015
• Studied effects of Rosiglitazone on iron markers and inflammation under Dr. Chad Hancock
• Presented co-authored poster at the Experimental Biology Conference in San Diego, CA in April 2014
• Presented co-authored poster at the American Diabetes Assoc. Conference in Boston, MA in June 2015

Sports Camp Counselor—Brigham Young University, Provo, UT
May – Aug., 2012
• Supervised activities of camp participants

Parts Runner—SA Recycling, Las Vegas, NV
June – Aug., 2011

Lab Assistant—Nevada Institute of Cancer, Las Vegas, NV
June – Aug., 2008
• Assisted in research lab attempting to crystallize the Bax protein under Dr. Tarmo Roosild

Volunteer Work

Primary Teacher—The Church of Jesus Christ of Latter-day Saints, Boston, MA
Feb., 2016 – Present
• Providing Sunday School instruction to a class of five year-olds

Emergency Department Assistant—Timpanogos Regional Hospital, Orem, UT
Sept., 2013 – Aug., 2015
• Communicating needs among patients and their families, nurses, and doctors
• Interpreting for Spanish-speaking patients
• Supporting nurses in transporting patients, cleaning rooms, and fulfilling other duties

Court Appointed Special Advocate—State of Utah, Utah Country
Oct., 2012 – Aug., 2015
• Reporting to state attorneys on the conditions of minors who have been removed from their homes
• Offering testimony and situational advice to a family court judge

Nursery Leader—The Church of Jesus Christ of Latter-day Saints, Orem, UT
• Tending and teaching 18-month to 4-year-old toddlers during church services

Racer Assistant—Miles for Smiles, Orem, UT
April, 2013 – Aug., 2015
Pushing wheelchairs of mentally handicapped participants in 5K races

**Volunteer Representative**—The Church of Jesus Christ of Latter-day Saints, Uruguay  Feb., 2009 – 2011
- Taught religious lessons and organized service activities
- Consistently worked 12 hour days
- Spent 15 months in leadership positions supervising and training missionaries

**Leadership**

**Young Men’s Secretary**—The Church of Jesus Christ of Latter-day Saints, Orem, UT  May – Aug., 2015
- Kept attendance, took notes of meeting, assisted in organizing activities for teenagers

- Organized weekly activities and supervised Sunday instruction

**Other Leadership**
- Team Captain in multiple university intramural sports

**Accomplishments and Interests**
- Fluent in Spanish with oral and written communication rated as “Advanced” according to ACTFL
- Nationally Certified Bilingual Healthcare Provider according to the National Certification for Bilingual Healthcare Providers with “Advanced Professional Proficiency”
- Owner of Diabetes y Tú, an app which helps Hispanic users learn about diabetes and find free or low-income health clinics in the state of Utah
- 70+ hours of physician shadowing
- Boy Scouts of America—Eagle Scout
- Three-sport athlete in high school and two-time Nevada State runner-up in volleyball
- Ran over 4,000 miles in the past four years, including a 1:25:08 time in the Nebo Half Marathon
- Backpacked through Europe in May, 2013
- Huge sports fan of the Arizona Diamondbacks, BYU, Real Salt Lake, FC Barcelona, Utah Jazz, San Francisco 49ers, Boston Bruins, Peñarol, and the Uruguayan National Fútbol Team
- Married with one child, a two-year-old son