

Children with Chronic Respiratory Complaints: When Does Normal Become Abnormal?

**Satellite Conference and Live Webcast
Wednesday, April 27, 2011
12:00 - 2:00 p.m. Central Time**

**Produced by the Alabama Department of Public Health
Video Communications and Distance Learning Division**

Faculty

J.P. Clancy, MD
Tom Boat Chair and Director of Cystic
Fibrosis Clinical and Translational
Research
Cincinnati Children's Hospital and Medical
Center
Cincinnati, Ohio

Angela Happeny
Parent of a Daughter Diagnosed with
Immotile Ciliary Syndrome
(Primary Ciliary Dyskinesia)

Learning Objectives

- To identify when common pediatric respiratory symptoms become excessive and beyond the normal range of care
- To state parental perspectives into the evaluation of chronic respiratory signs and symptoms

Overview of Presentation

- Case presentation and interview with parent
 - Daughter diagnosed with primary ciliary dyskinesia
 - PCD, or immotile cilia syndrome
 - Kartagener's syndrome

Overview of Presentation

- Medical background
 - Chronic respiratory symptoms and causes
- What are the factors that discriminate between normal and abnormal?
 - When to test and what to test for?
 - When to refer?

A Parent's Perspective: Chronic Respiratory Complaints

- Some background regarding daughter's birth and early symptoms
- The nature of daughter's symptoms through childhood
 - Types of evaluations

**A Parent's Perspective:
Chronic Respiratory Complaints**

- Stresses faced by your daughter, yourself and your family
 - Prior to diagnosis
 - After diagnosis
 - Today
- Messages for health care providers

**Part I
Common Respiratory
Complaints and Causes**

**Common Respiratory
Complaints and Causes**

- Provide a general framework for thinking about assessment of respiratory complaints
 - Etiologies based on symptoms
 - Segregate in broad groups

**Respiratory Complaints in
Primary Care**

- Common (up to 80% of sick patient encounters)
 - URIs
 - LRTIs
 - Asthma
 - Allergies
 - Noisy, spells, exercise symptoms
- Common symptoms
 - Cough
 - Wheeze
 - Tachypnea
 - Dyspnea

Chronic Respiratory Symptoms

- Cough (> 4 weeks)
 - Dry
 - Wet
 - Paroxysmal
 - Staccato
 - Honking

Chronic Respiratory Symptoms

- Noisy breathing
 - Inspiratory
 - Expiratory
- Wheezing
- Recurrent infections
- Tachypnea
- Dyspnea/exercise intolerance/pain

Chronic Respiratory Symptoms

- Apnea, ALTEs, and OSA

– Change and Glomb. Guidelines for evaluating chronic cough in children. *Chest*. 129; 260s – 283s (2006)



Cough: Daily, > 4 weeks

- Expected
- Specific
 - With associated findings
 - Typically requires further evaluation



Cough: Daily, > 4 weeks

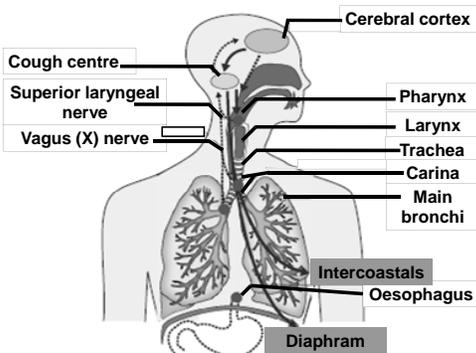
- Nonspecific
 - No associated findings
 - Watchful waiting

– Change and Glomb. Guidelines for evaluating chronic cough in children. *Chest*. 129; 260s – 283s (2006)



Why Do We Cough

- Sites of cough receptors
 - Larynx
 - Bifurcations
 - Distal esophagus



Chung, KF et al. Prevalence, pathogenesis, and causes of chronic cough. *The Lancet*. 371:1364-1374 (2008)

Examples of 'Expected' Chronic Cough

- Known underlying disorder that manifests with cough
 - Infections
 - Asthma
 - Mucus problem
 - Cystic fibrosis, primary ciliary dyskinesia

Examples of 'Expected' Chronic Cough

- Anatomic problem
 - Bronchiectasis, aspiration, compression, malacia, fistula, foreign body
- Airspace problem
- Interstitial lung disease
 - Chung, KF et al. Prevalence, pathogenesis, and causes of chronic cough. *The Lancet*. 371:1364-1374 (2008)

