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## Respiratory Disease in Snakes

Respiratory disease is a commonly diseased organ system in snakes in captivity. Snakes develop both upper and lower airway diseases. The range of respiratory diseases seen in captivity can be of many different etiologies, including bacterial, viral, parasitic, and fungal. Factors that contribute to the expression of the disease include captive husbandry, stress, cage spacing, genetics, physiological ecdysis or shedding, individual species characteristics, and cleanliness of habitat.

This article is designed to understand both the disease causing pathogens and the environmental husbandry factors which often suppress the immune system of the snake precipitating clinical disease. Developing a working knowledge of the physiological and anatomical differences between the mammalian and the reptilian respiratory systems is an important concept that impacts husbandry changes (prevention) and therapeutics. Diagnosing the respiratory dysfunction is done by the standard techniques used commonly in veterinary medicine including cultures, serology, radiology, parasite exams, cytology, etc... Diagnosing the potential underlying husbandry problem is often times a foreign concept that we as veterinarians have received little training. For this reason a review of the physics of thermoregulation will be discussed. Cage design and other husbandry considerations will also be conceptually explained. Lastly, therapeutics will be discussed including conventional and unconventional routes of administration.

Snakes are a fairly large and diverse group of reptiles utilizing niches in the trees, on land, sub-terrestrial, in fresh water and in the ocean. The shape of snakes varies little but the size can vary from inches to thirty feet. With the diversity of niches occupied and the size variability of snakes, challenges of captivity are related to space, knowledge of natural history, knowledge of captive manipulation, and current and past health status.

### Anatomy and Physiology

While the ecological niches occupied are diverse, the respiratory anatomy of commonly kept snakes is fairly constant. Snakes have an obvious, rostrally located glottis that fits into the choanal slit when the mouth is closed. When the snake is eating the mobile glottis can be position to maintain active respiration. The trachea, which is lined with more primitive endothelium (reduced function cilia), is "C-shaped" and ends at the level of the heart. The endothelial lining of the trachea functions ineffectively as a mucociliary escalator as a result. Snakes seem to use gravity and body positioning in order to clear the lungs and the trachea of mucous caused by infection. Certain snake species have a dorsally located tracheal lung, which may function in respiration upon lung and air sac compression after eating large meals. Most snakes have only a functional right lung, which is attached dorsally to the body wall. Boids have a vestigial but functional left lung. The normal lung is comprised of a cranial portion where gas exchange occurs across peripherally arranged simple alveoli. The right lung in the boidae and colubridae begin just caudal to the heart and extends to the dorsal surface of the liver. The remainder (caudal and central portion) of the lung is functionally an avascular air sac that in most snakes ends as a blind pouch as is approaches the stomach. Snakes have no diaphragm, which prevents effective coughing.

Respiration is controlled by groups of muscles attached to the ribs. Inspiration is controlled by muscle groups that expand the ribs; resulting in lower intrapulmonary pressure. The air pulled in from the atmosphere, which increases intrapulmonary pressure up to the point where the air sacs no longer expand. The passive expiratory phase begins by the relaxation of the inspiratory muscles. Relatively high intrapulmonary pressure and natural recoil of the lungs coupled with the glottis being open allows air to passively flow from the lungs. The stimulus for reptiles to take a breath is a low partial pressure of oxygen (pO<sub>2</sub>). This is unlike mammals in which high partial pressure of carbon dioxide (pCO<sub>2</sub>) stimulates respiration. The clinical significance of low partial pressure of oxygen being the stimulus for spontaneous

respiration is apparent when snakes are anesthetized. If too much positive pressure ventilation is administered during surgical procedures the partial pressure of oxygen is high. The patient may likely also be over anesthetized. Both conditions result in a prolonged recovery. Also pertinent to the concept is temperature control during anesthesia. Snakes need be kept in their preferred optimal temperature while anesthetized and recovered. If the temperature drops during anesthesia/recovery, then the demand for oxygen decreases. Body metabolism (including the anesthetic drug(s) of choice metabolism) decreases resulting in slowed recovery and delay in spontaneous respiration. If the temperature increases during anesthesia/recovery, the oxygen consumption increases as does drug metabolism resulting in more profound anesthetic depths; again resulting in prolonged recovery.

