HISTORY & PHYSICAL EXAM AND PFTs

Pulmonary diseases associated with smoking:
include Asthma, COPD, lung cancer, but also
Desquamative interstitial pneumonitis,
Respiratory bronchiolitis–interstitial lung disease,
Pulmonary Langerhans cell histiocytosis,
Goodpasture's disease, and
Pulmonary alveolar proteinosis

Acute pleuritic chest pain differential diagnosis includes asthma, pneumonia, pulmonary embolus, pneumothorax, and cholecystitis.

A fruity odor on the breath is usually found in diabetic ketoacidosis, which is associated with **Kussmaul's respirations** (deep, gasping respirations), or tachypnea with large tidal volumes.

Increased fremitus, bronchial breath sounds, egophony (E to A), whispered pectoriloquy (whisper 1,2,3) >> consolidated pneumonia.

Decreased tactile fremitus, dullness to percussion, decreased breath sounds, no voice transmission point to pleural effusion or atelectasis.

Absent fremitus, hyper-resonance, and absent breath sounds >> pneumothorax.

Tracheal deviation to left >> **right** pleural effusion OR **left** loss of volume (atelectasis due to obstructed bronchus).

Cyanosis that involves the skin and extremities: DVT, Raynaud's, cold exposure, and peripheral vascular disease.
Cyanosis that involves the skin and mucous membranes: methemoglobinemia and CO poisoning, right to left shunting, pulmonary AV malformations, and severe lung disease.

Digital clubbing can be caused by

>Many intrathoracic tumors: lung cancer and mesothelioma.
>Chronic intrathoracic non-malignant processes: bronchiectasis, lung abscess, pulmonary fibrosis
>Cardiac: SBE and congenital heart defects
>GI: cirrhosis and inflammatory bowel disease.

Severe kyphoscoliosis is associated with restrictive lung disease, alveolar hypoventilation, pulmonary hypertension, and v/q abnormalities with hypoxemia.

Cheyne-Stokes respirations, in which tidal volume and frequency wax and wane alternately, indicates decompensated heart failure. The mechanism is not known, but is possibly due to

increased circulatory time, alterations in acid-base status, and affects on the brainstem chemoreceptors that govern the respiratory pattern.

PFTs:

Reductions in DLCO results from obliteration of capillary bed volume: pulmonary fibrosis (e.g., due to scleroderma or bleomycin), pulmonary hypertension, chronic PTE,

Normal DLCO occurs in asthma and chronic bronchitis.

Increased DLCO is seen

a) when pulmonary capillary blood volume is increased: Obesity, early CHF, L.R shunts, Exercise, altitude, supine position.
b) With increased RBC's, e.g., With increased hematocrit or with alveolar hemorrhage.

In emphysema, one does not use spirometry to measure total lung capacity because it cannot account for residual volume. The most frequently used and accurate measures of lung volumes are steady-state helium dilution lung volumes and body plethysmography. Helium lung volumes are easier to perform for patients and staff and give reliable results in most circumstances.
In cardiopulmonary exercise testing:

Cardiopulmonary testing:
In patients with cardiovascular dysfunction, findings include a heart rate more than 85% of the maximum heart rate, a low anaerobic threshold, reduced maximum oxygen consumption, arrhythmia or ischemia on electrocardiography, and a drop in blood pressure without desaturation or achievement of the maximal predicted ventilation.

Conversely, pulmonary dysfunction is suggested by achieving or exceeding maximal ventilation, desaturation, a drop in FEV1 with exercise, and stability or an increase in the ratio of dead space to tidal volume without reaching 85% of the maximal heart rate or ischemic changes on electrocardiography.

In COPD, administration of oxygen does not suppress the respiratory drive. Rather the increase in the PCO2 is due to a) V/Q mismatch and b) the Haldane effect (Oxygen drives the release of CO2 bound to hemoglobin).

COUGH:

ACUTE:

URI, pertussis, allergic rhinitis, COPD exacerbation, asthma, acute sinusitis.

CHRONIC:

Post nasal drip

Vasomotor rhinitis

Chronic sinusitis

Cerumen impaction and ear canal hairs (irritating the tympanic membrane)

Chronic bronchitis

Post-infectious

Gastroesophageal reflux can be associated with a bitter taste or sore throat on awakening. 24-hour pH monitor accurately identifies this problem and can be used to correlate episodes of cough with reflux. However, A 24-hour pH monitor is invasive and often not necessary. Proton pump inhibitor therapy to block gastric acid production generally is required to attenuate cough associated with reflux. An empiric trial of an H-2 blocker; if unsuccessful, a proton pump inhibitor such as omeprazole may be used before 24 hour pH monitoring. The usual anti-reflux measures, such as avoiding fatty foods, alcohol, and food before bedtime, should be instituted as well. Prescribers must be aware that sometimes a complete resolution of cough takes months.

Occult asthma is also a common cause of undiagnosed chronic cough. Cough-variant asthma can be associated with normal pulmonary function tests but increased sensitivity of the airways to inhalation of methacholine or histamine. Treatment of cough-variant asthma can be difficult because the use of **inhalers may precipitate coughing episodes**. Therefore, **oral agents** such as oral long-acting β-agonists or leukotriene inhibitors may be more useful. In addition, short, tapering courses of corticosteroids may be very useful in decreasing cough resulting from asthma.

Bronchiectasis is also a cause of chronic cough, asthma is not a cause of this problem. Chronic cough resulting from bronchiectasis responds to rotating antibiotics.

Medications: ACE inhibitors, especially the nonselective agents, cause cough in approximately 10% of treated patients. The associated cough is generally nonproductive and may not clear for several days after discontinuation of the drug. Most asthma medications including albuterol and monteleukast. Amiodorone.

Malignancy.

Left ventricular dysfunction.

HEMOPTYSIS

CAUSES OF HEMOPTYSIS:

Vascular: PE, vasculitides (Goodpastures, Wegener's), arteriovenous malformation
Cardiac: CHF, mitral stenosis
Neoplastic: Bronchogenic carcinoma, metastatic disease
Connective tissue: Lupus, rheumatoid arthritis
Infectious: TB, bronchitis, pneumonia, abscess, aspergilloma (has opacities within cavities changing with position)
Drugs: tobacco, Anticoagulants, cocaine, solvents
Congenital: Hereditary hemorrhagic telangiectasia [1) personal epistaxis; 2) telangiectasias of mouth, nose or fingers; 3) AV malformations of the lung; 4) Family history.
Miscellaneous: Bronchiectasis, Trauma, foreign body, epistaxis, hematemesis, Antiphospholipid antibody syndrome.
In massive hemoptysis of bronchiectasis, the most likely cause is bronchial artery erosion, which is treated with embolization.

PNEUMONIA

CAP manifestations: tachypnea, purulent sputum, fever, crackles, and egophany. Rhinitis is a negative predictor.

