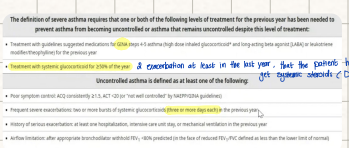
Medical Workbook

Respiratory internal medicine

Lecture one : Asthma

General characteristics:

- Chronic disease that is characterized by a triad: 1) Chronic inflx 2) Reversible airflow obstruction 3) Airway hyperresponsive
- It can begin at any age
- vary in severity from person to person
- Most are due to extrinsic asthma (Atopy, production of IgE due to triggers) and the rest are intrinsic (no Atopy)
- Severe VS uncontrolled asthma VS difficult to control (the patient is not adherant to his medications).



* Note: For the assessment of symptoms control we use ACT (Asthma control test) and ACQ (Asthma control questions)

- RF/Etiology: pollens, house dust, molds, occupation, western diet, smoking, pets, exercise or cold air, Medications (Aspirin and B-b), viral infx, GERD, sinusitis and rhinitis, prematurity and ↓ Maternal age, obesity, stress and emotional factors
- Asthma in Jordan: common, common in male children, increase by ↑2 in the last 10 years (Due to environmental factors).

Pathophysiology:

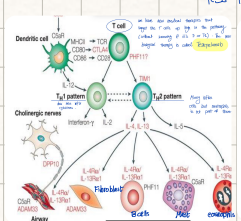
1) Chronic inflx 2) Reversible airflow obstruction
   - Due to eosinophils most of the time but could be neutrophils
   - By cells, mucus, Smooth muscle spasm, Goblet cell hyperplasia
     - early response: Acute bronchoconstriction by IgE mediator release
     - late response (6-24h)
     - then plug formation (weeks to resolve)
     - then remodelling
3) Airway hyperresponsive
   - Atopy
   - he would have V/Q mismatch,

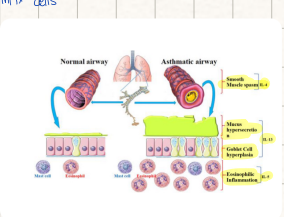
4 stages of blood gas progression with status asthmaticus

	PaO_2	$PaCO_2$
Stage 1	Decrease	Normal
Stage 2	Decrease	Decreased
Stage 3	NORMAL	Decreased
Stage 4	High	Decreased

* Note: if the patient has normal CO_2 in blood → he is in impending Rx arrest (a person with acute asthma attack should not have normal CO_2)

- you have to define the type of inflx (depending on the type of T cell).
  - T1: neutrophils with less inflx cells
  - T2: eosinophils with multiple inflx cells such as IL-4 (Mediates switch to IgE), IL-5 (attracts eosinophils), IL-13 [illegible] high eosinophilic count and high serum IgE





Clinical features:

They occur within 30 min of exposure to triggers.

1. Wheezing (Most common): usually at the end expiration (Mid Asthma), could be through expiration (increasing in severity) or inspiration (severe asthma) or absent (very severy obstruction even in small airways).
   Although asthma is the most common cause of wheezing, it could be associated with: 1) CF 2) HF 3) vocal cord dysfunction (Most imp DDx) → they present with wheezes, SOB and cough bc VC closes during insp and it happens in young patients with anxiety (wheeze is best heard over the laryngeal area) 4) Dynamic airway collapse: bronchomalacia or tracheomalacia (heard over the large airways)
2. Cough: non productive and non paroxysmal, may be the only symptom especially in exercise or nocturnal asthma (after midnight and early hours of mornings)
3. chest pain or tightness: in exercise and nocturnal asthma.
4. SOB
5. Nonspecific: Recurrent bronchitis, pneumonia, croup, rattling (in All children)

- When do we consider it as exacerbation Hx?