Reptiles are known very well for their ability to tolerate anoxia and hypoxia. The clinical significance of this fact is that despite major pulmonary pathology they are able to function in a somewhat normal physiological state. It is unclear how much anaerobic metabolism truly occurs during hypoxic periods. It is clear that during periods of hypoxemia some anaerobic metabolism occurs and some hypoxic depression occurs resulting in lower oxygen demand. This study was performed on the *Chelysemys scripta* turtles' heart and may be a species-specific phenomenon and may not necessarily be true with snakes. Severe pneumonia is compensated both behaviorally and physiologically. The inactive snake will refuse to eat and move around much. Arching the back at the level of the lungs or resting the head and upper one fourth of the snake in the vertical position is a common way snakes employ to keep purulent exudate from the active respiratory surface. Yawning is frequently observed sometimes with productive mucous.

## **Cage Requirements**

In captivity, cage design and space directly impact the health of the snake. The amount of space required for a snake depends on its genetic potential. As a rule of thumb for both juvenile and adult snakes captive caging should provide at the very minimum the ability to stretch out completely. This requirement is important due to the fact that the lung/air sac are able to completely exchange air in a single respiratory cycle. Cage width is not usually a problem for most snakes. Ideally, the enclosure should be large enough to exercise. Cage size affects several other parameters that impact the reptile husbandry including thermoregulation, humidity, and lastly degree of necessary sanitation.

## **Thermoregulation**

Understanding this concept is central to the health and life of a snake. Obviously, being ectothermic "cold-blooded" has its drawbacks. Especially when you, the reptile, are relying on the owner and your veterinarian to get this concept right. The basic knowledge of each species of snake must be known; continent of origin, climate of origin, period of activity, niche utilized, and chief food source. More detailed knowledge about the snakes microhabitat is useful such as seasonal highs/lows, periods of eating and reproducing etc.... When very little is known about the particular snake (reptile) it is essential to look at the form and function of the anatomy to make an educated guess as to the type of an environment it would come from. For instance, large snakes are not from the desert or snakes with eyes and nostrils located dorsally on the head are primarily aquatic. Consulting references via the internet and other text resources is also recommended for unfamiliar species. Husbandry is a species-specific process and knowledge in it develops over time. Educating clients to this concept is beneficial to their other reptilian pets. Problems can be associated with too large or too small of a cage. The basic goal of captive thermoregulation is to allow the reptile to control its' own temperature according to its biological needs. This concept is achieved through spacious caging that have established microenvironments in them. Cages should have a dry hot area, a warm humid area, a cool dry area, and a cool damp area. The amount and extent of these areas is species dependent. How the areas and environments are achieved is up to the pet owner and guidance from other professionals such as veterinarians and professional herpetoculturalist. Housecall veterinarians may provide the best information for captive environmental manipulations.

Relatively small caging with moderate heat sources will elevate temperatures throughout the cage. This causes loss of a thermal gradient (meaning the temperature is constant throughout the cage and the reptile cannot cool down). Loss of thermal gradients causes reptiles to have to drink more in order to maintain their hydration. Evaporation in small caging also occurs more quickly, which exacerbates dehydration and its effects. Chronic dehydration can lead to renal disease, respiratory disease, and stress that can exacerbate sub-clinical disease. Another potential problem associated with smaller caging is the relative increase in organic load. The larger the snake, the more metabolic waste that is created. More sanitation will be necessary in order to keep the reptile from being exposed to increased loads of organic waste.

Large cages cause fewer problems with overheating and more with under heating. Large cages have significant advantages to larger snakes in the fact that thermoregulation can be achieved by temperature gradients. A combination of heat sources must be used to achieve efficient thermoregulation. Heat lamps/emitters and room temperature (as set for the house) can be used to provide a range of temperatures that will be conducive to health for most species of large snakes. By checking surface and air temperature within the cage and adjusting the distance between the reptile and light, temperature can be controlled fairly efficiently. The simple element of having a large enough space allows the reptile to behaviorally thermoregulate. Heat rocks, heat tapes, and heat lamps cannot be used efficiently by themselves. Combinations of different heat sources may need to be utilized to achieve sufficient temperatures. A thermometer should be placed where heat is being achieved and preferably at the coolest place in the cage. A large range between the high and low temperatures is desirable. The range should encompass the Preferred Optimal Temperature Zone (POTZ).