RISK FACTORS FOR SPECIFIC BACTERIA in Community Acquired Pneumonia

Drug Resistant Strep pneumoniae:

age > 65
use of beta lactam Ab'cs in past 3 months
immuno-suppression
multiple medical co-morbidities
regular exposure to a child in day care

Gram negative organisms:

All of those for S. pneumoniae above PLUS
Residence in a nursing home
regular alcohol consumption.

Anaerobic bacteria:

Witnessed or suspected aspiration

Pseudomonas aeruginosa:

Cystic fibrosis and Bronchiectasis and other structural lung diseases
mechanical ventilation
daily steroids
recent broad spectrum antibiotic treatment
severe malnutrition.

Staphyloccocus aureus

Post Influenza

Cystic Fibrosis

SETTINGS FOR SPECIFIC PNEUMONIAS

Bronchiectasis is associated with
Moraxella
Pseudomonas
H Flu
Staph
Strep pneumoniae
(Rx with flouroquinoloines and aminoglycosides.)

Cystic Fibrosis
Ditto

COPD
Ditto plus
Atypical Mycobacteria
Influenza virus and parainfluenza virus

Atypical pneumonia, (e.g. from *L. pneumophila*, *M. pneumoniae*, or *C. pneumoniae)* is more commonly associated with systemic symptoms such as myalgias, anorexia, and pharyngitis.

Younger patients tend to get mycoplasma; older patients Chlamydia.

Approximately 50 to 70% of patients with **mycoplasma pneumonia** will develop **cold agglutinins** as a result of the development of IgM antibodies to the I-antigen on red blood cells. **Hemolytic anemia** may occur with a significant fall in the hematocrit (increase retics, MCV, indirect bilirubin, decrease haptoglobin). The Findingof **myringitis bullosa on the tympanic membrane** supports the diagnosis of mycoplasma pneumonia.

Post influenza: Although the incidence of pneumonia resulting from *S. aureus* is increased after influenza infection, the most common bacterial pathogen is S. pneumoniae. P. aeruginosa and H.. influenzae also occur. In fact, H. influenzae received its name because it was initially isolated from a patient with clinical influenza.

Ways in which organisms gain access to lower respiratory tract and cause pneumonia: 1) microaspiration of colonized oropharyngeal contents. 2) gross aspiration (stroke or seizures) 3) aerosol inhalation (histo, cocci, TB), 4) blood born (bacterial endocarditis), 5) extension from a contiguously infected site.

Prevention of CAP generally involves immunization with pneumococcal (every 6 years) or influenza (yearly) vaccine.

In CAP, patients treated with fluoroquinolones within the past 3 months, should not be retreated

with these.

In CAP, patients treated within 8 hours of arrival to the ER have a lower mortality than those in whom treatment is delayed.

CURB65 Stands for Confusion, uremia, respiratory rate greater than 30, blood pressure less than 90/60, and age 65+. A score of 2 indicates need for hospitalization; a score of 3+ is an indication for the ICU.

CAP recommendations for antibiotics. IDSA/ATS Guidelines 2007

OPD

Healthy, no AB'cs in prior 3 months: Macrolide (or Doxy)

Comorbidities or use of AB'cs in prior 3 months:

Levofloxacin or moxifloxacin OR

Beta lactam + macrolide

Hi rate of infection with macrolide resistant Strep, consider use of Levofloxacin

INPATIENTS

Non-ICU

Levofloxacin or moxifloxacin OR

Beta lactam + macrolide

ICU: beta lactam (cefotaxime, cetriaxone, or amp-sulbactam + either azithromycin OR respiratory fluoraquinolone.

Pseudomonas is a consideration (structural lung disease)

Piperacillin-tazobactam, cefepime, imipenem or meropenem +

Either cipro or levofloxacin (750mg)

OR

Beta lactam + aminoglycoside and azithromycin

OR

Beta lactam + aminoglycoside + cipro or levofloxacin

CAP-MRSA is a consideration: add vancomycin or linezolid.

Trade names:

3rd Gen

Ceftriaxone= Rocephin 1 to 2 gm

Cefotaxime: = Clarofan 1gm Q12

Cefixime = Suprax 400mg PO

4th Gen

Cefepime (Maxipime) 1 to 2gm Q12Hr

Piperacillin-Tazobactim= Zosyn (4th generation penicillin) 3.375 gm iv Q6Hr.

Ampicillin-sulbactam =Unasyn (3rd generation penicillin) 2gm iv Q6Hr.

Levofloxacin=Levoquin (3rd generation fluoroquinolone) 750 mg

Moxifloxacin=Avelox (4th generation fluoroquinolone) 400 mg

Linezolid=Zyvox 600mg Q12

Imipenem-cilastatin=Primaxin 500 Q6Hr

Meropenem=Merrem 1gm Q8Hr

Oseltamivir (Tamiflu) 75 PO BID

Eosinophilic pneumonia can be caused by nitrofurantoin, sulfa drugs, NSAIDS,penicillins, INH, thiazides, tricyclic antidepressants, hydralazine, and chlorpropramide.

BOOP (SEE BELOW)

ASTHMA and COPD:

Pathophysiology

> Histamine, a preformed mast cell mediator, has direct vasoactive and smooth muscle spasmogenic activity.

>Platelet activating factor is a mast cell-derived mediator that induces bronchospasm.

>Leukotriene B4 is a precursor to the sulfidopeptide leukotrienes C4, D_4, and E_4. All of these leukotrienes have some effect on airflow by modulating vascular permeability, smooth muscle constriction, and mucus secretion.

>Interleukin 5 supports the differentiation of cells into eosinophils, is a specific

chemotaxin for eosinophils, is important in immediate hypersensitivity and is a target of drug therapy investigation.

>Prostacyclin, a prostaglandin metabolite of arachidonic acid, has bronchodilating effects (hence the potential for bronchospasm with ASA and NSAIDS).

For exercise-induced asthma use inhaled beta agonists before exercise. Diagnose it by PFTs pre and post exercise.

Exercise induced asthma: Exercise-induced asthma is very common, occurring in 50 to 90% of asthmatics. Asthmatics manifest bronchodilation at early stages of exercise. Airway water loss during exercise may cause bronchospasm. and dry air worsens exercise-induced bronchospasm in affected asthmatics. In contrast, humid air improves symptoms.

Occupational Asthma: Allergy to agricultural grasses, etc. Acute wheezing and obstruction. NO FEVER.

>Isocyanates, chemicals used in spray paints and other industrial products, are an example of low-molecular-weight substances that cause asthma.

>Flour dust contains high-molecular-weight components, specifically proteins that induce antibody formation in some individuals and asthma in a subgroup of those individuals.

The initial symptom of byssinosis is chest tightness.