Exacerbation History

- Prodromal signs or symptoms
- Rapidity of onset
- Associated illnesses
- Number in the last year (2) at least
- Need for emergency department visits, hospitalizations, ICU admissions, intubations
- Missed days from work /school or activity limitation

Asthma and associated factors :

1. Aspirin induced: 3-10%, 3rd - 4th decade → Asthma + Aspirin sensitivity + nasal polyps, caused by: increase in eosinophils and cysteinyl leukotriens after exposure. Managed by: 1) Avoidance if you can 2) leukotriene antagonists (for cardiac and rheumatological patients) 3) Aspirin desensitizations (to decrease sinus symptoms).
2. GERD: improvement of Asthma, unexplained cough with Anti-reflux therapy in 64% of patients, 24% of patients have clinically silent reflux.
3. occupational Asthma: 15-20% of patients in High risk Jobs: Farmers, painters, plastic... , work exacerbated asthma: a patient who already has asthma but it's worsened by work factors

- Peak-flow monitoring during work (optimally, at least 4 times a day) for at least 2 weeks and a similar period away from work is one recommended method to establish the diagnosis.

to establish a dx:

4. Sinusitis: 50% of patients → treatement of sinusitis requires at least 10 days of Antibiotics to improve the asthma.

(5) Viruses and asthma: 80-85% of childhood asthma are associated with viral exposures → Rhinovirus (induces wheezing illnesses in a child with asthma), pneumonia had been found in more than 50%, RSV (associated with smoke exposure). (6) Exercise: in 50% they have silent asthma (except during exercising), they do have sensitivity towards cold and dry air (creates acute bronchoconstrictions), they would have symptoms such as cough, wheezing, SOB and chest pain after 10 min into exercise, treatment: warming up and b2 agonists. (Remember that they have normal resting spirometry)

(7) Pregnancy: severe and poorly controlled if: premature, low weight, perinatal mortality → prevent hypoxic episodes in the mother to maintain good O_2 to the baby

Nonpulmonary Manifestations

- Signs of atopy or allergic rhinitis, such as conjunctival congestion and inflammation, ocular shiners, a transverse crease on the nose due to constant rubbing
- Pale nasal mucosa
- Erythematous Turbinates
- Nasal polyps
- Atopic dermatitis
- Eczema

Physical examination:

- Mild episodes
  - Shortness of breath with physical activity
  - Can talk in sentences and lie down (imp)
  - May be agitated
  - Respiratory rate is increased
  - No use of accessory muscles
  - Heart rate is less than 100 bpm
  - Moderate expiratory wheezing
  - O2 saturation is greater than 95% (imp)

- Moderately severe episodes:
  - Use of accessory muscles
  - In children: supraclavicular and intercostal retractions, nasal flaring, abdominal breathing
  - The heart rate is 100-120 bpm
  - Loud wheezing
  - **Pulsus paradoxus**: (fall in systolic blood pressure during inspiration of10-20 mm Hg)
  - O2 sat is 91-95%
  - Sitting position

Severe episode
- Shortness of breath at rest
- Talk in words
- Respiratory rate: greater than 30/min
- Use of accessory muscles
- Heart rate is more than 120 bpm
- Loud biphasic (expiratory and inspiratory) wheezing
- Pulsus paradoxus is often present (20-40 mm Hg)
- O2 sat less than 91%
- Sitting position: tripod position.

Impending Respiratory Failure
- Drowsy and confused (tachy then brady then arrest)
- Thoracoabdominal movement
- Wheezing may be absent
- Severe hypoxemia, bradycardia
- Pulsus paradoxus may be absent: suggests respiratory muscle fatigue.
- Diaphoresis
- Rise in PCO_2 and hypoventilation
- Life-threatening hypoxia, advanced hypercarbia, bradypnea, somnolence

CLASSIFY SEVERITY
Clinical Features before Treatment

	Symptoms	Nocturnal Symptoms	FEV_1 or PEF
STEP 4 Severe Persistent	Continuous Limited physical activity	Frequent	< 60% predicted Variability > 30%
STEP 3 Moderate Persistent	Daily Attacks affect activity	> 1 time week	60 to 80% predicted Variability > 30%
STEP 2 Mild Persistent	> 1 time a week but < 1 time a day	> 2 times a month	> 80% predicted Variability 20 to 30%
STEP 1 Intermittent	< 1 time a week Asymptomatic and normal PEF between attacks	< 2 times a month	> 80% predicted Variability < 20%

Asthma classification:

1) intermittent 2) Mild persistant 3) Moderate persistant 4) Severe persistant } At any stage they could have exacerbation, one severe feature is enough to diagnose with severe persistant.

