Endoscopic evaluation of bronchial morphology in rabbits

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**Objective**—To evaluate bronchial morphology endoscopically in rabbits and develop a valid nomenclature for the endobronchial branching pattern.

**Animals**—10 mature New Zealand White rabbits.

**Procedures**—Flexible bronchoscopy was performed in rabbits anesthetized with isoflurane via nasal mask. Airways were systematically evaluated from the larynx to the terminal branches accessible with a 2.5-mm–outer diameter flexible endoscope. Airway branching patterns were identified and assessed for variation among subjects.

**Results**—Airways of all rabbits were readily examined with the 2.5-mm flexible endoscope. Laryngeal structure and function were normal in each rabbit, and airway branching patterns in all rabbits evaluated were identical. At the carina, branching into left and right principal bronchi was evident. The left principal bronchus divided immediately into the left cranial lobar bronchi. The left cranial lobe bronchus further divided into dorsal and ventral segmental bronchi. The left cranial lobe bronchus gave rise to branches originating dorsally, ventrally, and medially before continuing caudally. The right principal bronchus divided into the right cranial, right middle, and accessory lobar bronchi and continued distally as the right caudal lobar bronchus. The right cranial lobe bronchus also divided into dorsal and ventral segmental bronchi, and the right caudal lobe bronchus had branches that originated dorsally, ventrally, and medially.

**Conclusions and Clinical Relevance**—Definition of a standard nomenclature for airway branching in rabbits will allow precise localization of disease in clinical cases and accurate collection of airway samples in clinical and scientific evaluations. (Am J Vet Res 2007;68:1022–1027)

Bronchoscopy is a valuable tool in diagnosis and management of diseases of the lower portion of the respiratory tract in dogs, cats, horses, humans, and dolphins. This noninvasive technique is commonly used as a clinical tool for evaluation of respiratory tract disease and as a research tool for investigation of drug distribution in the respiratory tract or in assessment of response to treatment. Systematic classification of endobronchial morphology has long been established in human medicine, and such features have been described in dogs, horses, and dolphins. Knowledge of airway morphology has proved invaluable for visual inspection of a specific site within the lung as well as repeated sampling from a single lung region.

Of the mammalian species, other than primates, that have been evaluated to date, a monopodial or asymmetric branching pattern has been described, which is characterized by branching of each parent airway into 2 branches of unequal size, length, and diameter. Some methods for describing the morphology of airways attempt to incorporate this irregular dichotomy of branching through numeric identification systems that distinguish larger from smaller branch airways. Others have used sequential labeling of airways as they are encountered bronchoscopically or a combination of sequential labeling and identification of the origin of branching. Rabbits are commonly used in experimental evaluations of various pulmonary diseases, to assess airway deposition of particulate matter in air pollution studies, and for pharmacologic studies of aerosol drug distribution. In addition, pet rabbits are commonly affected by respiratory tract disease that can be clinically and radiographically unapparent, suggesting that development of bronchoscopy as a diagnostic procedure would be a valuable clinical tool. Evaluations of airway casts have established airway morphology in rabbits through determination of length, width, and branching angles of airways; however, clinical evaluation of these variables has not been performed. The purposes of the study reported here were to evaluate the airways bronchoscopically for uniformity in airway branching patterns and to develop a standardized nomenclature for airway branching in rabbits.

**Materials and Methods**

Ten mature sexually intact New Zealand White rabbits ranging in body weight from 2.75 to 4.35 kg that had been recently culled from other research protocols were transferred for use in this study. No respiratory procedures had been performed, and all rabbits were healthy. All stud-
ies were approved by the University of California, Davis, Internal Committee on Animal Care and Use. Rabbits were sedated via IM injection of xylazine and ketamine (3 mg/kg and 30 mg/kg, respectively). A rodent cheek dilator and mouth gag were fitted in place, and rabbits were maintained on a mixture of isoflurane (≤2%) and oxygen via nasal mask throughout the procedure. Bronchoscopy was performed with a 3.8 mm × 55 cm videobronchoscope for image capture and a 2.5 mm × 100 cm flexible fiberoptic endoscope for complete airway evaluation. Airways were systematically examined, and representative images and digital videos were recorded with a digital-image-capture system. Repetitive airway branching patterns were identified and subsequently described by determining the orientation of branching from the primary bronchus in comparison to a 12-hour clock face (ie, a branch originating from the dorsal aspect of the bronchus was assigned the 12-o’clock position). Primary, lobar, segmental, and subsegmental airways were identified and compared via standard nomenclature as used in dogs.