RADS: Reactive Airway disease syndrome) is caused by a ingle toxic irritant exposure (e.g., chlorine gas). The subsequent asthma is confirmed by methacoline challenge test. A similar syndrome can follow a severe pulmonary infection.

Allergic bronchopulmonary aspergillosis is characterized by asthma, central bronchiectasis, peripheral eosinophilia, an immediate type of reaction to skin test reactivity, increased IgE in serum, and aspergilla precipitins in serum. It is a hypersensitivity pneumonitis that involves an allergic reaction to antigens from Aspergillus spp., most commonly A. fumigatus.

Diagnostic criteria:

1) Asthma,

2) Antigenic skin testing is positive in immediate (type I, wheal-and-flare) reaction, and reaction after 4 to 6 h (type III, erythema and induration).

3) Serum precipitins to aspergilli.

Supportive criteria:

IgE > 1 mgm/ml

Peripheral eosinophilia > 500/ml

Lung infiltrates

Bronchiectasis

Aspergilli in the sputum.

Lymphocytic alveolitis on BAL (sensitive but not specific).

COPD MAINTENANCE: Emerging data suggest that ipratropium bromide treatment improves prognosis in patients with COPD. Patients with this disorder commonly respond to ipratropium more favorably than asthmatics.

Anticholinergics are as, or more effective, than beta 2 agonists in COPD !! (Differs from asthma).

DIFFERENTIAL DIAGNOSIS OF ACUTE ASTHMA:

*Mechanical obstruction (a peanut)

*Vocal cord dysfunction

*Bronchiolitis

*Pneumonia

*CHF

*PE

ACUTE EXACERBATION OF ASTHMA & COPD

ASTHMA exacerbation:

Causes: Dust, chemicals, allergens, Beta antagonists, NSAIDs, GERD, Exercise

Assessing severity:

Clinical: Pulsus paradoxus (> 12 mmHg decrease in arterial pressure with inspiration), accessory muscles, diaphoresis, orthopnea.

Peak Flow:

<200 ("ml/min" is the unit) means severe. If < 100, this is life threatening.

PEFR nl is 80%-100% of patient's best.

PEFR < 70% means to treat

Treatment:

Albuterol (Beta agonist) – MDI or via nebulization.

Methylprednisolone IV.

Ipratroprium, if asthma is very severe or if there is no improvement with albuterol

Mg Sulfate IV (smooth muscle relaxant)

NO Chest physiotherapy

NO Antibiotics unless there is pneumonia

NO inhaled steroids for acute attack.

Re-Evaluate after 4 to 6 hours:

If PEFR > 70%, discharge on prednisone with taper.

If PEFR < 40%, admit.

If PEFR 40%-70% individualize. Any of the following factors might be sufficient for admission:

Poor Self care

Poor Home support

New Onset Asthma (1st ever attack)

Multiple prior hospitalizations or ER visits

Steroids at presentation.

Theophylline:

Conditions & Drugs <u>reducing theopylline levels</u> via liver metabolism:

>cigarette smoking, rifampin, phenytoin, and barbiturates

Conditions & drugs <u>increasing theophylline levels</u>:

>cimetidine, allopurinol, erythromycin, **<u>ciprofloxacin, oral contraceptives, propranolol</u>**, and clarithromycin, and cirrhosis, congestive heart failure, and febrile viral illness.

Ciprofloxacin inhibits the CYP 1A2 in the cyt p 450 system. Theophylline clearance is reduced.

Beneficial effects of theophylline include augmentation of cardiac output, enhancement of diaphragmatic strength, and bronchodilation.

<u>COPD exacerbation</u> (from Sthi S, Murfphy T. NEJM 2008; 359:2355.)

Roushmedicine.com

Cardinal symptoms: increased dyspnea, sputum volume, and purulence.

Risk factors: age 65+, FEV1 ≤ 50% predicted, 3+ exacerbations annually, heart disease.

Mild: 1 cardinal symptom: No antibiotics. Increase bronchodilator.

Moderate, uncomplicated: 2+ cardinal symptoms, no risk factors: Ab'c: azithromycin, cefuroxime, doxy, or TMP/SMX.

Moderate-Severe, complicated: 2+ cardinal symptoms, 1+ risk factors: Moxi, Amox-clav, or cipro (if pseudomonas expected). (Use alternative class if antibiotics were given ≤ 3 months ago.)

Albuterol doses are much lower than in asthma

Alpha 1 anti-trypsin deficiency now has a synonym: alpha 1 anti-protease deficiency. Prevalence is 0.06% in Sweden.

CM's: COPD in those less than 40. No cigarette smoking, positive family history. PE: Tympanitic chest, and decreased breast sounds, Chest x-ray: **lower lobe** emphysema (pan acinar–entire alveolus), cirrhosis, and panniculitis (with subcutaneous nodules and infiltration of fat lobules with acute inflammatory cells). Associated liver disease.

Obtain alpha 1 antitrypsin level.

Smoking	Lung apices	central acinar, central part of alveolus
alpha 1 anti-trypsin	Lung bases	pan-acinar, entire alveolus

Therapy is with infusion and is costly.

Cystic fibrosis has persistent asthma, airflow obstruction, and sputum cultures growing P. aeruginosa and S. aureus coupled with bilateral upper lobe infiltrates.

Bronchitis: Cotton dust and grain dust exposures. Endotoxins within these dusts are probably the inciting components for this syndrome. Both of these dusts can also cause fever in the absence of pulmonary symptoms, also probably resulting from endotoxin inhalation. Bronchitis secondary to cotton dust exposure tends to improve with continued exposure during the work week but worsen once again after returning to work from a period off the job.

Bronchiectasis:

>Symptoms: cough, copious mucopurulent sputum, and fetid breath.

>Causes of bronchiectasis by type:

Focal:

>Infections: Viral, staph, klebsiella, mycobacterium (tuberculous or avium)

>enlarged lymph nodes, endobronchial carcinoid or endobronchial lung cancer.

Central: Allergic bronchopumonary aspergillosis.

Diffuse: Impaired host defense mechanisms such as cystic fibrosis, immunodeficiency such as with panhypogammaglobulinemia and HIV, and ciliary dysfunction as in Kartagener's syndrome (immotile sperm, infertility).

>Treatment includes reversal (if possible) of the underlying cause and reduction in recurrent infections

using prophylactic rotating antibiotic regimens.

IPF, idiopathic pulmonary fibrosis, is characterized by oxygen desaturation with exercise and velcro like inspiratory crackles.

Pulmonary fibrosis is associated with

>Connective tissue disease: rheumatoid arthritis, scleroderma, and SLE.

>Pulmonary hypertension, pleural effusions, aspiration resulting from esophageal dysfunction, and obstructive lung disease

>Ankylosing spondylitis

>Neurofibromatosis (neurofibromas in the skin and other sites, cafe au lait spots, and axillary freckles).