Asthma DDX:

(1) VC dysfunction: May disappear during speech or laughter → you should do direct laryngeoscopy during the episodes or after exercise • the presence of the inspiratory limb of the flow-volume loop = suggestive of VC dysfunction. (2) CHF (interstitial pul. edema and engorged pul. vessels = ↓ lung compliance = SOB and wheezes so any wheezing 2° to bronchospasm = paraxysmal nocturnal SOB and nocturnal cough. (3) Forign body (4) Bronchial lesions (5) Sinus disease (6) GERD

Asthma diagnosis:

(1) PFT → they show decreased FEV1, decrease expiratory flow rate and decreased FEV1 / FVC ratio < 0.70 (2) Spirometry (Before and after bronchodilators): if increase in FEV1 or FVC by at least 12% = Asthma. (3) Methacholine test (when spirometry is normal or intermittent asthma or exercise induced): +ve if 20% decrease in FEV1 and if +ve it excludes Asthma. { if FEV1 is 65-70% avoid the test } (4) Mannitol: +ve if decrease FEV1 by 15%. (5) peak flow monitoring (used to assist the severity (< 50 is severe)): very common in ED (the quickest test for dx if the patient is in ED) → variability of 20% between morning and night (you should perform it on 5 days *if the patient is not in ED*) (6) CXR: normal in mild to moderate, but severe could reveal hyperinflation → imp to exclude pneumothorax or forign bodies (7) chest CT: only in specific patients. (8) ABGs: hypocarbia is common, if $PaCO_2$ is normal or increased = patient needs admission (a sign of severe obstruction) (9) Blood and sputum eosinophilia + serum IgE:

- Blood and sputum eosinophilia:
  - Greater than 4% (blood) supports the diagnosis of asthma
  - Its absence does not exclude asthma
  - Greater than 8% may be observed in patients with:
    - Atopic dermatitis. (Skin rash)
    - Allergic bronchopulmonary aspergillosis. (IgE serum > 1000 and parenchymal changes (not found in Asthma))
    - EGPA
    - Eosinophilic pneumonia
  - Use mepolizumab (anti-IL-5 antibody) if counts 150 cells/µL or an eosinophil count of 300 cells/µL within the past 12 months
  - Adjust ICS with sputum eosinophilia

- Serum Immunoglobulin E:
  - Total serum immunoglobulin E levels greater than 100 IU are frequently observed in patients experiencing allergic reactions
  - Observed also in: (allergic bronchopulmonary aspergillosis, EGPA)
  - Normal levels do not exclude the diagnosis of asthma
  - Elevated levels are required for chronic asthma patients to be treated with omalizumab (Xolair)

Asthma treatment:

GINA goal of asthma management

The goal is to achieve the **best possible long-term asthma outcomes** for each patient:

- Long-term symptom control, which may include:
  - Few/no asthma symptoms, quickly relieved
  - No sleep disturbance
  - Unimpaired physical activity
- Long-term asthma risk minimization, which may include:
  - No exacerbations
  - Improved or stable personal best lung function
  - No requirement for maintenance oral corticosteroids
  - No medication side-effects

When discussing best possible long-term outcomes with a patient, consider:
- Their asthma phenotype
- Clinical features
- Multimorbidity
- Risk factors (e.g. poor adherence, smoking, persistent airflow limitation)
- Availability, cost and adverse effects of medications
- The patient's goals (these may be different from medical goals)

- Assessing symptom control is not enough! Patients with few asthma symptoms can still have severe or fatal exacerbations related to individual risk factors or external triggers (viruses, allergen, pollution)
- Encourage referral for expert advice for patients with difficult-to-treat or severe asthma

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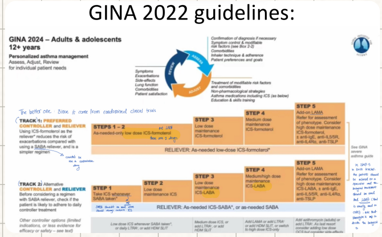
• We start with quick releive medications including rapid acting B2 agonists → if used more than 2 days a week for symptoms you should step up to treatement.

