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Minimizing Trauma to the Upper Airway: A Ferret Model of Neonatal Intubation

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Our objective was to determine whether an adult ferret can be intubated as many as 10 times per training session without resulting in trauma to the upper airway. In this program, 8 male ferrets rotated through intubation laboratories, limiting the use of each animal to once every 3 mo. Animals were examined by the veterinary staff after intubations to assess for trauma to upper airway tissue. Each examination was given a trauma grade of 0 for no visible signs of trauma, 1 if erythema of the larynx was present, 2 if visible excoriation of the mucus membranes was present, and 3 if bleeding (frank hemorrhage) was observed. The number of intubation attempts was restricted to 10 per animal per training session. A total of 170 intubations were completed on the ferrets during a 12-mo period. The average number of intubations per laboratory was 8.1 intubations per ferret. In addition, 1.8% of the intubations resulted in erythema (score, 1) after training, and 0.6% of the intubations resulted in excoriation (score, 2). Frank hemorrhage (score, 3) was not noted. The overall percentage of intubations resulting in any trauma during a training session was 0.02%. None of the animals have experienced any major complications to date. This ongoing training program has been used to teach neonatal intubation skills to emergency medicine residents for the past 12 mo. Ensuring the health and safety of the ferrets was paramount. Our results suggest that as many as 10 intubation attempts per session can be performed safely on each ferret without causing excessive trauma.

Cardiopulmonary arrest in neonatal patients results when respiratory failure or shock is not identified and treated in the early stages.[3] Unlike in adults, cardiopulmonary arrest in infants is due to asphyxial rather than cardiogenic causes; therefore airway management is crucial to pediatric resuscitation.[4] More than 5 million neonatal deaths occur worldwide each year, and asphyxia is estimated to account for 19% of these deaths.[30] Undeniably, early recognition and intervention prevent deterioration to cardiopulmonary arrest and probable death.[9] The emergency medicine physician is often required to rapidly assess and manage pediatric airways. However, a 2008 survey of emergency physicians found that although more than 90% of physicians felt usually or always confident of their skills in performing peripheral vascular access, procedural sedation, fluid resuscitation, tube thoracostomy, managing patients with altered conscious state, cardiac emergencies, behavioral disturbance, and interpreting acid base, and other blood tests, fewer than 50% felt confident managing pediatric respiratory emergencies.[20] Pediatric intubation requires knowledge, skill, and experience; if the procedure is performed by inexperienced providers, it can result in life-threatening complications.[18] A study of the intubation skills of pediatric residents revealed a high failure rate of attempted intubations and several concerning deficiencies in acute airway management.[19] Competency in endotracheal intubation of children is an overlooked, but critical, component of the emergency physician's arsenal.

Historically, intubation training has involved plastic models and kittens (*Felis domesticus*, also known as *Felis catus*). The more advanced plastic models are excellent teaching tools and are used routinely at our hospital to enable residents and interns to gain initial neonatal intubation skills. However, the plastic models continue to lack the 'true-to-life' experience required to obtain the confidence and necessary skills to intubate neonatal patients successfully. A 2006 study comparing the use of mannequins versus the head of a whitetail deer revealed that the real animal tissue provided a superior learning experience for the students.[5] Kittens have served as successful pediatric intubation models in the past;[12] however, because the kittens mature into adult cats, the larynxes become too large to simulate the human neonate patient.

The respiratory system of the domestic ferret (*Mustela putorius furo*) shows remarkable similarities to that of humans. The ferret commonly serves as a model in biomedical research in the field of respiratory disease, including the study of influenza,[17,26] avian influenza A (H5N1) virus,[31] severe acute respiratory syndrome (SARS),[6,23,29] and as an airway xenograft model of cystic fibrosis.[7,28] In addition, the ferret upper respiratory tract is comparable in physiology, appearance, and size to that of human neonatal patients. Therefore, the ferret has proven a beneficial representation for pediatric endotracheal intubation techniques in a previous model.[22] However, in contrast to the aforementioned model, our study revealed that ferrets can be intubated safely more times per session than was previously described.