Interstitial lung disease:

>PMN's occur in: asbestosis and idiopathic pulmonary fibrosis.

>Lymphocytes occur in sarcoid and hypersensitivity pneumonitis.

>Langerhans cells, a form of monocyte, points to eosinophilc granuloma (histiocytosis X)

>Proliferating smooth muscle cells: lympangioleiomyomatosis.

Methotrexate pulmonary toxicity can include hypersensitivity pneumonitis, pulmonary fibrosis, pleural effusion, or non-cardiogenic pulmonary edema.

Asbestosis refers to interstitial lung disease, generally with fibrosis, seen in the lower lung fields of a chest radiogram or chest CT and an associated restrictive ventilatory defect. This patient, although he has pleural plaques suggesting asbestosis exposure, does not have interstitial changes on chest radiography and has no restriction on pulmonary function tests; therefore, he does not have asbestosis.

There are three types of lung disease in farmers

Asthma Allergy to agricultural grasses, etc. Acute wheezing and obstruction. NO FEVER.

Silo Filer's Disease: Oxides of nitrogen released at top of silo lead to initial chest tightness. After an interval of non-exposure of days to weeks, with relatively few symptoms, there can develop an irreversible obstruction due to bronhiolitis obliterans with a marked decrease in FEV1

Farmer's lung: **A hypersensitivity pneumonities**, a delayed hypersensitivity reaction, due to inhalation of spores of thermoactinomyces from moldy hay, which induces interstitial inflammation and loosely formed granbulomas. Onset is within hours of exposure, with fever, cough, dyspnea, bibasilar crackles. Diagnosis is by History of exposure and removal of exposure. I

In hypersensitivity pneumonitis (extrinsic allergic alveolitis), the pathogenic immune response is not an allergic reaction, but rather a delayed hypersensitivity reaction.

Most hypersensitivity pneumonitis syndromes (e.g. bagassosis (sugar cane) bird fancier's, humidifier lung, etc) involve exposure to organic compounds, usually molds. Also mycobacterium avium (hot tub lung). And methotrexate.

Hypersensitivity pneumonitis can develop to rat urine.

Sarcoidosis

>Sarcoid inheritance is supported by monozygotic twin studies.

> Kveim antigen is a suspension of sarcoid tissue that causes characteristic skin granulomas when injected intradermally in up to 80% of patients with early sarcoidosis.

>Absolute indications for corticosteroid therapy of sarcoidosis include (1) hypercalcemia, (2) cardiac involvement, (3) ocular involvement (uveitis), (4) disfiguring skin disease, and (5) central nervous system involvement. The utility of corticosteroids in the treatment of other sequelae of sarcoidosis, including lung involvement, is controversial.

>Slit lamp examination is imperative for all patients with sarcoidosis to prevent resulting blindness(uveitis in 20%).

>For biopsy, choose skin and lung which are rarely be involved with noncaseating granulomatous inflammation from other disorders. (Don't biopsy liver or lymph nodes where granulomas occur from other disease.)

Sarcoid can have cranial nerve palsies and EN.

Berylliosis, like sarcoid, has inflammatory granulomas and is treated with steroids. Exposures occur in aluminum alloy processes and fluorescent light industry.

Pulmonary cavities:

Less likely to cause cavities: H. influenzae, M. pneumoniae, and other type serotypes of S. pneumoniae other than III.

Pulmonary cavities due to tissue necrosis: S. aureus, S. penumoniae serotype III, aerobic gram-negative bacilli, oral anaerobes, M. tuberculosis, and fungi.

Upper lobe cavities: M TB.

Lower lobe cavity with air fluid level and sulfur granules in subcutaneous tissues: The anaerobe, Actinomyces.

OSA may present with personality changes !

Triple test for an pleural effusion exudates: Any of :

Cholesterol >45

Protein >3

LDH >1.6 x upper limit of normal serum level.

Adenosine deaminase concentrations are elevated in tuberculous pleural effusions: the sensitivity of an adenosine deaminase pleural fluid level greater than 47 IU/L was 100% and specificity was 91%.

An indication for IVC filter is severe COPD, wherein minor compromise due to PE would cause death.

In pneumocystis, LDH is elevated. Levels greater than 600 IU/ml indicate a poor prognosis.

In pleural fluid exudates, low glucose can be caused by rheumatoid arthritis (classic), esophogeal rupture, TB, and malignancy.

PLEURAL FLUID ANALYSIS: The Rule of "15" or 29-49-60 for 2.9 protein, 49 cholesterol, and 60 LDH.

For an exudate, any of the following must be true:

Protein > 2.9 gm/dL

Cholesterol > 45 mg/dL

LDH > 60% of upper limit of normal of serum LDH (usually 60U/L).

Otherwise, it is a transudate.

DRUG INDUCED PULMONARY DISEASE (from Robbins) July 14, 2004

Pneumonitis & Fibrosis	Bleomycin Amiodarone
Hypersensitivity pneumonitis	Methotrexate Nitrofurantoin
Bronchospasm	Aspirin beta-blockers

Name	pathology	Radiologic	CMs	RX
Idiopathic* pulmonary fibrosis (= Usual interstitial pneumonitis)	Patchy, heterogenous disease Sub-pleural honeycomb fibrosis Proliferating fibroblast foci Minimal inflammation.	Non-Uniform. Lower lobe, pleura Honey combing	Cough, Dyspnea	
Desquamative Interstitial pneumonitis*	Pigmented Macrophages in distal air spaces. Peribronchiolar inflammation with little fibrosis. Desquamation of epithelial cells into air spaces.	Uniform Lower lobe Ground glass	Smokers	Steroids
Bronchiolitis obliterans organizing pneumonia (BOOP)= Cryptogenic Organizing Pneumonia (COP) *, (2)	Bronchiolocentric inflammation. Airspaces plugged with granulation tissue	Non-uniform ground glass peripheral	H/o Rx for penumonia. No fever. Bilateral crackles. PFTS: Mixed obstructive & restrictive.	Steroids
Hypersensi-tivity pneumonitis (Delayed hypersensitivity) (2)	Interstitial pneumonitis with lymphs, plasma cells, & macrophages. Interstitial fibrosis. Obliterative bronchiolitis. Granuloma formation	Ground glass Nodular Patchy	Acute(4-6hrs) ^T, cough, dyspnea. Resolves in 2 ds. ^ PMNs. Ab's to specific Ag (2) PFT's: Restrictive.	
Goodpasture's syndrome	Necrotizing, hemorrhaging IS pneumonitis: Intra-alveolar hemorrage, fibrous thickening of septa, hemosiderin laden macrophages. Linear deposits of Immunoglobulins along BM of septal walls (as in glomerular BM).			
Idiopathic pulmonary hemosiderosis	shedding & hyperplasia of alveolar epithelial cells. Blood in alveoli.			
Pulmonary alveolar proteinosis	Intra-alveolar dense granular material: lipid and PAS positive.		Cough with gelatinous sputum.	