GINA 2022 guidelines:



Biological classes:

IgE against IgE

Class	Name	Age*	Asthma indication*	Other indications*
Anti-IgE	Omalizumab (SC)	≥6 years	Severe allergic asthma	Nasal polyposis, chronic spontaneous urticaria
Anti-IL5	Mepolizumab (SC) Reslizumab (IV)	≥6 years ≥18 years	Severe eosinophilic/Type 2 asthma	Mepolizumab: EGPA, CRSwNP, hypereosinophilic syndrome
Anti-IL5R	Benralizumab (SC)	≥12 years		
Anti-IL4R	Dupilumab (SC)	≥6 years	Severe eosinophilic/Type 2 asthma, or maintenance OCS	Moderate-severe atopic dermatitis, CRSwNP
Anti-TSLP	Tezepelumab (SC)	≥12 years	Severe asthma	

Questions in pp:
4, 7, 8, 14, 15, 17, 19, 20, 22, 44, 65, 81

• you could also do Bronchial thermoplasty for smooth muscle spasm: but it's done for certain patients and not recommended initially

• For acute exacerbations → (1) short acting bronchodilators: Salbutamol 2) Steroids 3) Heliox (O2 + helium) 80:20 4) intubation

• Extra note: complications of Asthma: 1) Status asthmaticus 2) Acute RF 3) pneumothorax 4) Atelectasis.

Lecture 2 : COPD

General characteristics:

- Heterogeneous lung disease. • it has 2 classic types : 1) chronic bronchitis : chronic cough and productive for 3 months over 2 years 2) emphysema: permanent enlargement of air spaces distal to terminal bronchioles due to destruction in the walls these 2 usually coexist but you can find pure bronchitis or emphysema. • Both conditions are progressive, persistant and causes airway obstruction. • it's the 3rd leading cause of death. • More common in elderly (≥ 65) • M=W (But 20 y ago M>F) · due to smoking habits.

Pathophysiology:

(1) chronic bronchitis: walls are thick, inflammed and mucus is made more than usual (Smooth muscle hyperplasia). → ciliary dysfunction and increased goblet cells size size and number (2) Emphysema: loss of elasticity of air sacs with destruction of the walls between them → Extra note Macrophages and PMN produces proteases that inhibits α1-Antitrypsin = More free radicles and destruction * Note (Extra): Two types of emphysema: centriacinar : due to smoking (Destruction of proximal acini) AND panlobular : due to AIAT deficiency (Distal and proximal acini) Both conditions are irreversible.

Risk factors and causes:

Proposed Taxonomy (Etiotypes) for COPD

Classification	Description
Genetically determined COPD (COPD-G)	Alpha-1 antitrypsin deficiency (AATD) Other genetic variants with smaller effects acting in combination
COPD due to abnormal lung development (COPD-D)	Early life events, including premature birth and low birthweight, among others
Environmental COPD	
Cigarette smoking COPD (COPD-C)	• Exposure to tobacco smoke, including *in utero* or via passive smoking • Vaping or e-cigarette use • Cannabis
Biomass and pollution exposure COPD (COPD-P)	Exposure to household pollution, ambient air pollution, wildfire smoke, occupational hazards
COPD due to infections (COPD-I)	Childhood infections, tuberculosis-associated COPD, HIV-associated COPD
COPD & asthma (COPD-A)	Particularly childhood asthma
COPD of unknown cause (COPD-U)	

Clinical features:

Clinical Indicators for Considering a Diagnosis of COPD

Consider the diagnosis of COPD, and perform spirometry, if any of these clinical indicators are present: (these indicators are not diagnostic themselves, but the presence of multiple key indicators increases the probability of the presence of COPD; in any case, spirometry is required to establish a diagnosis of COPD)

Dyspnea that is	Progressive over time Worse with exercise → earliest symptom is exertional dyspnea. Persistent
Recurrent wheeze	
Chronic cough	May be intermittent and may be unproductive
Recurrent lower respiratory tract infections	
History of risk factors	Tobacco smoke (including popular local preparations) Smoke from home cooking and heating fuels Occupational dusts, vapors, fumes, gases and other chemicals Host factors (e.g., genetic factors, developmental abnormalities, low birthweight, prematurity, childhood respiratory infections etc.)

Physical examination:

Early in the disease you can't detect easily but later on you could see:

(1) prolonged exp time (2) Signs of hyperinflation: Barrel chest, decreased breathing sounds, distant heart sounds and increased resonance (3) End expiratory wheezes (Doesn't necessarily relate to the severity of airflow obstruction) (4) Tachypnea (5) Tachycardia (6) tripod position (7) pursed lip (to create a +ve pressure) (8) Signs of cor pulmonale (swelling of the ankles) (9) tar stains. (10) usage of Accessory muscles.