'Specific' Chronic Cough: Associated Findings

Table 1.—Pointers to the Presence of Specific Cough

Abnormality	Example of Etiology
Auscultatory findings	Wheeze—asthma; any lesion (eg, tracheomalacia, asthma); crackles, any airway lesion; fine crackles, or parenchyma disease such as interstitial disease
Cough characteristics	Associated airway abnormalities, asthma, infection
Chest pain	Asthma, infection
Dyspnea or tachypnea	Any pulmonary airway or parenchymal disease
Chest wall deformity	Any pulmonary airway or parenchymal disease
Dental chloasma	Suppurative lung disease
Daily nocturnal or paroxysmal cough	Suppurative lung disease
Exercise-induced dyspnea	Any airway or parenchymal disease
Fatigue or weight loss	Any serious systemic condition including pulmonary infection such as cystic fibrosis
Feeding difficulties	Any serious systemic condition including pulmonary infection, aspiration
Hemoptysis	Suppurative lung disease, vascular abnormalities
Hypoxemia	Any airway or parenchyma disease, cardiac disease
Immune deficiency	Suppurative lung disease or atypical infection
Neurodevelopmental abnormality	Aspiration lung disease
Recent pneumonia	Immunodeficiency, atypical infection, suppurative lung disease, congenital lung abnormalities, tracheo-oesophageal H fistula

Change and Glomb. Guidelines for evaluating chronic cough in children. *Chest*. 129:260s–283s (2006)

Causes of 'Non-specific' Chronic Cough

- Lack clear etiology
- Lack associated 'pointers'
- Extend beyond the expected timeframe from post-infectious or exposure causes
 - > 4 weeks

Causes of 'Non-specific' Chronic Cough

- Often lead to empiric trials of therapies
 - Unresponsive - Consideration of habit cough
 - Chung, KF et al. Prevalence, pathogenesis, and causes of chronic cough. *The Lancet*. 371:1364-1374 (2008)

Noisy Breathing

- Inspiratory
 - Extrathoracic
 - Stridor
- Expiratory
 - Intrathoracic
 - Wheeze

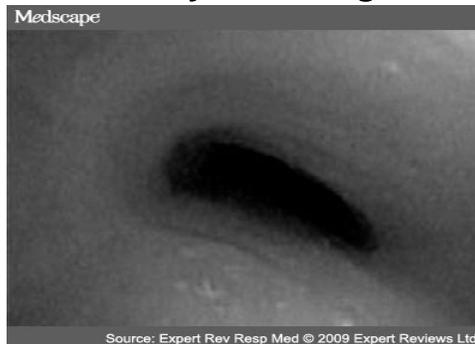
Noisy Breathing

- Both
 - Fixed abnormality, or mixture

Noisy Breathing



Noisy Breathing

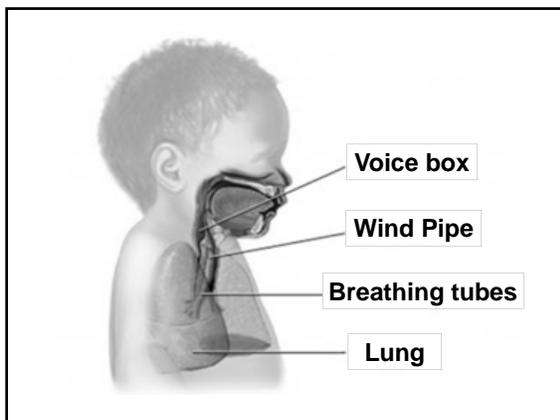


Noisy Breathing

- **Inspiratory**
 - **Supraglottic, glottic, and subglottic**
 - **Laryngomalacia**
 - **Croup**
 - **Anatomic**

Noisy Breathing

- **Expiratory**
 - **Airways**
 - **Tracheomalacia, bronchomalacia**
 - **Anatomic**



Noisy Breathing

- **Inspiratory and expiratory**
 - **Fixed abnormality**
 - **Vocal cords, subglottic stenosis, laryngeal web, large airway lesion**