*An "Idiopathic Insterstial Pneumonia".

(1) BOOP has many causes ore associations other than "idopathic", including post-infectious, drug related (amiodarine, bleo, MTX, cocaine), rheumatologic (RA, SLE), Immunologic (common variable immuno deficiency, essential mixed cryoglobulinemia), organ transplant, and other associations.

(2) Etiologies are myriad organic compounds: e.g., Farmer's lung (moldy hay, grain, silage), Bird Fancier's lung (Avian droppings), woodworker's lung, hot tub lung (mold on ceiling). Methotrexate. HVAC lung. Tissue Bx is not necessary for Dx. Method of diagnosis is by history of exposure and removal from agent.

NOTES:

Solitary pulmonary nodule

If all of these are true

—

Age < 40

Non-smoker

no prior CA

Nodule < 1 CM

Benign calcification pattern (diffuse, central, or laminar ("popcorn")

Middle or lower lobe location (**NOT** upper lobe)

Not a spiculated edge and with smooth borders

—

Then you can follow patient with CXR.

If there is any doubt, do a PET scan. (Sens & Spec > 95%).

False negatives are due to bronchoalveolar ca or hyperglycemia.

Presentations of lung tumors:

Adenocarcinoma: peripheral location and non-calcified. Most likely to have a single brain met. Associated with IPF.

Broncho-alveolar ca: non-resolving pulmonary infiltrate with air bronchogram. Associated with IPF.

Squamous cell ca: central lung mass, hypercalcemia.

Small cell ca: Central lung mass, hepatomegaly, lymphadenopathy, proximal muscle weakness, paresthesias (Eaton-Lambert) or SIADH.

Bronchial carcinoid: Atelectasis, hypervascular pedunculated mass, liver nodules, wheezing, diarrhea, and flushing.

TYPES OF DYSPNEA

SETTING	ONSET	AIRWAY & LUNG PATHOLOGY
Persulfates in hair dressers	Minutes to hours	irritant asthma
Sugar Can, Bird Droppings, or moldy hay	5 hours	Hypersensitivity pneumonitis
Latex exposure (health workers)	weeks to years	immunologic asthma
Silo-fillers disease or oxides of nitrogen	immediate (but see to right)	Chest tightness, rinorrhea, laryngeal symptoms (later, there can be irreversible bronchiolitis obliterans)
Phosgene (fire fighters)	6 hours to days	Bronchitis, alveolitis

ABNORMAL HEMOGLOBIN OR 02 CARRYING CAPACITY

	CO poisoning	Methemoglobinemia*
O2% by Pulse oximetry	NL	Decreased but still over estimate & plateaus at 85%
O2% by usual ABGs	NL	NL
PaO2	NL	NL
O2% by co-oximetry	Decreased (accurate)	Decreased (accurate)

*Acquired methemoglobinemia can result from dapsone (e.g., for dermetitis herpetiformis or for prophylaxis against pneumocystis in HIV patients) which oxidizes ferrous (Fe2+) to ferric (Fe3+) state. This results in a functional anemia and hypoxemia and may even be fatal (Pallais NEJM 2011;364:957).

IF THERE IS HYPOXEMIA ON ROOM AIR, and the FiO2 is increased to 100%,

the PaO2 may increase dramatically, e.g., to from 50 to 613, indicates

V/Q mismatch, as in pulmonary embolus, COPD, or interstitial lung disease.

If the PaO2 increases modestly from 50 to 75, this indicates a

Shunt, due to atelectasis, pneumonia, ARDS, cardiogenic pulmonary edema, pulmonary infarct or intra-cardiac right to left shunt. (See Cecil, Figure 99-2.)

Even when the PaO2 is correctable, there is still lung disease, manifest by the increased A-a Gradient. Partial pressure of air = 760 mmHg - 47 mmHg = 713. (Where 47= partial pressure of water vapor).

A-a gradient = 713*FiO2 - 5/4 * PCO2 - PaO2 For example,

at FiO2 = 21%, PCO2=52, and PaO2 = 50

=713*.21 - 5/4 * 52 - 50

= 150 - 65 - 50 = 35.

Or, at the FiO2, where the PaO2 is 613, the result is 713-65-613=35.
Normally the A-a gradient is 10 to 30, from 30 to 100 years of age.
At age 65 it is normally around 20.

	Summary	ch in HC03	HCO3	ch in pCO2	pCO2	ph chng	ph
Normal		0		0			
			24		40		7.40
Met Acidosis	ch in pCO2 is 110% of ch in HCO3	-10		-11			
			14		29		
Met Alkalosis	ch in pCO2 is 70% of ch in HCO3	+10		+7			
			34		47		
Resp Acidosis-Acute	ch in HCO3 is 10% of ch in pCO2	+1		+10		-.08	
	(DUE to buffering)		25		50		7.32
Resp Acidosis-Chron	ch in HCO3 is 40% of ch in pCO2	+4		+10		-.04	
	(Due to kidneys)		28		50		7.36
Resp Alkalosis-Acute	ch in HCO3 is 20% of ch in pCO2	-2		-10		+.08	
	(Due to buffering)		22		30		7.48
Resp Alkalosis-Chron	ch in HCO3 is 40% of ch in pCO2	-4		-10		+.04	
	(Due to kidneys)		20		30		7.44

For metabolic acidosis, you can use the winter formula: PC02 = 1.5 * Bicarb + 8.

For anion gap metabolic acidosis, you can calculate

Change in Anion Gap / Change in Bicarb. = 1 to 2

If the entire process is attributable to the abnormal anions.

If Ratio > 2, there is also a metabolic alkalosis.

If the ratio is < 1, there is an additional non-anion gap metabolic acidosis.

Passive smoking is associated with increased cardiac mortality, respiratory illness, and lung cancer.

In TB, the pathology is the caseating or necrotizing granuloma. Pleural biopsy is positive for non-caseating granulomas and TB, but cultures of pleural fluid are usually negative.

Patients from high risk areas of the world where tuberculosis is highly prevalent (as evidenced by use of BCG vaccine) and who have been vaccinated with BCG, have their BCG vaccine ignored in interpreting the PPD and are treated for latent TB on the basis of an induration of greater than 10 MM (because they are from a location with high prevalence and therefore have intermediate pre-test probability of TB).

Treat hepatic hydrothorax (transudative, right pleural effusion associated with hepatitis) with a)diuretics and salt restriction, b) possibly TIPS, c) and, finally, if those don't work, pleurodesis.

In lung transplant patients, the greatest risk of infection at 1 week is bacterial, at 1 - 6 months it is CMV, and then after 6 months it is bacterial again.