COPD DDX :

Differential Diagnosis of COPD

Diagnosis	Suggestive Features
COPD	Symptoms slowly progressive History of tobacco smoking or other risk factors
Asthma	Variable airflow obstruction Symptoms vary widely from day to day Symptoms worse at night/early morning Allergy, rhinitis, and/or eczema also present Often occurs in children Family history of asthma
Congestive heart failure (Cor pulmonale)	Chest X-ray shows dilated heart, pulmonary edema Pulmonary function tests indicate volume restriction and airflow obstruction
Bronchiectasis	Large volumes of purulent sputum Commonly associated with bacterial infection Chest X-ray/HRCT shows bronchial dilation
Tuberculosis	Onset all ages Chest X-ray shows lung infiltrate Microbiological confirmation High local prevalence of tuberculosis
Obliterative bronchiolitis	Can occur in children Seen after lung or bone marrow transplantation HRCT or biopsy confirms hypodense areas
Diffuse panbronchiolitis	Predominantly seen in patients of Asian descent Most patients are male and nonsmokers Almost all have chronic sinusitis Chest X-ray & HRCT show diffuse small centrilobular nodular opacities & hyperinflation

These features tend to be characteristic of the respective diseases, but are not mandatory. For example, a person who has never smoked may develop COPD (especially in LMICs where other risk factors may be more important than cigarette smoking).

Prevention of COPD:

(1) Primary prevention : Avoidance of tobacco smoking (passive and active)

BRIEF STRATEGIES TO HELP THE PATIENT WILLING TO QUIT (3 As strategy)

• ASK:	Systematically identify all tobacco users at every visit. *Implement an office-wide system that ensures that, for EVERY patient at EVERY clinic visit, tobacco-use status is queried and documented.*
• ADVISE:	Strongly urge all tobacco users to quit. *In a clear, strong, and personalized manner, urge every tobacco user to quit.*
• ASSESS:	Determine willingness and rationale of patient's desire to make a quit attempt. *Ask every tobacco user if he or she is willing to make a quit attempt at this time (e.g., within the next 30 days).*
• ASSIST:	Aid the patient in quitting. *Help the patient with a quit plan; provide practical counseling; provide intra-treatment social support; help the patient obtain extra-treatment social support; recommend use of approved pharmacotherapy except in special circumstances; provide supplementary materials.*
• ARRANGE:	Schedule follow-up contact. *Schedule follow-up contact, either in person or via telephone.*

(2) 2ird prevention: Smoking cessation (the disease could be slowed by cutting off smoking) Although smoking cannot results in complete reversal • Respiratory Symptoms improve within 1 year of quitting • Some patients would have weight gain and constipations after the cessation • Some studies showed that 25% of the patient had long term quit after trying to quit • 3 minute counselling by the physician could help with encouraging the patient to stop smoking.

Difference between pink puffers(emphysema). and blue bloaters(chronic bronchitis):

TABLE 2-1 COPD—Emphysema and Chronic Bronchitis

Predominant Emphysema ("Pink Puffers")	Predominant Chronic Bronchitis ("Blue Bloaters")
• Patients tend to be thin due to increased energy expenditure during breathing. (Hyperventilation) • When sitting, patients tend to lean forward. • Patients have a barrel chest (increased AP diameter of chest).	• Patients tend to be overweight and cyanotic (secondary to chronic hypercapnia and hypoxemia). • Chronic cough and sputum production are characteristic. • Signs of cor pulmonale may be present in severe or long-standing disease.
Tachypnea with prolonged expiration through pursed lips is present.	Respiratory rate is normal or slightly increased. • Hyperventilation • greater V/Q mismatch → more hypoxemia and cyanosis.