At the end of the procedure, rabbits were euthanized with an overdose of IV barbiturate. Lungs were immediately removed from the thoracic cavity and rinsed free of blood by continual rinsing with water. Dried lung models were made by use of constant inflation with air through the trachea for 48 to 72 hours, as described. Airway casts were made from 4 lung models by injecting colored latex into the trachea, allowing the material to set, and digesting existing tissue by immersion in sodium hypochlorite. Bronchoscopic morphology was determined by comparison of digital images to latex casts of the airways.

Results

Viewing the larynx required displacement of the soft palate. The epithelial surface of the larynx was hyperemic and granular in appearance in all rabbits. Corniculate processes of the arytenoid cartilages were seen dorsolaterally as broad cartilage plates. Ventrally, the epiglottis was prominent and visible as 2 vertically oriented protrusions (Figure 1), and the origin of these structures was confirmed via postmortem dissection. Laryngeal abduction was seen on inspiration in all rabbits. Mild laryngospasm was encountered during endoscopic intubation, but the larynx was easily entered because of use of the endoscope.

The 3.8-mm endoscope provided excellent observation of the trachea and principal bronchi with divisions into the primary lobar bronchi. In the proximal...
cervical region, tracheal rings appeared U-shaped, which gave a slight elliptical appearance to the largest airway at its origin (Figure 2). The epithelium covering the rings was markedly hyperemic in each rabbit, and the submucosal vasculature was not visible. At the level of the carina, airway hyperemia resolved fairly abruptly, and the remainder of the examination revealed pale-pink epithelium with visible bronchial vasculature. A mild glistening appearance to the airways was considered to represent normal respiratory secretions, and no mucus accumulation was seen in any rabbit. The carina was readily identified by the iniminate branching into the left and right principal bronchi, which were designated the LPB and RPB, respectively (Figure 3). The carina was sharply angled in all rabbits, the left mainstem bronchus appeared to have a slightly smaller diameter than the right, and the angle of bifurcation for division into the left and right lung lobes was symmetric.

To enter all lobar bronchi and identify segmental branching within each lobe, the 2.5-mm endoscope was required. Endobronchial morphology and appearance were essentially identical in all rabbits. A system of nomenclature that used a combination of sequential labeling with identification of the origin of branching was adapted from nomenclature used in dogs (Figure 4). The primary difference between the 2 species was evident in the cranial lung lobes. In dogs, the left cranial lung lobe has a distinct exterior margin that divides the lobe into cranial and caudal subsegments, and the caudal subsegment of the left cranial lobe forms a pseudo–left-middle lung lobe. In rabbits, the exterior aspect of the left cranial lung lobe was not subdivided into cranial and caudal segments and the first lobar bronchus (designated LB1) arose from the lateral aspect of the LPB and continued into the left cranial lung lobe. The LB1 divided immediately into dorsal and ventral segments (Figure 5).

The caudal continuation of the left principal bronchus was designated LB2. The first dorsal branch from LB2 (designated LB2D1) arose at the 10- to 12-o’clock position almost directly opposite the branching into LB1, and the first ventral branch (designated LB2V1) arose at the 4- to 5-o’clock position slightly caudal to the dorsal branch (Figures 5 and 6). These segmental airways could be entered with the 2.5-mm endoscope in some but not all rabbits and immediately divided into smaller branches. An extremely small medial branch that was too narrow to allow entry of the bronchoscope originated from the 7- to 8-o’clock position from LB2. From the continuation of LB2 caudally, a dorsal, ventral, and medial branch originated from the parent bronchus in a spiral fashion with slight changes in orientation from the parent branch (Figures 4 and 6). In individual rabbits, LB2 could be followed to the level of the third to fourth segmental bronchi. Beyond this point caudally, the branching pattern became less obviously oriented in ventral and dorsal positions because of the closeness of the individual branches.