In HIV, a person with latent tuberculosis who acquires HIV infection is estimated to have a 3 to 15% annual risk of developing active tuberculosis, which is substantially higher than the risk in HIV-uninfected individuals. Active tuberculosis may develop at any point in the course of HIV infection. The clinical presentation varies with the degree of immune suppression. Typical upper lobe cavitary disease is common early in the course of HIV infection, when immune suppression is least. As the degree of immune suppression becomes more advanced, extrapulmonary or atypical presentations such as mediastinal lymph node, disseminated, and meningeal disease become more common. HIV-infected patients have a decreased frequency of sputum smear–positive disease that in conjunction with the atypical presentations makes diagnosis often more difficult than is the case in HIV-uninfected individuals.

In post transplant patients, human herpesvirus type 8 (HHV-8) is causally associated with primary effusion lymphoma as well as Kaposi's sarcoma and multicentric Castleman's disease.

In these patients, Epstein-Barr virus can cause posttransplant B cell lymphoproliferative disease.

It is stated that in a patient with chronic hypoxemia and Obesity Hypoventilation Syndrome (Pickwickian), the over correction of hypoxemia led to decrease respiratory drive and respiratory arrest. In OHS, remember to screen for hypothyroidism.

Patients who develop postpolio syndrome tend to have affliction of the same muscle groups that were affected in the original presentation. This patient presents with symptoms of diaphragmatic muscle weakness 40 years after the initial presentation with poliomyelitis.

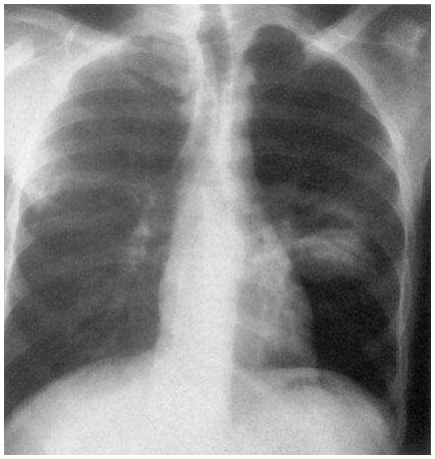
The most common cause of ambulatory care visits in the US is rhinovirus infection.

Reverse pulmonary edema and peripheral blood eosinophilia: hypereosinophilic syndrome.

Factor V Leiden deficiency – with protein C resistance --is the most frequent cause of PE in white populations.

Loffler's syndrome: pneumonitis+eosinophilia 2nd to Ascaris Lumbricoides.

For PE, the classic EKG is an SI, QIII



This is a left lower lobe lung abscess in a 60 y.o. man with a 2 week history of cough and fever. Sputum is foul smelling. This is an abscess, likely due to anaerobes. It is best treated by clindamycin or metronidazole. (It used to be treated with penicillin, but not anymore.)

MEDSTUDY Pulmonary questions

ciprofloxacin increases theophylline levels.

Chronic eosinophilic pneumonia: peripheral infiltrates (i.e., photo negative of pulmonary edema), eosinophilia.

In INH therapy, baseline and repeat LFTs are not indicated unless there is a co-existing liver disease. Clinical monitoring is done monthly for signs of INH-hepatitis : Anorexia, N,V, dark urine, rash, icterus, persistant parathesias of hands and feet, fatigue, weakness, fever, abodominal pain, arthralgias, and easy bruising.

Eosinophilic granuloma: In a smoker, on cxr honey comb changes with small cystic spaces in upper lung fields, and may have abnormalities related to pituitary insufficiency due to granulomas there (e.g., diabetes insipidus).

Length of treatment for DVT/PE:

Warfarin Life long: 2+ unprovoked DVT, 2 DVTs with any type of thrombophilia, or one DVT in an unusual site, or PE with APLAB.

Heparin Life long: DVT or PE secondary to cancer.

Warfarin for 12 months: 1 unprovoked PE (or one of which would be with an unprovoked proximal DVT) OR one unprovoked PE with an irremovable risk factor (e.g., ACLA or Factor V Leiden).

Warfarin for 6 months: 1st unprovoked DVT.

Warfarin 3 - 6 months: one DVT with removable risk factor.

CPAP must be used cautiously because it can increase the work of breathing. It is particularly contraindicated in ALS because it can cause tiring and death.

BI-PAP means that the pressure can be set differently for inspiration and expiration. E.G.: for expiration the pressure can be set to drop and make breathing more easily. It is particularly important to use BI-PAP for neuromuscular (ALS) or chest wall disease (scoliosis).

Alpha 1 ATT deficiency: CM's: Emphysema ≤ 45y.o. or in absence of smoking or occupation or in the lower lungs. Bronchiectasis with etiology. Asthma with persistent airflow obstruction post treatment. Unexplained liver disease. Necrotizing panniculitis.

Serum ATT is used for presumptive diagnosis: 100 - 300 mg/dL. < 80 indicates significant risk.

Phenotyping is required to confirm, if the serum ATT is borderline or if considering Rx.

PiZZ phenotype in serum is responsible for nearly all cases. Genotyping can be done on mouth

swabs. In ATT deficiency pulmonary disease, the pathogenesis is proteolysis.

In ATT liver disease, the pathogenesis is accumulation of ATT protein in hepatocytes.

Rx for pulmonary disease is by ATT mist. Rx for liver disease is renal transplant.

Cystic fibrosis (JAMA 2007;298:1787): This is a pearl: Think of cystic fibrosis in the following situtions:

Bronchiectasis plus any of the following a) male infertility (congenital bilateral absence of the vas deferens), b) recurrent idiopathic pancreatitis (10 - 20% of individuals with chronic idiopathic pancreatitis care cystic fibrosis mutations), or c) recurrent sinusitis with nasal polyposis.

Recent treatments include:

Better manual compression techniques.

Mucolytic dornase alfa (nebulized) (breaks up DNA from PMNs)

Nebulized antibiotics.

Oral azithromycin

Nutritional support (because of malaborption these patients are undernourished).

Replacement of ADEK.

EOSINOPHILIC LUNG DISEASE: Increased eosinophils in the lung with or without peripheral blood eosinophilia.

These can be divided into Airway disorders and parenchymal disorders

Airway Disorders	Parenchymal disorders
	Hypereosinophilic syndromes
Asthma	Eosinophilic pneumonias
Non asthmatic eosinophilic bronchitis	Pulmonary vasculitis
Allergic bronchopulmonary aspergillosis	Malignancies
	Infections
	Drugs
	Interstitial lung disease

Non asthmatic eosinophilic bronchitis: Hallmark=Chronic cough. (No bronchial hyper-responsiveness.

Allergic bronchopulmonary aspergillosis: Hallmark=Asthma, infiltrates on CXR, High IgE. Precipitins for aspergilla. Stages are: 1. Acute asthma with infiltrates. 2. Remission. 3. Exacerbation with 2x higher IgE. 4. Steroid dependency where the taper worsens the asthma. 5. A fibrotic end stage with cor pulmonale. Rx: oral steroids until CXR clears. Ketoconazole or Itraconazole.