Naval Medical Center Portsmouth is a tertiary care military teaching hospital, with multiple residencies including emergency medicine. The center annually trains approximately 75 interns of various specialty services (general surgery, internal medicine, pediatrics, obstetrics and gynecology, orthopedics, psychiatry, and transitional). The emergency department treats approximately 80,000 patients annually, with 25% to 33% of those being pediatric patients. There is limited experience with neonatal intubations. We designed a curriculum to use the ferret as a neonatal training model for our emergency medicine residents. This report is intended to describe the number of intubations that resulted in trauma to the ferrets and the methods

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we used to safely perform as many as 10 intubations per animal during each training session.

Materials and Methods

Animals. Conventional male ferrets (n = 8; weight, 1.25 to 1.75 kg) were purchased from Marshall Farms (North Rose, NY). All animals were housed in pairs in 2-story stainless steel ferret cages and allowed to socialize and play in groups in a specially constructed play room. Animals were housed on a 12:12-h light:dark cycle. Animal rooms were maintained at 15 to 17 °C with a relative humidity of 40% to 65% and 12 to 15 air changes hourly. Animals were fed (Global Ferret Diet, Harlan Teklad, Madison, WI) and provided water via water bottles ad libitum. The use of the animals in our training program was conducted in compliance with the Animal Welfare Act and other federal statutes and regulations pertaining to animals and the use of animals in training procedures and adhered to the principles stated in the *Guide for the Care and Use of Laboratory Animals*.[11] The intubation training laboratory was approved by our institutional animal care and use committee. The facility where the training and housing of the ferrets was conducted is fully AAALAC-accredited.

On receipt at the facility, ferrets received individual microchips (Home Again Pet Recovery System, Schering-Plough, Kenilworth, NJ) for identification purposes. Daily health care and maintenance and twice daily rounds for monitoring animal health were completed by the animal care staff. Animals were examined by the attending veterinarian on receipt and after release from a 14-d quarantine. In addition, each ferret was given a physical exam prior to each training session to assess general health status before undergoing anesthesia. During the intubation laboratory, each ferret's laryngeal area was examined after every intubation attempt. Each examination was given a trauma grade of 0 for no visible signs of trauma (normal); 1 if erythema of the larynx was present; 2 if visible excoriation of the mucus membranes was present; and 3 if bleeding (frank hemorrhage) was observed. After the completion of all intubation procedures and before anesthesia was reversed, each ferret was given a final physical exam, with particular attention paid to the laryngeal region and proximal trachea. Animals received annual vaccinations as required, annual heartworm testing for *Dirofilaria immitis*, and annual deworming as required. In addition, each animal received monthly heartworm prevention consisting of ivermectin at a dose of 0.006 mg/kg PO (Heartgard, Merial, Duluth, GA). Plastic balls and PVC pipe were placed in a dedicated playroom for daily environmental enrichment and to allow social interaction. A lambswool sheet was provided for bedding, along with cloth hammocks, washable 'snooze tubes,' and a mouse cage to serve as a house. Treats appropriate for the species also were provided. In addition, all ferrets received daily human interaction via treats, gentle handling, and monthly bathing and nail clipping.

Training course design. Before any in vivo training, all emergency medicine residents began the course by practicing intubation techniques on pediatric mannequins. Most residents had limited experience with neonatal intubation and had not received prior training with live animals. On completion of mannequin training, the students then proceeded to the live-tissue training portion of the course. All residents received a 30-min didactic session before starting the intubation procedure. The session detailed specifics regarding indications, complications, and techniques of pediatric and neonatal intubation. In addition, the attending veterinarian instructed all residents in general ferret health, upper airway anatomy, and special considerations for the use of the ferret as laboratory animal. Once the classroom session was complete, all residents entered the procedural portion of the training course.