The RPB originated at the carina, and the opening to the right cranial lobe (designated RB1) was visible at

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**Figure 4**—Diagram of the bronchial tree of a rabbit (dorsoventral view [with the rabbit in sternal recumbency]). The left cranial lobar bronchus (LB1) bifurcates into ventral (LB1V1) and dorsal (LB1D1) segments. The left caudal lobar bronchus (LB2) gives rise to dorsal (LB2D1), medial (LB2M1), and ventral (LB2V1) branches. A second series of dorsal (LB2D2), medial (LB2M2), and ventral (LB2V2) branches are also illustrated. The right cranial lobar bronchus (RB1) branches into dorsal (RB1D1) and ventral (RB1V1) segments. The right middle lobar bronchus (RB2) and accessory lobar bronchus (RB3) give rise to several smaller branches. The branching pattern of the right caudal lobar bronchus (RB4) mimics that of LB2, with dorsal (RB4D1), ventral (RB4V1), and medial (RB4M1) branches arising as the first series, followed by a second series (RB4D2, RB4V2, and RB4M2).

**Figure 5**—Endoscopic view of the openings to LB1 and LB2 in a rabbit. Notice that LB1 immediately branches into LB1D1 and LB1V1. The LB2D1 is also evident. See Figure 4 for key.
9 o’clock. The right middle lung lobe bronchus (designated RB2) was found at 6 o’clock, the accessory lung lobe bronchus (designated RB3) originated from the medial aspect of the RPB at 3 o’clock, and the bronchus to the right caudal lobe (designated RB4) represented the continuation of the right principal bronchus (Figure 7). Bronchial divisions in the right cranial lung lobe were similar to those in the left, with dorsal and ventral segmental branches originating from the primary lobar bronchus. The right middle lobar bronchus gave rise to lateral and medial branches, whereas the accessory lobe bronchus gave rise to dorsal and ventrally oriented segmental bronchi. The branching pattern in the right caudal lung lobe mimicked that found in the left caudal lobe. The first dorsal branch of the right caudal lobe (RB4D1) arose at the 10 o’clock position and divided into 2 smaller airways. The ventral branch (RB4V1) arose at the 7 o’clock position and a small medial branch at the 4 o’clock position. The second series of dorsal, ventral, and medial branches was oriented in a spiral fashion off the right caudal lobar bronchus (Figure 8). In individual rabbits, RB4 could be followed to the level of the third to fourth segmental bronchi.

Measurements of airway diameters made from lung casts were not considered likely to represent actual diameters in vivo because the dried lung model from which the casts were made shrinks during processing; however, the relative diameters of the branching airways could be interpreted. The airways branched in monopodial fashion, and ventral branches were consistently slightly larger than dorsal branches. The medial branches detected in the caudal lobes were extremely small.

Discussion

The lungs of all rabbits comprised left and right lung lobes. At the carina, the trachea bifurcated into left and right principal bronchi at a relatively acute angle. The angle of bifurcation was slightly different from that typically seen in horses, dogs, and cats, in which the right principal bronchus can appear as a continuation of the trachea, with less angulation from the trachea than the left principal bronchus. In all rabbits, the left principal bronchus subjectively appeared to have a smaller diameter than the right. This is consistent with 1 author’s (LRJ) experience in other species such as dogs, cats, and pigs, in which the left mainstem bronchus is of somewhat smaller diameter than the right. It is also consistent with a report of children in which the diameter of the left mainstem bronchus is 79% that of the right.
Flexible bronchoscopy in the 10 mature rabbits reported here revealed reproducible findings in airway morphology. The left lung consisted of cranial and caudal lung lobes, and the right lung consisted of cranial, middle, accessory, and caudal lobes as is typical of dogs, cats, and horses. Bronchoscopic images and dissections of lung casts revealed a similar branching pattern in all rabbits examined, suggesting that the proposed nomenclature for airway morphology will be useful in clinical and research applications. The benefits of defining the airway branching pattern include the ability for repetitive sampling of specific lung segments, localizing disease to certain lung segments, and facilitating interpretation of radiographs. Specific nomenclature will also prove useful in standardizing clinical and research investigations of respiratory physiology and disease in rabbits.