Acute eosinophilic pneumonia: Hallmark=pneumonia with BAL eosinophils > 25%. Steroid responsive without relaps.

Chronic eosinophilic pneumonia. Peripheral infiltrates ("Photonegative infiltrates") BAL eos > 40%. Steroid responsive but relapses occur.

Idiopathic hyper-eosinophilic syndrome: Hallmark = multi-organ disease. Arterial and venous thrombi.

Churg Strauss syndrome: pulmonary-renal syndrome. Ashma, rhinitis, and peripheral blood eosinophilia. Vasculitis. P-ANCA positive.

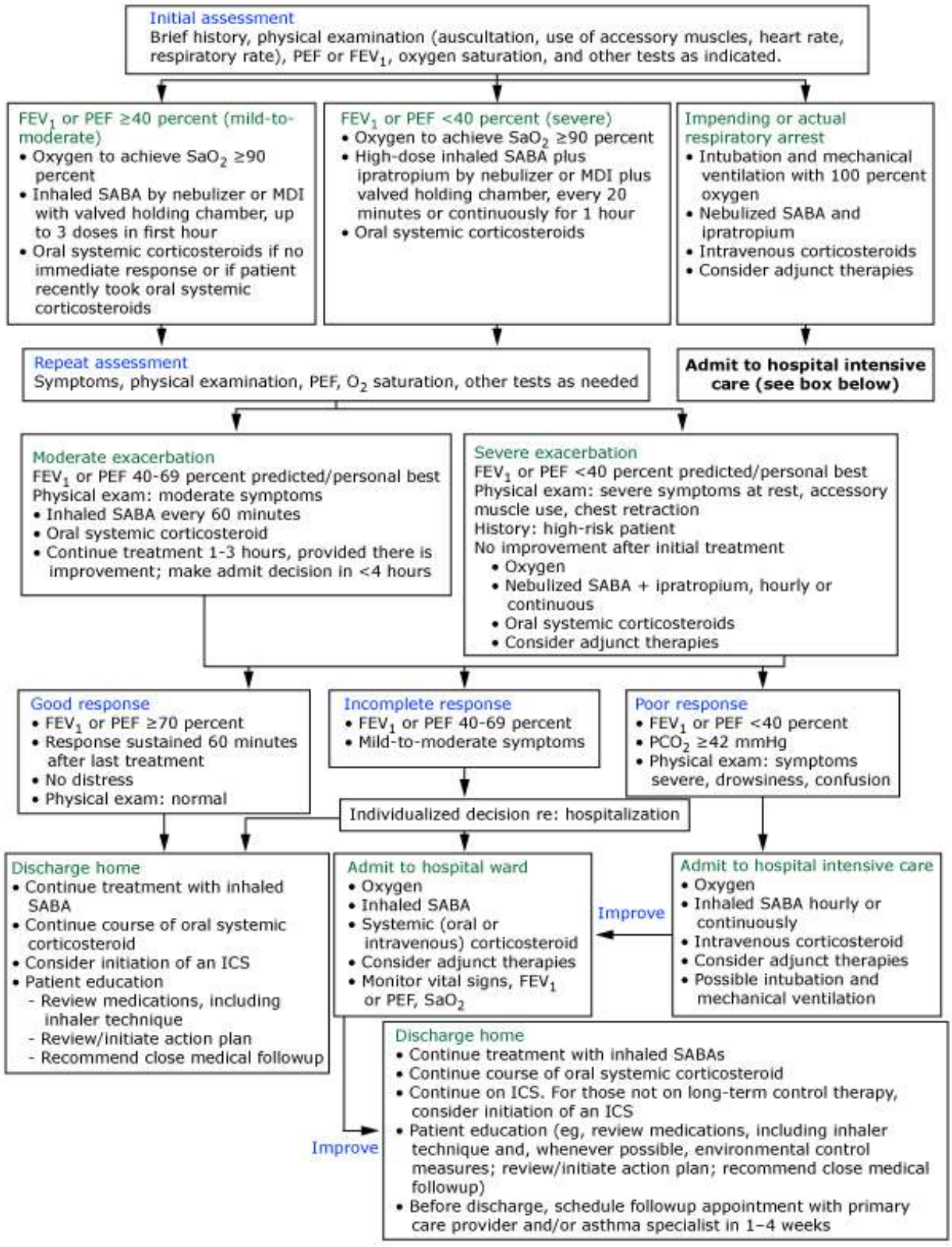
Parasitic infections causing pulmonary disease and peripheral blood eosinophilia.

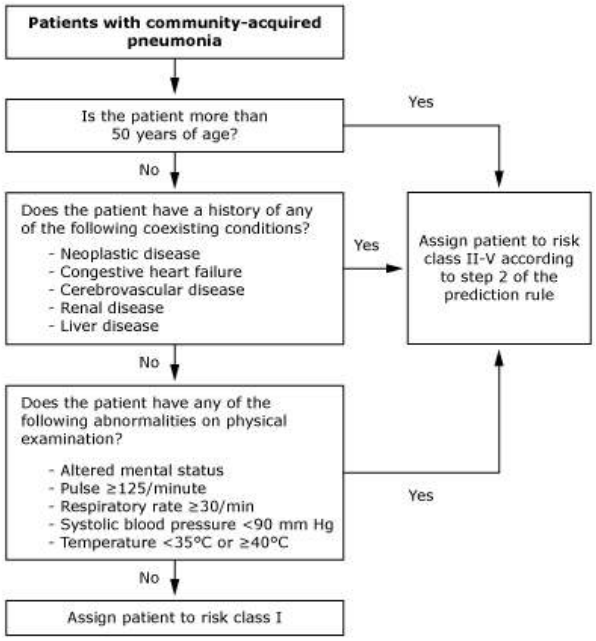
Parenchymal invasion with hemoptysis, CXR infiltrates and pleural effusions: Paragonimus, echinococcus, and cystercicosis.

Hematogenous spread: Hookworm, Ascaris, and Strongyloides. Cough & wheezing.

Various other disease can give eosinophilic pulmonary disease: sacrcoid, lung cancer, Hodgkin's disease, medications such as ASA, amiodarone, bleomycin, captopril, dilantin.