• less hypoxic (they appear pink)

Difference between asthma and COPD

	Asthma	COPD
Onset	Anytime (often childhood or youth)	Later in life
Etiology	Allergic, family history	Smoking, other noxious exposures
Course	Intermittent	Chronic progressive
Clinical features	Wheeze, episodic dyspnea, cough	Persistent dyspnea, productive cough
Pattern of Symptoms	Variable day to day, more at night/early morning	Less variable, more on exertion
Inflammatory cells and mediators	Eosinophils, mast cells, Th-2 type	Neutrophils, macrophages, Th-1 type
Response to Bronchodilators	Largely reversible	Partially reversible or irreversible
Response to steroids	Substantial	Partial

• Hyperventilation • Hypoventilation

Diagnosis of COPD :

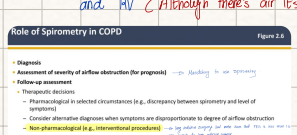
(1) Starts with Hx then PF (as mentioned above)

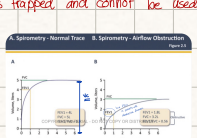
Early :
1) Exertional SOB
2) Mild recurrent cough
3) clearing throat in mornings
4) skipping stairs and physical activities

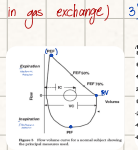
late :
1) SOB after minimal exertion
2) Wheezes during exhalation
3) chest tightness
4) chronic cough
5) Frequent FLU

→ in very late stages: Fatigue, wt loss, Swelling in feet, ankles or legs → signs of cor pulmonale.

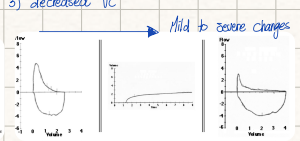
(2) PFT (Spirometry) : The definitive diagnostic test , you should find: 1) Decreased FEV_1 and FVC/FEV_1 ratio 2) increased TLC and RV (Although there's air it's trapped and cannot be used in gas exchange) 3) decreased VC







Mild to severe changes



[3] CXR: Hyperinflation signs [4] Measures α1 AT [5] ABGs: Chronic pCO2 retention and decreased PO2

GOLD grades and other tools :

GOLD Grades and Severity of Airflow Obstruction in COPD (based on post-bronchodilator FEV1)

Figure 2.7

In COPD patients (FEV1/FVC < 0.7):

GOLD 1:	Mild	FEV1 ≥ 80% predicted
GOLD 2:	Moderate	50% ≤ FEV1 < 80% predicted
GOLD 3:	Severe	30% ≤ FEV1 < 50% predicted
GOLD 4:	Very Severe	FEV1 < 30% predicted

GOLD ABE Assessment Tool

Figure 2.10

Spirometrically confirmed diagnosis (For dx) imp → Assessment of airflow obstruction (By using of GOLD grades) → Assessment of symptoms/risk of exacerbations

Post-bronchodilator FEV1/FVC < 0.7 (Since it's irreversible)

GRADE	FEV1 (% predicted)
GOLD 1	≥ 80
GOLD 2	50-79
GOLD 3	30-49
GOLD 4	< 30

EXACERBATION HISTORY (PER YEAR)		
≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	E	
0 or 1 moderate exacerbations (not leading to hospitalization)	A (less symptom and exacerbation)	B (more symptom and less exacerbation)
	mMRC 0-1, CAT < 10	mMRC ≥ 2, CAT ≥ 10

Modified MRC Dyspnea Scale

Figure 2.8

PLEASE TICK IN THE BOX THAT APPLIES TO YOU | ONE BOX ONLY | Grades 0 - 4

mMRC Grade 0	mMRC Grade 1	mMRC Grade 2	mMRC Grade 3	mMRC Grade 4
I only get breathless with strenuous exercise	I get short of breath when hurrying on the level or walking up a slight hill	I walk slower than people of the same age on the level because of breathlessness, or I have to stop for breath when walking on my own pace on the level	I stop for breath after walking about 100 meters or after a few minutes on the level	I am too breathless to leave the house or I am breathless when dressing or undressing
☐	☐	☐	☐	☐

CAT™ Assessment

Figure 2.9

For each item below, place a mark (x) in the box that best describes you currently. Be sure to only select one response for each question.