Animal protocol. Ferrets were divided into groups of 2 or 3. One group was used per training session, with intubation laboratories performed once monthly. Emergency medicine residents participated in each session, which was staffed by an attending emergency physician trained in ferret intubation. During each intubation laboratory, a maximum of 3 ferrets were used. Our training protocol allowed each ferret to participate in a training laboratory once every 3 mo. Before induction of anesthesia, ferrets were fasted for 12 h and were allowed access to water until 1 h prior to induction. Animals then received acepromazine (0.1 to 0.3 mg/kg SC, 25-gauge needle) for mild tranquilization and glycopyrrolate (0.01 mg/kg SC, 25-gauge needle) to counteract salivation and reflexive bradycardia due to vagal stimulation during intubation. At 20 to 30 min after premedication injections, a combination of tiletamine–zolazepam (1.5 mg/kg) and xylazine (1.5 mg/kg) were injected subcutaneously with a 25-gauge needle. Ophthalmic lubricant was applied to the eyes once sedation was achieved. The animals were placed in dorsal recumbency on a heated operating table. Strips of rolled gauze were used to hold the animals' jaws gently open and to allow insertion of the laryngoscope (Figure 1). Cotton-tipped applicators were used to apply 2% lidocaine topically to the vocal cords to prevent laryngospasm. Depth of anesthesia was monitored every 10 min during the exercise and as the ferret awoke from anesthesia. A stethoscope was used to monitor heart and respiratory rates. Veterinary staff also monitored mucus membrane color and capillary refill time throughout the procedure and during recovery. The gag reflex was used to determine whether additional anesthesia was needed; a small amount of gag reflex was expected to be present when the tracheal tube passed between the laryngeal folds. However, if the gag reflex persisted or the animal started chewing, additional anesthesia in the amount of 1/4 to 1/2 of the initial dose of tiletamine–xylazine would be given; we have not encountered this situation to date, as the procedure usually was completed in 10 to 15 min.

Intubation procedure. As many as 10 physicians rotated through each laboratory for pediatric intubation training. The safety and health of the ferrets was paramount, and intubation training was monitored closely by instructors and the veterinary staff. At the beginning of the procedural portion of the laboratory, an instructor discussed and then demonstrated correct endotracheal intubation of the ferret. After the demonstration and under close supervision by the instructor, each student then was allowed to intubate the ferret with a 2.5-mm endotracheal tube by using a laryngoscope equipped with a straight blade (size 0). Figure 2 shows a view of the glottis as seen through the laryngoscope. Each resident was given a chance to intubate a ferret correctly. Students observed to be having difficulty with the intubation procedure received additional 'bedside' instruction by the instructor on intubation procedures. Successful endotracheal intubation was confirmed through use of a pediatric end-tidal CO_2 detector (Figure 3), as is currently recommended for pediatric intubation practices.[2] End-tidal CO_2 detectors quantify the amount of exhaled carbon dioxide and allow the operator to determine whether or not the endotracheal tube has been inserted into the trachea. An indicator color change from purple to yellow denotes the presence of carbon dioxide. A separate CO_2 detector was used for each ferret during the intubation session, and each session was short enough to allow for repeated use of the CO_2 detector. Each

Figure 1. Insertion of the laryngoscope in an anesthetized ferret.

Figure 2. View of the glottis as seen through the laryngoscope; ferret positioned in dorsal recumbency.

ferret was examined by a member of the veterinary staff after every intubation attempt to assess for trauma to upper airway tissue. A maximum of 10 intubation attempts were allowed for each animal. Any trauma to the larynx or trachea resulted in immediate removal of that animal from the training laboratory. A more detailed examination of the entire upper airway then was performed by the attending veterinarian to assess the animal's condition and provide treatment as required.

After the laboratory session, yohimbine (1 mg/mL; 1.5 mg/kg, SC) was administered to reverse xylazine-induced bradycardia and to reduce recovery time and minimize potential anesthetic complications. Reversal of the effects of xylazine usually began to occur within 3 to 4 min after injection of yohimbine. To reduce possible edema and inflammation, dexamethasone (0.5 mg/kg SC) was administered once postprocedurally to all ferrets. Animals recovered in a warmed incubator and were monitored closely during the recovery period. Once fully alert and active, ferrets were returned to their cages and monitored by the animal care staff. Canned kitten food was offered to each ferret as an alternative to their regular diet for 24 h after undergoing intubation. Any ferret that we felt might be experiencing discomfort received 1/2 of an 80-mg baby aspirin (or other analgesic as determined by the veterinarian). Ferrets were

