

NHLBI Workshop
Developmental Aspects of the Upper Airway

Executive Summary

The upper airway serves three important functions: respiration, swallowing, and speech. In order to accommodate these functions its shape is actively modulated neuronally, but is passively collapsible at times. During development it undergoes significant structural and functional changes that affect its size, shape, and mechanical properties. Another important characteristic of the upper airway is that it is a virtual conduit. Its anatomical boundaries are defined by other tissues that determine its properties at each moment. Abnormalities of the upper airway require prompt attention since these often alter ventilatory patterns and gas exchange, particularly during sleep when upper airway motor tone and ventilatory drive are diminished.

Treatment options for severe upper airway anomalies are predominantly surgical, are marginally efficacious, and often create other long-term morbidities. While these treatment options are helpful, they do not address the underlying pathology. Difficulties in maintaining upper airway patency arise in intensive care units when neonates and children fail extubation due to poor upper airway control and for 20% of children who fail to resolve obstructive sleep apnea after tonsillectomy and adenoidectomy. Improvements of effective intervention remains limited by a lack of knowledge regarding molecular mechanisms of development, growth, and neuromotor responses to maintain a functional upper airway.

Recognizing the relationship of early life events on lung health and disease, the National Heart, Lung, and Blood Institute (NHLBI) convened extramural experts, from many disciplines (neonatology, pediatrics, otolaryngology, plastic surgery, bioengineering, imaging, sleep disorders, lung development, genetics), at a Workshop "Developmental Aspects of the Upper Airway" on March 5-6, 2009.

The objective of the workshop was: 1) To review the state of science in pediatric upper airway disorders; 2) To make recommendations to the Institute to fill gaps; 3) To prioritize new research directions; and, 4) To capitalize on scientific opportunities. Experts from multiple fields participated, who made recommendations that could facilitate translation of basic research findings into practice to better diagnose, treat, and prevent airway compromise in children. The priority areas identified for research in upper airway development included: 1) Larynx/trachea/soft tissue development, 2) Craniofacial development, 3) Neuromotor development, and 4) Evaluation of the upper airway using imaging and other techniques.

Recommendations:

- Define the epidemiology, natural history, genetic and epigenetic basis of syndromes that impact the upper airway, with the goal of understanding the molecular biology of normal and abnormal upper airway development
- Creation of animal models to aid in the understanding of both congenital and acquired upper airway anomalies.
- To determine strategies for prevention of iatrogenic injury and improve interventions for upper airway compromise

- Define the role of developmental plasticity in neuromotor control of the upper airways.
- Understand the modifying effects of infection/inflammation on neuromotor responses of the upper airway
- Determine the state dependence (wake/sleep) of neuromotor activity to protect against upper airway compromise
- Determine the developmental changes in upper airway anatomy and function during childhood (neonatal through puberty), across genders, and ethnicities.
- Apply imaging modalities or other techniques to determine the pathophysiological mechanisms that lead or predict morbidity in children with altered upper airway anatomy and or function
- Study upper airway mechanics using advanced dynamic imaging modalities

The meeting was held on March 5-6, 2009 in Bethesda, Maryland

Workshop Members

Co-Chairs—Carole Marcus, M.D. (Philadelphia, PA), Richard Smith, M.D., (Iowa City, IA);

Participants— Raanan Arens, M.D. (Bronx, NY), Ravindhra G. Elluru, M.D., Ph.D. (Cincinnati, OH), Vito Forte, M.D. (Toronto, Ontario), Steven Goudy, M.D. (Nashville, TN), Ethylin Wang Jabs, M.D. (New York, NY), Alex A. Kane, M.D., (St. Louis, MO), Eliot Katz, M.D. (Boston, MA), Leila Mankarious, (Boston, MA), Gordon S. Mitchell, Ph.D. (Madison, WI), David Paydarfar, M.D. (Worcester, MA), Kevin D. Pereira, M.D., M.S. (Baltimore, MD), Joseph M. Reinhardt, Ph.D. (Iowa City, IA), Roger H. Reeves, Ph.D. (Baltimore, MD), Joan T. Richtsmeier, Ph.D., (University Park, PA), Ramon L. Ruiz, D.M.D., M.D. (Orlando, FL), Elisabeth B. Salisbury (Worcester, MA), Bradley T. Thach (St. Louis, MO), David E. Tunkel (Baltimore, MD), Jeffrey A. Whitsett, M.D. (Cincinnati, OH), David Wootton, Ph.D. (New York, NY)

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