

*Diseases of the Oropharynx  
and Esophagus*

Chair: P. Jay Pasricha, MD

Vice Chair: David A. Lieberman, MD

# Research Goal 1

Understand the neurobiology of oropharyngeal structure and function in health and disease.

# Research Goal 1

## Objectives

- Develop useful animal models of oropharyngeal swallowing disorders to facilitate neuropathological studies of central and peripheral components and evaluate the effects of interventions directed at specific molecular and/or cellular targets.
- Conduct clinical studies of recovery and plasticity with creative use of functional imaging and novel interventional techniques.

# Research Goal 1

## Objectives (continued)

- Understand physiological and pathological communication between the functional components of the aerodigestive tract.
- Understand the effects of gastroesophageal reflux on the airways including the larynx and bronchi.
- Define the effects of sleep abnormalities on upper GI tract physiology.

## Research Goal 2

Fully understand the clinico-pathological mechanisms leading to and/or associated with GERD and identify novel molecular, physiological and anatomical targets for more effective and rational treatment.

# Research Goal 2

## Objectives

- Understand the clinical spectrum, outcomes and natural history of childhood reflux and its relationship/evolution into adult patterns of disease.
- Validate and develop more effective and/or less invasive long-term approaches to GERD and identify more precisely the clinical, anatomical and/or functional predictors of response.

# Research Goal 2

## Objectives (continued)

- Understand the biological basis of gastroesophageal reflux, hiatal hernia and GERD-associated esophageal dysmotility, including the role of biomechanical factors and longitudinal muscle.

# Research Goal 3

Define the mechanisms responsible for esophageal injury and repair with particular emphasis on the interactions between components of the esophageal wall (epithelial, neuromuscular and neurohormonal, interstitial, and immunological).

# Research Goal 3

## Objectives

- Elucidate mechanisms of increased permeability in esophageal epithelium.
- Understand the role of neural and muscular elements in modulation or enhancement of esophageal injury.
- Characterize acute and chronic mechanisms responsible for esophageal epithelial squamous cell repair.

# Research Goal 3

## Objectives (continued)

- Determine the role of food/aero /environmental allergens in promoting eosinophilic esophagitis and the underlying mechanisms.
- Define basic pathogenic mechanisms by which eosinophils mediate esophageal dysfunction- eosinophil homing, esophageal contraction, and fibrosis.

# Research Goal 4

Understand the epidemiology, natural history and outcomes of eosinophilic esophagitis and identify targets for more rational and effective therapy.

# Research Goal 4

## Objectives

- Determine risk factors, natural history and outcomes of patients with eosinophilic esophagitis and identify biomarkers for disease activity and progression.
- Identify novel targets and interventions for more effective and rational therapeutic approaches to eosinophilic esophagitis and other inflammatory disorders of the esophagus.

# Research Goal 5

Understand the etiopathogenesis of Barrett's esophagus, determine risk factors associated with its progression and identify novel targets and/or therapies for its chemoprevention and treatment.

# Research Goal 5

## Objectives

- Understand the initiation of Barrett's with particular emphasis on identifying the putative stem cell and studying its biology.
- Define the contribution and etiopathogenic role of environmental (e.g. smoking) and genetic/familial factors in the development of Barrett's.

# Research Goal 5

## Objectives (continued)

- Develop biomarkers that reliably predict dysplastic and neoplastic progression.
- Identify novel molecular targets for pharmacological approaches to restoring a stable epithelial phenotype in patients with Barrett's esophagus.

# Research Goal 5

## Objectives (continued)

- Conduct (plausible American ?) chemoprevention studies in subjects with Barrett's based on molecular pathways identified through ongoing studies on human tissue and animal models.

# Research Goal 6

Understand the etiology and biology of esophageal neuromuscular function in health and disease.

# Research Goal 6

## Objectives

- Understand the neurobiology of normal and abnormal esophageal sensation and identify novel molecular targets for more effective and rational treatment of esophageal hypersensitivity associated with disorders such as non-cardiac chest pain and non-erosive reflux disease (NERD).

# Research Goal 6

## Objectives (continued)

- Understand the etiopathogenesis, genetic predisposition and risk factors for esophageal motility and functional disorders including the role of autoimmunity, environmental factors (e.g. viruses), relationship to GERD and genetic factors and molecular candidates (e.g. ALADIN).

# Research Goal 6

## Objectives (continued)

- Identify novel therapeutic targets for pharmacological, cellular (e.g. stem cell treatment) and physical (e.g. endoscopic) approaches for more effective and rational treatment for esophageal motility disorders.

# Major Challenges/Steps To Achieve Goals

- Animal models
- Standards for diagnosis
- Interdisciplinary research
- Disease definitions
- Validation of novel interventions
- National research resources
- Advanced technology

# Major Challenges/Steps To Achieve Goals

## **Animal Models**

- Experimental models for diseases of the oropharynx and esophagus, including GERD

## **Standards for Diagnosis**

- Means to overcome:
  - small number of patients seen by any one center,
  - the absence of uniform diagnostic criteria,
  - the lack of generally available and reliable methods for physiological testing
  - the inaccessibility of tissue for histopathological correlation
- Ways to minimize variations in practice management to obtain a true epidemiological and clinical picture of these disorders

# Major Challenges/Steps To Achieve Goals

## **Interdisciplinary Research**

- Cross-fertilization amongst disciplines, for example
  - swallowing disorders secondary to central nervous system (CNS) pathology: neuroscience and gastrointestinal specialties
  - eosinophilic esophagitis: gastroenterologists, immunologists and allergy experts

## **Disease Definitions**

- A multi-national consensus conference to arrive at standardized disease definitions

# Major Challenges/Steps To Achieve Goals

## **Validation of Novel Interventions**

- Rigorous testing of new imaging and therapeutic technology
- New approaches to limiting cancer in the setting of Barrett's beyond the current focus on subjects with chronic GERD symptoms

## **National Research Resources**

- Multicenter consortia with the ability to build large databases and patient registries
- Collaborative trial groups with experts from relevant disciplines (e.g., immunology, oncology, and surgery) to validate clinical protocols for diagnosis and management and to conduct trials for prevention and therapy

# Major Challenges/Steps To Achieve Goals

## **Advanced Technology**

- Technological research and development
  - endoscopic access for obtaining tissue samples from deeper layers of the esophagus
  - better physiological tests and less invasive and more effective anatomical and physiological approaches to treatment