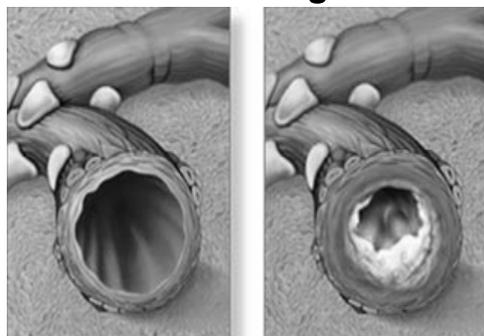
Noisy Breathing

- Mixture of extra and intrathoracic sources
- Laryngomalacia + tracheobronchomalacia
- Croup + bronchiolitis

Wheezing

- Commonly described
- Expiratory
- Airflow obstruction
 - Mucus
 - Constriction
 - Compression
 - Luminal process

Wheezing



Wheezing

- Causes
 - Asthma
 - Bronchiolitis
 - Atypical LRTIs
 - Fixed airway obstruction
 - Cardiac
 - Failure, vascular anomaly



Recurrent Infections

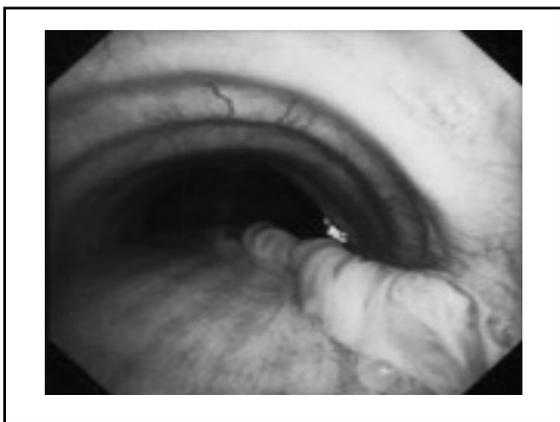
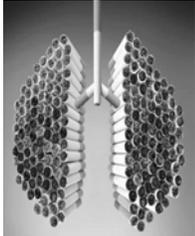
- Sino-pulmonary infections
 - Pneumonia
 - Bronchiolitis
 - Bronchiectasis
 - Acute sinusitis
 - Chronic sinusitis





Recurrent Infections

- **Host anatomy**
 - Failure to clear secretions
- **Host immunity**
 - Failure to kill bugs
 - Innate or acquired immune system
- **Host exposures**



Tachypnea

- **Resting respiratory rate**

↓

- **Associated findings**
 - Retractions
 - Flaring
 - Head bobbing
 - Accessory muscles



Normal Nostrils	Flared Nostrils
	

ADAM.

Tachypnea

- Pulmonary and non-pulmonary
 - CO₂ removal/acidosis
 - Oxygenation
 - VQ mismatch
 - Diffusion
 - Hypoventilation
 - Shunt
 - Altitude



Dyspnea/Exercise Intolerance

- More common outside of infancy and toddlers
- Keeping up with peers
- Onset
- Associated symptoms



Dyspnea/Exercise Intolerance

- Pulmonary
 - Primary or secondary
- Cardiac
- Hematologic
- Endocrine
- Infectious
- Rheumatologic
- Deconditioning



Apnea, ALTEs, and OSA

- ALTEs
 - Apparent Life Threatening Events
 - Acute change in consciousness, tone, color
 - With or without apnea



Apnea, ALTEs, and OSA

- ALTEs
 - 2-5% of all infants
 - Weak association with SIDS
 - 50% with diagnosis
 - All organ systems

Apnea, ALTEs, and OSA

- Obstructive Sleep Apnea
 - Increasing prevalence
 - Relationship to behavior and school performance
 - Central and anatomic causes



Apnea, ALTEs, and OSA



Summary – Etiology of Chronic Respiratory Symptoms

- **Pulmonary disorder**
 - Airway or airspace
 - Abnormal anatomy
 - Infectious
 - Exposures
- **Other organ or systemic disorder**
- **Not mutually exclusive**

Part II
What are the Factors that Discriminate Normal from Abnormal?