	Bronchitis	Emphysema
age	40-45	50 - 75
dyspnea	Mild: late	Severe: early
cough	early, copious sputum	late; scanty sputum
infections	common	occasional
respiratory insufficiency	repeated	terminal
cor pulmonale	common	rare; terminal
airway resistance	increased	normal or slight increase
elastic recoil	normal	low
CXR	prominent vessels; large heart	hyperinflation; small heart
Appearance	blue bloater	pink puffer


Initial assessment
Brief history, physical examination (auscultation, use of accessory muscles, heart rate, respiratory rate), PEF or FEV1, oxygen saturation, and other tests as indicated.
FEV1 or PEF ≥40 percent (mild-to-moderate)
• Oxygen to achieve SaO2 ≥90 percent
• Inhaled SABA by nebulizer or MDI with valved holding chamber, up to 3 doses in first hour
• Oral systemic corticosteroids if no immediate response or if patient recently took oral systemic corticosteroids
FEV1 or PEF <40 percent (severe)
• Oxygen to achieve SaO2 ≥90 percent
• High-dose inhaled SABA plus ipratropium by nebulizer or MDI plus valved holding chamber, every 20 minutes or continuously for 1 hour
• Oral systemic corticosteroids
Impending or actual respiratory arrest
• Intubation and mechanical ventilation with 100 percent oxygen
• Nebulized SABA and ipratropium
• Intravenous corticosteroids
• Consider adjunct therapies
Repeat assessment
Symptoms, physical examination, PEF, O2 saturation, other tests as needed
Admit to hospital intensive care (see box below)
Moderate exacerbation
FEV1 or PEF 40-69 percent predicted/personal best
Physical exam: moderate symptoms
• Inhaled SABA every 60 minutes
• Oral systemic corticosteroid
• Continue treatment 1-3 hours, provided there is improvement; make admit decision in <4 hours
Severe exacerbation
FEV1 or PEF <40 percent predicted/personal best
Physical exam: severe symptoms at rest, accessory muscle use, chest retraction
History: high-risk patient
No improvement after initial treatment
• Oxygen
• Nebulized SABA + ipratropium, hourly or continuous
• Oral systemic corticosteroids
• Consider adjunct therapies
Good response
• FEV1 or PEF ≥70 percent
• Response sustained 60 minutes after last treatment
• No distress
• Physical exam: normal
Incomplete response
• FEV1 or PEF 40-69 percent
• Mild-to-moderate symptoms
Poor response
• FEV1 or PEF <40 percent
• PCO2 ≥42 mmHg
• Physical exam: symptoms severe, drowsiness, confusion
Individualized decision re: hospitalization
Discharge home
• Continue treatment with inhaled SABA
• Continue course of oral systemic corticosteroid
• Consider initiation of an ICS
• Patient education
- Review medications, including inhaler technique
- Review/initiate action plan
- Recommend close medical followup
Admit to hospital ward
• Oxygen
• Inhaled SABA
• Systemic (oral or intravenous) corticosteroid
• Consider adjunct therapies
• Monitor vital signs, FEV1 or PEF, SaO2
Improve
Admit to hospital intensive care
• Oxygen
• Inhaled SABA hourly or continuously
• Intravenous corticosteroid
• Consider adjunct therapies
• Possible intubation and mechanical ventilation
Improve
Discharge home
• Continue treatment with inhaled SABAs
• Continue course of oral systemic corticosteroid
• Continue on ICS. For those not on long-term control therapy, consider initiation of an ICS
• Patient education (eg, review medications, including inhaler technique and, whenever possible, environmental control measures; review/initiate action plan; recommend close medical followup)
• Before discharge, schedule followup appointment with primary care provider and/or asthma specialist in 1–4 weeks



Age in years: Men, Women -10, NH residents + 10.

Comorbidities: Neoplastic 30, Liver disease 20, other of those in the figure 10.

Each of the Physical exam abnormalities get 10 to 20.

Lab abnormalities: Low sodium, ph < 7.35, BUN >30, glucose > 250, HCT < 30, POa2<60, pleural effusion: each of these gets 10 to 30.

< 70	0.6%
71-90	0.9
91-130	9.3
>130	27.0%

Class Points Mortality, percent

I No predictors 0.1

II <70 0.6

III 71-90 0.9

IV 91-130 9.3

V >130 27.0

CURB 65

Confusion
Urea Nitrogen > 20
Respiratory Rate >30
Blood pressure < 0-
Age > 65

Number of factors & 30 day mortality rate:
0: 0.6%,
1: 2.1%,
2: 9.2%,
3: 14.5%,
4: 40%

SHUNTING AND DISEASE CORELATIONS

Shunting absent:
IPF (idiopathic pulmonary fibrosis)
COPD
Asthma
A1ATD

Shunting present:
Hereditary hemorrhagic telangiectasia (Osler-Rendu-Weber)
Right to left shunts in heart disease; VSD
Pulmonary edema

HHT: Classically: epistaxis, GI bleed, iron deficiency, and telangiectasias of the mouth and fingers. The criteria are: 1) epistaxis, 2) telangiectasia of the mouth and fingers, 3) AVM of the lung, cerebrum and liver, 4) autosomal dominant pattern. The condition is associated with pulmonary hypertension.

	Low	Intermediate	High
Nodule (cm)	<1.5	1.5-2.2	>2.2
age	<45	45-60	>60
smoking	Never	current, ≤ 1PPD	current, >1PPD
smoking cessation	Quite > 7rs ago or never	quit < 7 years ago	current
nodule margins	Smooth	Scalloped	corona radiata or spiculated

In patients on a ventilator, peak pressure is the highest pressure achieved on forced inspiration.

Plateau pressure (ideally less than 30) follows the peak pressure and reflects the distension of the alveoli.

Positive End Expiratory pressure (PEEP) occurs after releasing the forced inspiration.

Resistance is defined as the difference in pressure between the peak pressure and the plateau pressure.

Static compliance = Tidal Volume/(Plateau pressure - PEEP).

It is decreased by pneumonia, edema, atelectasis, pneumothorax or endobronchial intubation.

Dynamic compliance = TV/(Peak pressure - PEEP).

It is decreased by bronchospasm, mucus plugging, kinked tube.

PULMONARY EMBOLISM PRETEST PROBABILITY

Feature	Points
Signs and symptoms of DVT	3
Alternative diagnosis equally or less probable	3
Heart rate > 100	1.5
Immobilization or surgery in prior 4 weeks	1.5
Prior history of DVT or PE	1.5
Hemoptysis	1
Malignancy (or treatment within 6 months)	1

Probability Low: < 2/ Intermediate 2-6/ High > 6.

PE is characterized by dyspnea, pleuritic pain, cough, hemoptysis, fever, increased Aa gradient, RV strain, clear CXR.

From Wells PS et al. Ann Int Med 1998; 129:997-1005.

DEEP VEIN THROMBOSIS PRETEST PROBABLITY:

History of Cancer 1

Immobilization 1

Bedd ridden 1

Thigh or calf tenderness 1

Calf swelling 1

Pitting edema 1

Collateral vein distension 1

Varicosities 1

Alternative diagnosis: -2

Pulmonary hypertension can be caused by nocturnal hypoxemia: Q 48, MKSAP 14, Pulmonary.