## **Humidity**

Humidity also impacts thermoregulation and is critical to the respiratory health of large tropical snakes. High humidity holds heat. Dryness allows heat to escape. The concept is best illustrated by observing weather patterns in the tropics. Cloud cover protects the land from evaporation. Evaporation is a cooling process. Less evaporation means there is more moisture in the air and therefore humidity is higher. The water in humid air has a high specific heat, which allows heat to accumulate in collective molecules. Therefore, less change in temperature occurs when nightfall comes because humidity is maintaining the heat in the water molecule. Deserts are relatively dry and cloudless (low rain). As the sun beats down on the earth, evaporation occurs. Water leaves the plant life and turns it brown. As evaporation (a cooling process) occurs temperatures drop tremendously. Temperature variability is great because water has evaporated and is not holding the heat in its collective molecules. For instance, temperatures can be as high as 110 F in the day and 70 F at night in the Sonoran Desert. In the tropical rainforest, temperatures rarely drop below 75 F and where large snakes inhabit rarely over 90 F. Dry cage environments also have drops in temperatures if the heat source is turned off at night. The drop in temperature certainly can be immunosuppressive, especially in captive environments in houses with winters.

When tropical snakes are kept in a dry environment, insensible water loss is greater. Respiratory secretions are viscous. The normal secretions tend to accumulate in the respiratory system. As mucous accumulates, it acts as a medium for potential infections or acute obstructions.

## **Cage Manipulation**

Captive cage manipulation is necessary to simulate the natural environment. Temperature was mentioned previously in the fact that the goal is to have multiple microenvironments set up within the cage. This is achieved best by compartmentalizing heat and water. The warm and dry area should be confined to a large area that is closed off from the cool area in the cage. The cool area in the cage should have water and an appropriate substrate that holds moisture or maintains dryness (depends on species-specific needs). Refer to the general drawing of a compartmentalized cage. If a glass aquarium is used to house a particular snake several inexpensive steps may be done to increase the humidity and maintain a more constant temperature. Screen tops can be partially covered with plastic wrap or Plexiglas. Glass or Plexiglas can be used inside the cage to compartmentalize the heat on one side of the cage. The water may be placed over the top of a heating pad to increase the humidity as well. Also, moisture-holding substrates such as cypress mulch may be used to maintain humidity/heat. Plastic rubber boxes can also be used with appropriate high moisture substrates in them such as sphagnum moss. More expensive and more effective ways of maintaining humidity are using humidifiers. This method also forces cage ventilation measures. Hygrometers are a very effective tool for measuring the cage humidity. Cage perching is also important even in non-arboreal snakes. Perching areas allow larger snakes to use gravity in order to help expel purulent exudate or mucous from the air sacs.

Ventilation and oxygenation of the cage are essential. Both heat and humidity escape as ventilation increases. Experience and studies in herpetoculture and keeping will help in balancing temperature, humidity and ventilation. Captivity management is an oversimplification of the complexity of the natural environment.

## Sanitation

More infections occur in snakes kept in cages that are hard to clean. The type of caging that is hard to clean is typically painted plywood. As mentioned previously, the relative snake size to cage size determines the quantity of organic load that an individual may produce and contact. Many owners of Boidae have the uncontrollable urge to power feed their snake. These fast growing power fed snakes produce copious amount of stool. This makes effective cleaning an essential tool for long term health. Most boids live only 5-7 years of age in captivity as a result from a relatively small cage with high organic loads that eventually leads to both immunosuppression and opportunistic infections. Larger snakes, particularly the boids, are the poster children for pneumonia.

Cleansing agents recommended by the author are warm soapy water and/or bleach, chlorhexidine scrub, and quaternary ammonium compounds. Thorough rinsing and drying are important after using any cleansing agent.

## Differentials and Treatment for Respiratory Dysfunction

Clinical signs associated with respiratory dysfunction can be anorexia, lethargy, weight loss, vomiting, diarrhea, skin opacity, dysecdysis, rostral abrasion, stomatitis, yawning, cyanotic mucous membranes, discharge from glottis, exaggerated breathing, superior ventral/ upper body positioning in the cage, lung elevating, dyspnea, head shaking, abortion/egg retention, and death. Feeding, stooling, and shedding records are an excellent way to suspect subclinical respiratory infection as anorexia, constipation/diarrhea and dysecdysis are physical signs that meticulous keepers can monitor.