The branching pattern of rabbit lungs has been described by use of the Horsfield scheme, which incorporates the asymmetry in airway branching that has been detected in animal species. The Horsfield scheme catalogues airways by starting at the terminal airways and moving proximally. Although useful in estimating pulmonary mechanics and determinants of airflow, the technique has little application to clinical medicine or in vivo research studies. In contrast, bronchoscopic evaluation of the airways originates in the trachea and progresses through the airways distally, thus providing a readily followed map of the airway.

The branching pattern of airways in the rabbits examined here was monopodial, as has been described in most other animal species, with a series of segmental bronchi originating dorsally and ventrally from the parent lobar bronchi. In the caudal lobes, a small medial segmental bronchus was evident. This is in contrast to the dichotomous airway branching observed in humans and nonhuman primates. Knowledge of this branching pattern is of value when performing bronchoscopy because the largest airway is always the parent (lobar) bronchus and gives rise to smaller branches. In rabbits, ventrally oriented branches were consistently larger than dorsally oriented branches. Similar to the morphology of the lungs of dogs and horses, segmental bronchi originated in spiral fashion from the caudal lobar bronchi.

Use of flexible bronchoscopy allowed viewing of all lobar bronchi in the rabbits, and segmental airways could be entered with the smaller endoscope. Evaluation of the extent of the bronchial tree in various species is related to the size of the patient and the bronchoscope, and it is unlikely that an endoscope with > 3.8-mm outer diameter would be of any use in rabbit species, other than allowing an assessment of the upper portion of the airway and trachea. A flexible endoscope with < 2.5-mm outer diameter would likely provide access to more subsegmental airways, although the usefulness of a smaller endoscope could be limited by a smaller field of view and insufficient light transmission. Rigid bronchoscopy with a smaller telescope might provide good viewing of the primary airways; however, maneuverability through the airways with this type of endoscope is limited, and the technique was not evaluated here.

Bronchoscopy was performed with ease in all rabbits reported here. In a preliminary study, 2 rabbits were anesthetized with only the injectable anesthetic agents used as induction agents in this study, and both had marked airway responses and coughing during the procedure, which precluded a complete examination. When inhalant anesthesia was used in combination with the injectable induction medications, rabbits tolerated the procedure readily and examinations could be performed in 15 to 20 minutes. Although this was the only anesthetic protocol evaluated in the bronchoscopic procedure reported here, in clinical practice or in research applications, other anesthetic protocols could be equally effective in minimizing airway responses during the procedure.

An important finding in all rabbits was evidence of severe hyperemia in the trachea. The deep-red color of the epithelium typically did not involve the dorsal tracheal membrane and vanished relatively abruptly at the level of the carina. This finding has been reported when rabbits are used for pediatric bronchoscopy, and because it was seen in the 10 rabbits reported here, it is possible that this is normal for rabbits, whereas the mucosa of the trachea is pale pink in dogs and cats. It is also possible that the hyperemia represented a response to environmental irritants, chemicals, or pathogens that were in the housing environment of these laboratory rabbits. In dogs, diffuse bronchial hyperemia is associated with airway inflammation, such as with chronic bronchitis or cosmetic bronchopneumopath; however, focal tracheal hyperemia has not been reported. Further examination of rabbits with and without respiratory tract disease as well as histologic examinations are required to determine the effect of pathologic processes on the appearance of tracheal and bronchial mucosa.

References