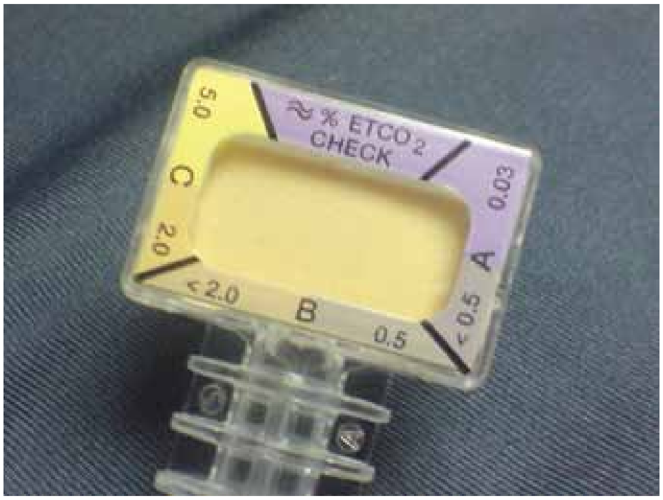

Figure 3. End-tidal CO_2 detector.

reevaluated by the attending veterinarian for signs of discomfort the morning after the laboratory.

All ferrets eventually will be retired from the protocol at the discretion of the attending veterinarian and investigator and will be adopted as pets. Retired ferrets may be replaced by alternates in the laboratory in order to continue the training protocol for future emergency medicine residents.

Results

During a 12-mo period, a total of 170 intubations were completed on the 8 ferrets. The range of intubations was 6 to 10 intubations per ferret during each of the training laboratories. The average number of intubations during the training sessions was 8.1 intubations per ferret. Examination after each intubation revealed that 2 of the animals had erythema in the laryngeal region, and another 1 ferret had visible excoriation of the mucus membranes. One of the 2 ferrets with erythema had erythema in the laryngeal region twice during other training laboratories, therefore giving a total of 3 episodes of erythema. The percentage of ferrets having erythema during the training sessions was 1.76%. Visible excoriation of the mucus membranes was observed once, giving a 0.6% rate of occurrence. No frank bleeding was observed (Table 1). Therefore, as determined by a goodness-of-fit test, the probability that a ferret may sustain any trauma to the laryngeal region during a pediatric intubation training laboratory was 0.02. None of the animals have suffered any major complications as a result of trauma to the laryngeal region. All of our ferrets have recovered well from the procedure, and no changes in appetite or activity have been observed.

Discussion

This ongoing training program has been used successfully for the past 12 mo. We have found that as many as 10 intubation attempts can be performed safely on each ferret without resulting in trauma. Each resident generally required 2 to 3 attempts at intubation before successful intubation was achieved. The instructor monitored each student's attempts, and successful intubation was verified by use of a CO_2 detector.

Airway management is the most essential skill in emergency medicine.[27] However, the emergency physician's lack of confidence in pediatric intubation techniques has been confirmed through surveys[20] and verified by our own residents. Pediatric specialists stress that adult-oriented health care providers should not be inhibited from the emergency care of a child's

Table 1. Frequency and percentage of observations of trauma in intubated ferrets

Description (grade)	Frequency	%	95% Confidence interval
No visual trauma (0)	166	97.64	0.939–0.993
Erythema of larynx (1)	3	1.76	0.004–0.053
Excoriation of mucus membranes (2)	1	0.06	<0.001–0.036
Bleeding (3)	0	0.00	0.000–0.027

airway from fear of doing harm if there is no pediatric specialist immediately available.[4] Skillful intubation can mean the difference between life and death in the infant experiencing respiratory failure, and it is the goal of our training to provide competency in this procedure to our emergency medicine residents. There are advantages and disadvantages to each of the traditional methods of airway training, including the use of animals.[24] Ethical and logistic concerns provide motivation for seeking alternatives. The aim of future critical care teaching methods is to reduce or eliminate the need for live tissue training through replacement with high-quality and effective new measures. New endeavors into this field, such as 'augmented reality technology,' provide prospects for the development of suitable models of intubation. However, even the creators of the augmented-reality system acknowledge that this new technology is envisioned as a supplement to, rather than a replacement for, current methods of teaching.[13] Therefore, the need for traditional models of intubation has not yet been eliminated.

The current study used an alternate species in place of live humans; for ethical reasons, training cannot be performed on human infants. Mannequins are used as an adjunct to our ferret training, but do not replace experience with a breathing animal, and the difficulties that may be associated with intubating a live being. Ferrets were used because of their anatomical similarities to human infants—the airway of an adult ferret is similar in size to a human neonate.[1] The domestic cat, although useful as an intubation model, has a larynx that is too large to simulate that of an infant. Informal surveys of students upon completion of the lab have revealed a marked increase in confidence in intubation skills. However, only emergency medicine residents, with a relatively predictable and consistent set of skills, enroll in our course, and their outcome may not necessarily reflect the benefits that might be gained by a group of trainees with a broader range of intubation abilities and experiences.