Normal vs. Abnormal

- **‘Normal’**
 - Symptoms anticipated to self-resolve without intervention
- **‘Abnormal’**
 - Symptoms that warrant further work-up

Normal vs. Abnormal

- **Diagnostic testing**
- **Referral for further evaluation**
- **Duration**

Symptoms in Combination that Frequently Warrant Further Work-up + Persistence



(4 weeks)

- Abnormality
-
- Auscultatory findings
 - Cough**
 - Cardiac abnormalities
 - Chest pain
 - Dyspnea or tachypnea
 - Chest wall deformity
 - Digital clubbing
 - Daily moist or productive cough
 - Exertional dyspnea
 - Failure to thrive
 - Feeding difficulties
 - Hemoptysis
 - Hypoxia/cyanosis
 - Immune deficiency
 - Neurodevelopmental abnormality
 - Recurrent pneumonia

Chang and Glomb. Guidelines for evaluating chronic cough in children. Chest. 129: 2609–2634 (2006)

Chest Examination Abnormalities

- Auscultatory
 - pulmonary
- Cardiac findings
 - History and auscultatory
- Chest pain
- Chest deformity



Chest Examination Abnormalities

- Reduced saturations
- Productive cough
- Hemoptysis
- Symptoms related to specific activities
 - Change and Glomb. Guidelines for evaluating chronic cough in children. *Chest.* 129; 260s – 283s (2006)

Chest Examination Abnormalities

- Auscultatory (pulmonary)
 - Stridor
 - Sleeping obstructive symptoms
 - Wheeze
 - Rhonchi
 - Rales
 - Sidedness/localization
- * New onset without clear URI/LRTI prodrome



Chest Examination Abnormalities

- Cardiac findings (history and auscultatory)
 - History
 - ‘Racing’ heart, pain, syncope, poor feeding



Chest Examination Abnormalities

- Exam
 - Murmurs
 - Gallops
 - Resting tachycardia
 - Right sided heart sounds

Chest Examination Abnormalities

- Chest pain (cardiopulmonary, musculoskeletal, referred)
 - Localization
 - Provocative activities

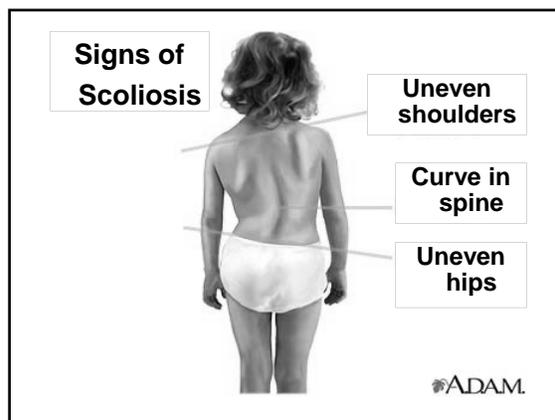
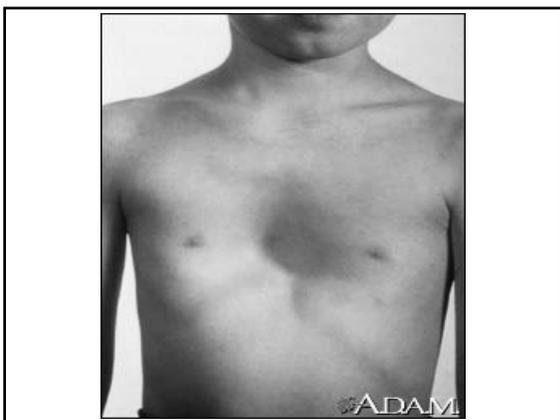


Chest Examination Abnormalities

- Nature
 - Sharp
 - Dull
 - Tight
 - Inspiratory/expiratory

Chest Examination Abnormalities

- Chest deformity
 - Typically not a 'new' symptom
 - Frequent restrictive disease
 - Pectus excavatum
 - Pectus carinatum
 - Rib anomalies
 - Significant scoliosis



Chest Examination Abnormalities

- Reduced saturations
 - Most commonly part of an acute (infectious) process
 - V/Q mismatch
 - When identified as part of chronic symptoms
 - Shunt
 - Cardiac

Chest Examination Abnormalities

- Diffusion abnormality
 - Airspace
- Hypoventilation
 - Central vs. obstructive



Chest Examination Abnormalities

- Productive cough
 - ‘Moist’, sputum
 - Rhonchi, rales or wheeze (localization)
 - Asymmetric exam
 - Diminished or phase lag

