Asthma Review—

ETIOLOGY

Airflow limitation is caused by the following:
- bronchoconstriction
- mucous pluggin
- airway inflammation

Sudden death
- heavy mucous plugging is common
- typically occurs between MN and 4am
- nonwhite, urban, lower socioeconomic status, older
- predicted by recent near death or recent uncontrolled sx
- most common eosinophil, slow, and mucous plugging
- less common neutrophil, fast, NSAIDS?

Symptoms are worse at night and in the morning and includes cough, whz, chest tightness.

Epidemiology
- 8% of US population
- Increasing in Africa, Asia, Latin America
- Mortality not associated with prevalence due to socioeconomic factors
- In childhood it affects more boys than girls but this flips by puberty and ultimately higher in women
- More in blacks than whites (even when social corrected)
- Urban more than rural (cockroaches?)
- Obesity strongly related
  - Linear relationship between obesity and asthma in studies
    - Probably over-stated though as 40% negative challenge study
    - Be careful with steroids if asthma dx not solid

Pathophysiology
- Genetic susceptibility with environmental triggers
- Genetic (no single gene), sex, obesity
- Inflammation Science
    - T-lymphoctyes (T2) -> IL-3 + IL-5
    - Eosinophils (major)
    - Neutrophils (more in death)
    - Mast Cells
- Inflammation Effects
    - Smooth muscle constriction
    - Vascular permeability
    - Mucosal thickening and mucous production (MUC5AC gene)

- Path
    - Basement membrane thickening (diagnostic on bx)
    - Denuding of epithelium
    - Increased smooth muscle and collagen
    - Increased myofibroblasts

Neurogenic
    - autonomic: tone, secretions and feedbacks to create more inflammation with more autonomic stimulation
    - nonadrenergic, noncholingeric - promotes cough

Classification
- Extrensic
    - atopic
    - IgE
    - Not in infants. Peaks in teenage years
    - Strong family and seasonal hx
- Intrinsic
    - non-atopic
    - Later onset
    - Greater inflammation
    - Probably more viral causes

Diagnosis
- No one test diagnoses asthma
- usually made clinically (symptoms and clinical tests / reversibility)
- 12% reversibility FEV1 or 200-400ml
- Diurnal variability in peak flow > 20%
- Lowest lung function of the day occurs at 4am.
- Bronchial hyperreactivity testing
    - methylcholine directly activates smooth muscles
    - Sensitive but not specific. Many things will be positive other than asthma.
    - Drop 20% 8mg/ml or less is positive

TREATMENT

- Switching from old classification to symptom control

- What are the components of control (goal)?
    - Daytime sx (< 2wk)
    - Nightime sx (none)
    - Activity limitations (none)
    - Rescue inhaler use (< 2wk)
    - Lung function (FEV1 or Peak flow >80%)

- Step 1 - SABA

- Step 2 - low dose ICS
- Step 3 - med ICS or low ICS + LABA
- Step 4 - med ICS + LABA (consider LTRA, theophylline, etc)
- Step 5 - high ICS + LABA (consider omalizumab in allergic patients)
- Step 6 - high ICS + LABA + steroids

Tiotropium not on guidelines but an effective step up after ICS or ICS+LABA.

When can you step down therapy? After 3 months of being controlled.
Salmeterol deaths? Doesn't decrease death and increases death in AA. (SMART trial)
Salmeterol deaths probably due to lack of ICS.

Consider ABPA or Churg-Strauss Syndrome if difficult to control

Adrenal suppression and osteopenia can occur with high dose ICS use (typically above 1000mcg daily)
ICS + LABA is superior to higher doses of ICS
LTRA (leukotriene receptor antagonist like Singulair) more helpful in smokers and premenstrual.

Bone mineral density
- Steroids > 3 months postmenopausal and > 6 months premenopausal or any fracture.
- Stop smoking, exercise, calcium supplementation.