Infectious causes of respiratory issues can be of bacterial, viral, fungal, or parasitic etiologies. Bacterial pneumonia is by far the most common. This statement is biased by the fact that bacterial cultures are commonly done as a first diagnostic step. Secondary bacterial infections are being mistaken for primary infections. It is the authors opinion that viral, fungal, and parasitic infections are under diagnosed. Bacterial pathogens of the respiratory tract are primarily gram negative aerobes. *Pseudomonas* sp., *Klebsiella* sp., *Aeromonas* sp., *E. coli.*, and *Proteus* are common isolates in the authors practice. Atypical bacterial are occasionally found including *Mycoplasma* sp., *Chlamydia* sp., and *Mycobacteriosis*. Performing culture and sensitivity on snakes suspected of having bacterial diseases is important for both diagnostics and treatment. The best samples to cultures are those obtained by a transtracheal wash. The mouth opening device of choice for the authors practice is a cookie spatula. Using sterile technique, a red rubber catheter of the appropriate size is inserted into the trachea. A saline filled syringe with up to 1% of the snakes body weight (in fluid volume) is connected to the catheter. The saline is introduced into the snake. The snake is then rolled around up and down for a brief time. The fluid is re-aspirated. It is common to get only a small volume back from this procedure. Cultures and cytology should be done on the fluid.

Antimicrobial therapy should be initiated immediately and changed if the sensitivity deems it necessary. Because most respiratory diseases are chronic upon presentation, the authors treatment for bacterial pneumonia is very aggressive and done for at least a three week period. The preference is to use the same technique for a transtracheal wash. Instead of using a red rubber catheter, a sterile interavenous catheter is used. The normal injectable antibiotic dose is mixed in the syringe with the saline and introduced to the snake being held in the vertical

Viral etiologies are under diagnosed cause of respiratory disease due to the fact that few tests are developed to diagnose them. Many times virally infected snakes have a secondary bacterial pneumonia. The secondary pneumonia is diagnosed by culture or therapeutically treated with antibiotics.

Inclusion body disease of boidae is caused by a retrovirus. Currently it is thought to be transmitted through bites from snake mites (*Ophionyssus natricus*). The author suspects vertical transmission as well (transovarially). The virus causes a multitude of signs and symptoms including anorexia, vomiting (intermittant or chronic), diarrhea, decreased locomotion, respiratory disease and/or neurologic disease. The clinical signs manifested are variable and probably depend on the amount of virus present and the site the virus is infecting. Secondary bacterial infection occur commonly in the respiratory tract, bone, and gastrointestinal systems. Diarrhea and anorexia is usually due to enteritis caused by gram negative bacteria, anaerobes, or protozoal overgrowth. Neurologic signs are variable. Signs may be slight paresis to the classical "star-gazing". Several snakes the author has seen developed a severe spondylolytic osteomyelitis similar to what Frye calls Paget's disease.

There is currently no serologic test available for virus detection as funding thus far has been limited. Current antemortem diagnosis is done by a combination of methods including complete blood counts, endoscopy, and biopsies. White esophageal plaques are sometimes present in snakes that are positive for the viral inclusions. A confirmatory biopsy should be done to identify inclusions. A laparotomy is necessary to perform the liver and kidney biopsy. Eosinophilic intracytoplasmic inclusions are evident in most positively infected animals. This virus is certainly under diagnosed as generalized immune suppression tends to cause further manifestations of more common problems (respiratory disease and enteritis). Inclusion Body Disease of Boids (IBD) is usually not evident until neurologic signs are manifested.

Paramyxovirus is a virus that targets respiratory system. Central nuerologic disease occasionally accompanies clinical respiratory disease. Clinical signs can be subclinical and non-specific or multiple including flaccidity of the body, open-mouthed breathing, tracheal/pharyngeal hemorrhage with mucous, seizures/convulsions and acute death. Cases involving a fer-de-lance involved 4 stages in an epizootic. Stage 1 lasting 5 to 12 days and is characterized by loss of muscle tone and linear body positioning. Stage 2 was characterized by restlessness in the cage with partially opened mouths and lasted 1-2 days. The eyes were also dilated and the tongues were incompletely withdrawn into the sheaths. Stage 3 is marked by a several hours to one day of complete mouth opening and purulent glottal exudate. Stage 4 was seen 1 minute to one hour antemortem. Signs included excessive activity, dilated pupils, and the mouth wide open. Paramyxovirus is primarily in viperid snakes. Titers and clinical disease are seen less commonly but increasingly in boids. Inclusion Body Disease of Boids should be considered as a primary differential. Severe lower respiratory disease including mucous and secondary bacterial invaders may be present.