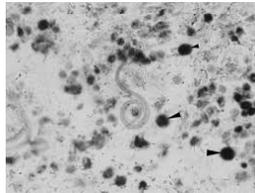


Chest Examination Abnormalities

- Considerations:
 - Post nasal drip, foreign body, aspiration, bronchiectasis, ‘mucus problem’
 - Change and Glomb. Guidelines for evaluating chronic cough in children. *Chest.* 129; 260s – 283s (2006)

Chest Examination Abnormalities

- Hemoptysis
 - Always concerning
 - Typically justifies evaluation
 - Frequently not serious



Chest Examination Abnormalities

- Source?
 - Upper airway
 - GI tract
 - Lower airway or airspace

Chest Examination Abnormalities

- Symptoms related to specific activities
 - Feeding
 - GERD, aspiration
 - Exercise
 - Asthma, cardiac
 - Sleep
 - Asthma, OSA

Chest Examination Abnormalities

- Stress triggers
 - Asthma, vocal cord dysfunction
- Exposures
 - Environmental tobacco smoke, viral infections

Abnormalities Outside of the Respiratory System

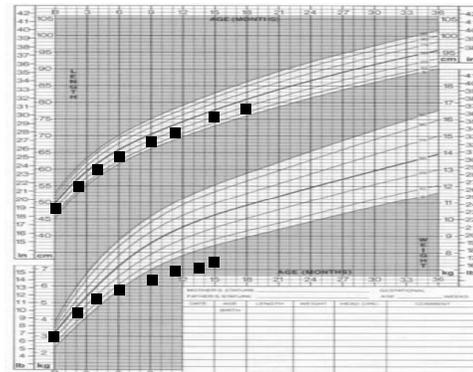
- Failure to thrive
- Infections outside of respiratory system
- Digital clubbing
- Neurodevelopmental abnormalities
- Exercise intolerance
- Syncope

Abnormalities Outside of the Respiratory System

- Failure to thrive
 - A symptom warranting further evaluation
 - Associated symptoms
 - Respiratory
 - Infections

Abnormalities Outside of the Respiratory System

- GI
 - Feeding, vomiting, diarrhea
- Rashes, fevers, arthritis



Abnormalities Outside of the Respiratory System

- Infections outside of respiratory system
 - Bacterial
 - Viral
 - Fungal

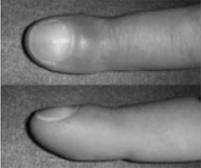


Abnormalities Outside of the Respiratory System

- Immunodeficiency considerations:
 - IgA deficiency, common variable or severe combined immune deficiency, complement deficiency, T cell defect, neutrophil defect (CGD, LAD), Job's syndrome, Wiskott-Aldrich syndrome

Abnormalities Outside of the Respiratory System

- Digital clubbing
- Implies chronic purulent respiratory disorder
 - CF
 - PCD
 - Tb/post-infectious
 - Other causes of bronchiectasis



Abnormalities Outside of the Respiratory System

- Neurodevelopmental abnormalities
 - High risk:
 - Swallowing difficulties
 - Aspiration
 - Sleeping/recumbent symptoms
 - OSA

Abnormalities Outside of the Respiratory System

- Mucus clearance
 - Poor or ineffective cough
- Scoliosis

Abnormalities Outside of the Respiratory System

- Exercise intolerance
 - Syncope/dizziness
 - Cardiac or neurologic

Abnormalities Outside of the Respiratory System

- General fatigue
 - Hematologic
 - Infectious
 - Rheumatologic
 - Endocrine



Part III
Testing and Interventions

Testing and Interventions

- What types of tests can be performed from the pediatrician's office?
- What tests are typically performed out of the specialists' office?
- Empiric therapeutic trials

Next Steps in Evaluation

"Your Office"	"My Office"
Saturations	PFTs, walk test
Imaging (chest X-ray, decubitus films)	Imaging (CT, UGI, swallow, airway fluoroscopy)
Laboratory studies -CBC, metabolic profile, UA, endocrine, ESR, CRP -Quantitative immunoglobulins	Laboratory studies -Sweat Cl, cilia
Skin test	Pre/post antibody titres
	Bronchoscopy

Next Steps in Evaluation

- Send films prior to work-up
- Conversation with specialist

Empiric Therapeutic Trials

- Antibiotics
- Asthma rescue +/- asthma controller
- H2 blocker or proton pump inhibitor
- Antihistamine
- Leukotriene receptor antagonist