Trigges
- airborne - cockroach, dust mite, pet, smoke, perfume
- URI
- Exercise
- Hormones
- Food very rare except sulfites (5%)
- Medications - ASA, NSAIDS, Beta blockers
- GERD (probably)

When immunotherapy (like Xolair)?
- Uncontrolled with obvious allergy exposures and failing med ICS + LABA
- Target IgE levels
- Want to avoid or had bad affects to other meds

Does it work?
- yes with typical allergens
- not recommended with people with FEV1 < 75% due to decompensation
- chronic steroids or recent exacerbations are much higher risks of decompensation

Omalizumab (Xolair)
- monoclonal that binds IgE
- decreases AE rate, number, and steroids in moderate

- only for sure improves QOL in severe
- Age > 12
- Failing ICS + LABA + leukotriene antagonist
- elevated IgE
- Positive allergy testing

Risks:
- analphalyxis (<0.1%)
- cost
- cancer
- parasites

Acute bronchospasm treatment
- ipatropium added to beta agonist gives more relief
- nebs not proven better than MDI
- post treatment PEF < 40% baseline = admission
- systemic steroids started if not response within an hour
- 3 to 10 days without taper of oral steroids is sufficient typically
- long acting IM steroids if noncompliant
- admission recommended if no better 4 hours in ED
- must be started ICS upon d/c

Bronchial thermoplasty
- distal to proximal
- outpatient, multiple
- avoid in patient's with AICD or pacemaker
- Benefits:
  - decreased AE
  - stablizes FEV1
  - lower ICS dosing
- Risks:
  - more atelectasis and hemoptysis

Aspirin-Related Asthma
- Typically occurs ages 30-40s
- Classic triad: Nasal Polyps, ASA sensitivity, Asthma
- Other sx: rhinorrhea, conjunctivitis, **head/neck flushing 30min-3hr after exposure
- Sx typically progress with subsequent attacks
- Can be diagnosed after introduction to a COX-1 inhibitor with severe AE of asthma and bronchospasm
- Treatment:
  - Avoid COX-1 inhibitors
  - Best NSAID salicylsalicylic acid
  - LTRA work best for acute attacks

Exercise-Induced Asthma

- Few minutes AFTER exercise
- More rare during exercise due to circulating catecholamines
- ***Cough is common
- Typically spontaneously resolves in 30-45 min
- Worse in cold, dry air as dry air causes mast cell degranulation
- Dx: hx, response to medications, 8 min post-exercise spirometry (10-12% drop in FEV1)
- Treat: Pre-exercise SABA or cromlyn. LTRA are also an option.

Asthma in Pregnancy
- Don't use methylcholine challenge during prego
- 1/3 better, 1/3 unchanged, 1/3 worse
- Uncontrolled asthma probably more likely to get worse with prego
- How mother did with first prego will likely be repeated with subsequent pregos
- Poor control causes fetal and mother harm
- Uncontrolled problems far exceed risk of asthma medications
- Well-controlled = non-asthmatic outcomes
- AE most common during 2nd trimester and rare complicating delivery
- Treatment:
    - Budesonide best studied ICS
    - Avoid Zileuton*
    - LTRA animal studies suggest they are safe
    - Salmeterol best studied LABA
    - Theophylline should be avoided if possible due to difficult dosing and metabolism

Vocal Cord Dysfunction
- Female with very-short AE that fails standard asthma therapy
- Frequent intubations. Often immediately better with intubation.
- Related to anxiety
- Diagnosis
    - Inspiratory flow loop is flatted compared to baseline (almost impossible to catch though)
    - Adduction of the cords (together) during inspiration seen via laryngoscopy or bronchoscopy
- Treatment
    - Difficult
    - Avoid treating "asthma" and over-medicating
    - Speech path and relaxation techniques