Our study has several relevant differences from the ferret model of pediatric intubation published in 1991.[22] In that study, 29% of ferrets showed trauma to the larynx or trachea after 5 attempts; 100% of animals that were intubated 10 times or more experienced trauma. In contrast, our intubation procedures allow each animal to support as many as 10 intubation attempts with minimal risk of sustaining trauma to the larynx. Our methods differ from this previous model in several key ways. For instance, the earlier protocol used both male and female ferrets weighing between 0.64 and 1.44 kg, which were intubated with 2.5- to 3.0-mm endotracheal tubes. We have attempted to minimize trauma by using only large male ferrets between 1.25 and 1.75 kg and intubating with the 2.5-mm tubes. Ferrets were examined for injury after each intubation attempt in our study, whereas in the earlier study, trauma was assessed only on necropsy after 5, 10, 15, and 20 intubations. Our method of frequent appraisals allows us to withdraw an animal from the laboratory as soon as minimal trauma is detected. Dexamethasone is administered postprocedurally to all animals during our training sessions. In clinical trials, dexamethasone has been shown to reduce postextubation inflammation, airway obstruction, and laryngeal edema in both animals and humans,[8,14-16] as well as to ameliorate sore throats in humans.[21,25] Also in contrast to the previous study, in which intubations were performed over a period of 45 to 60 min, our intubations typically are completed within a shorter time frame (5 to 10 min), minimizing the period of anesthesia. Importantly, we use a pediatric end-tidal CO_2 detector to verify correct placement of the endotracheal tube. We have found that use of the CO_2 detector is paramount in confirming reliable placement of the endotracheal tube. Many participants believe they have successfully intubated the ferret when the tube is actually in the esophagus. The detector easily confirms placement with the animal's normal breathing pattern. Conversely, placement of the endotracheal tube in the earlier study was determined by ausculting bilateral breath sounds or by observing condensation in the tube during exhalation. In addition, all of our students receive training on mannequins prior to attempting intubation on live animals, in order to gain initial procedural skills. Students also attend a didactic session before the laboratory to develop a better understanding of the upper airway anatomy and special considerations for the use of the ferret as an intubation model. Our procedure represents both a reduction in animal use and a refinement of an existing animal model for neonatal intubation. By using these minor methodologic adjustments, we were able increase the number of intubations per animal while reducing the incidence of laryngeal trauma after 10 intubations from the historic 100% to just 2%.

Due to ferret anatomy, intubation techniques have been modified for this course. Although the ferret is an ideal neonatal model, some important differences should be considered prior to and during intubation training. One key point is that the ferrets are sedated rather than paralyzed. The normal use of a straight blade mounted on a laryngeal scope is to lift up the epiglottis and directly visualize the vocal cords. This method would be the standard technique in an unresponsive neonatal patient or 1 who was paralyzed during rapid sequence induction. However, ferrets are difficult to intubate if the blade is placed deep enough in the hypopharynx to lift the epiglottis. We find that once the blade tip enters the hypopharynx, a gagging reflex is produced. However, placing the straight blade in the vallecula (depression on each side of the median glossoepiglottic fold) to lift the epiglottis indirectly produces almost no gag reflex. We continue to use only a straight blade (size 0) instead of a curved blade, because we believe that a straight blade is most likely to be used during a human neonatal intubation procedure.

If any degree of trauma is observed at any point during the training, the ferret is retired from the session immediately and examined by veterinary staff to determine appropriate treatment. The animals receive a reasonable period of rest between training sessions. Limiting use to a maximum of 1 session every 3 mo has been well tolerated by the animals. Ultimately, all animals will be retired from the program and offered as pets. A previous survey of laboratory ferret adopters revealed that 91% of former instructional ferrets rated as good or excellent pets.[10] The ferret model and procedures outlined here allow as many as 10 intubations per animal during each training session. To better quantify the benefits of this model in teaching intubation technique, we plan to conduct a future study to assess the confidence levels and procedural skills obtained from the in vivo training course versus that of training strictly with mannequins.

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