Empiric Therapeutic Trials

- 'No role for over the counter cough suppressants, particularly young children'
- * Be systematic, not just additive
 - Change and Glomb. Guidelines for evaluating chronic cough in children. *Chest.* 129; 260s – 283s (2006)

Cochrane Reviews Prolonged Cough in Children

- Antibiotics
 - Randomized controlled trials with placebo group (2)
 - Cough greater than 10 days
 - Mean 3 - 4 weeks
 - Predominance of *Moraxella catarrhalis* in N/P cultures

**Cochrane Reviews
Prolonged Cough in Children**

- Treatment arms improved relative to placebo
- High self-resolution rate
- Uncomplicated pediatric acute sinusitis
 - Clinical improvement = 88% with antibiotics, 60% with placebo

Change and Glomb. Guidelines for evaluating chronic cough in children. *Chest*. 129; 260s – 283s (2006)

Prolonged Nonspecific Cough in Children

- Asthma therapy
 - ‘Children with nonspecific chronic cough and asthma risk factors, a short trial (2 - 4 weeks) of ICS (budesonide) may be warranted’
 - Most kids with nonspecific cough do not have asthma

Prolonged Nonspecific Cough in Children

- Reevaluate, and don’t escalate if no response
- Typically should be able to discontinue treatment
 - Change and Glomb. Guidelines for evaluating chronic cough in children. *Chest*. 129; 260s – 283s (2006)

Potential Side Effects of ICS

- Many potential side effects described
- Very difficult to demonstrate long-term side effects in children
 - HPA suppression
 - Bone mineral density
 - Growth
 - Cataracts

Potential Local and Systemic Side Effects of Inhaled Corticosteroids

Local adverse effects	Systemic side effects
Pharyngitis	Suppressed HPA-axis function
Dysphonia	Adrenal crisis (with insufficiency)
Reflex cough	Suppressed growth velocity in children
Bronchospasm	Decreased lower-leg length in children
Oropharyngeal candidiasis	Reduced bone mineral density
	Suppressed HPA-axis function
	Bone fractures
	Osteoporosis
	Skin thinning
	Skin bruising
	Cataracts
	Glaucoma

HPA = Hypothalamic-pituitary-adrenal.
- Dahl, R. Systemic side effects of inhaled corticosteroids in patients with asthma. *Resp Med*. 100, 1307-17 (2006)

**Cochrane Reviews
Prolonged Cough in Children**

- GERD therapy
 - Cochrane review failed to demonstrate benefits of milk thickening, cisapride, or domperidone in pediatric GERD

Cochrane Reviews Prolonged Cough in Children

- **Separate Cochrane review of metoclopramide for GERD in children < 2 yo – no benefit demonstrated (did not monitor cough)**
- **No RCT has been conducted on the use of PPIs for the treatment of cough in children**

– Chang and Glomb. Guidelines for evaluating chronic cough in children. *Chest*. 129; 260s – 283s (2006)

Cochrane Reviews – Prolonged Nonspecific Cough in Children

- **Antihistamines**
 - **Randomized controlled trials with placebo group (3)**
 - **Therapeutic studies demonstrated similar improvements in active treatment and placebo arms (n~160)**

Cochrane Reviews – Prolonged Nonspecific Cough in Children

- **Some benefit of antihistamine in seasonal allergy (within two weeks)**
- **Leukotriene receptor antagonists**
 - **Randomized controlled trials with placebo group (2)**

Cochrane Reviews – Prolonged Nonspecific Cough in Children

- **No significant difference in all study endpoints between LRTA and placebo groups (n~260)**

– Chang, AB et al. Antihistamines for prolonged nonspecific cough in children. *Cochrane Reviews*. April 16;(2) (2008)

Summary

- **Listen to (don't just hear) caregivers**
- **Persistent respiratory symptoms typically warrant further evaluation (> 4 weeks)**
- **Combinations of symptoms provide evidence of more significant disorder**

Summary

- **Respiratory symptoms can be primary or secondary**
- **Empiric trials should have start and endpoint**

Thank You

- **Pediatric Pulmonary Center at UAB**
 - Nancy Wooldridge, Claire Lenker, Wyn Hoover, Brad Troxler, Heather Hathorne, and former faculty:
Janet Johnston, Julie McDougal
 - Advisory committee members