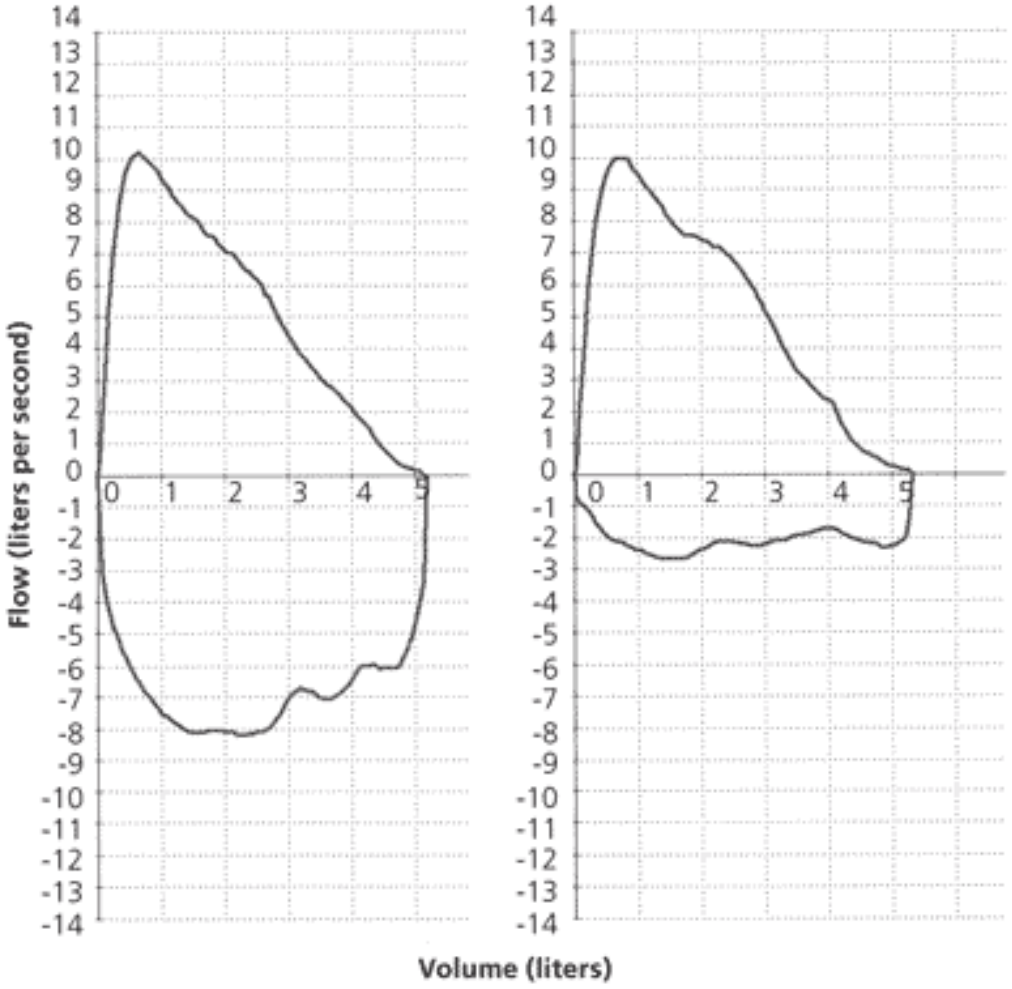
Occupational Asthma
- Hints: improved s/sx and peak flows on weekends and vacations
- Consider w/u in all adults or people with change in baseline s/sx
- Avoidance therapy is ideal
- Pharm therapy is same as any other asthma
    - Not typically IgE mediated
    - Anti-IgE typically doesn't work unless related to animal dander

- Causes are extremely varied

Allergic Bronchopulmonary Aspergillosis (ABPA)
- Causes because IgE and IgG responses increase risk of fungal colonization
- Other fungi other than Aspergillosis can cause this including Candida Albicans
- Typically occurs in asthma and CF
- CT
    - Upper lobe mucous plugging and bronchiectasis
    - Mucous may be higher intensity than expected (hyper-dense areas in plugging and infiltrate)
        - Associated with high eosinophils, higher IgE, and more relapses
- Diagnosis
    - Consider getting screen aspergillosis skin testing in all asthma patients
    - IgE level if skin test is positive. If IgE > 1000 IUml, needs complete eval.
    - Would love to dx early before bronchiectasis
    - Can check IgE specific to aspergillosis, presence of IgG to aspergillosis
    - Peripheral eosinophilia and proximal bronchiectasis
- Treatment
    - System steroids 40-60mg daily (ICS not enough)
    - Itraconazole improves response (vori also works)

Churg-Strauss Syndrome
- Eosinophilic Granulomatosis with Polyangiitis
- Small to Medium Vessel
- P-ANCA
- Diagnosis (very specific. need 4 out of 6)
    - asthma
    - Fleeting pulm infiltrates
    - peripheral eosinophilia > 10%
    - mono or poly neuropathy
    - extravascular eosinophils on histopath
    - paranasal sinus abnormalities
- Treatment
    - Acute: Systemic steroids
    - Severe Acute (additional non pulmonary s/sx) - add cyclophosphamide
    - Chronic remission control with azathioprine or methotrexate

Normal vs Flat inspiratory flow loop in VCD
Source: http://www.aafp.org/afp/2010/0115/afp20100115p156-f1.gif


Flow (liters per second)
14
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1
-2
-3
-4
-5
-6
-7
-8
-9
-10
-11
-12
-13
-14
0 1 2 3 4 5
0 1 2 3 4 5
Volume (liters)

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