* More than 10 → symptomatic
* More than 20 → severely symptomatic

EXAMPLE: I am very happy	0 X 2 3 4 5	I am very sad	Score
I never cough	0 1 2 3 4 5	I cough all the time	
I have no phlegm (mucus) in my chest at all	0 1 2 3 4 5	My chest is completely full of phlegm (mucus)	
My chest does not feel tight at all	0 1 2 3 4 5	My chest feels very tight	
When I walk up a hill or one flight of stairs I am not breathless	0 1 2 3 4 5	When I walk up a hill or one flight of stairs I am very breathless	
I am not limited doing any activities at home	0 1 2 3 4 5	I am very limited doing activities at home	
I am confident leaving my home despite my lung condition	0 1 2 3 4 5	I am not at all confident leaving my home because of my lung condition	
I sleep soundly	0 1 2 3 4 5	I don't sleep soundly because of my lung condition	
I have lots of energy	0 1 2 3 4 5	I have no energy at all	

Use of CT in Stable COPD

Figure 2.11

① Differential Diagnosis	• Frequent exacerbations with excessive cough with sputum production, raising concern for bronchiectasis or atypical infection • Symptoms out of proportion to disease severity based on lung function testing
② Lung Volume Reduction (if you want to do lung reduction surgery)	• Endobronchial valve therapy may be a therapeutic option for patients if they demonstrate postbronchodilator FEV1 between 15% to 45% and evidence of hyperinflation • Lung volume reduction surgery may be a therapeutic option for patients with hyperinflation, severe upper lobe predominant emphysema and low exercise capacity after pulmonary rehabilitation
③ Lung Cancer Screening	• Annual low-dose CT scan is recommended for lung cancer screening in patients with COPD due to smoking according to recommendations for the general population

Common Risk Factors for the Development of Lung Cancer

Figure 5.1

- Age > 55 years
- Smoking history > 30 pack years
- Presence of emphysema by CT scan
- Presence of airflow limitation FEV1/FVC < 0.7
- BMI < 25 kg/m²
- Family history of lung cancer

Treatment:

Goals for Treatment of Stable COPD

Figure 3.1

- Relieve Symptoms
- Improve Exercise Tolerance
- Improve Health Status

→ REDUCE SYMPTOMS

AND

- Prevent Disease Progression
- Prevent and Treat Exacerbations
- Reduce Mortality

→ REDUCE RISK

Treatment

- Reducing risk factor exposure · Most imp one is smoking
- Appropriate assessment of disease
- Patient education
- Pharmacological and non-pharmacological management of stable COPD
- Prevention and treatment of acute COPD exacerbations

Nonpharmacological treatment(stable COPD)

(improve survival)

- Smoking cessation
- Education , self management and pulmonary rehabilitation
- Vaccinations (specifically influenza)
- Nutrition
- End of life and palliative care
- Treatment of hypoxia
- Treatment of hypercapnia (Reduce exacerbations but not survival)
- Intervention bronchoscopy and surgery

* non of the treatment of inhalers can improve survival but non pharmacological can improve survival.

* What is COPD exacerbations:

SOB, cough, sputum that worsens ≤ 14 days which is accompanied by tachypnea, tachycardia is often associated by airway viral infection, pollutions or other insult to the airway

Non-Pharmacological Management of COPD*

Figure 3.12

Patient Group	Essential	Recommended	Depending on Local Guidelines
A	Smoking cessation (can include pharmacological treatment)	Physical activity	① Influenza vaccination ② COVID-19 vaccinations ③ Pneumococcal vaccination Pertussis vaccination Shingles vaccination RSV vaccination
B and E	Smoking cessation (can include pharmacological treatment) Pulmonary rehabilitation	Physical activity	Influenza vaccination COVID-19 vaccinations Pneumococcal vaccination Pertussis vaccination Shingles vaccination RSV vaccination

(importance)

Prescription of Supplemental Oxygen to COPD Patients

Figure 3.15

Arterial hypoxemia defined as: PaO_2 ≤ 55 mmHg (7.3 kPa) or SaO_2 < 88% or PaO_2 > 55 but < 60 mmHg (> 7.3 kPa but < 8 kPa) with right heart failure or erythrocytosis

↓

Prescribe supplemental oxygen and titrate to keep SaO_2 ≥ 90%

↓

Recheck in 60 to 90 days to assess:
- If supplemental oxygen is still indicated
- If prescribed supplemental oxygen is effective

Initial Pharmacological Treatment

Figure 3.7

(Based on symptom group)

≥ 2 moderate exacerbations or ≥ 1 leading to hospitalization	GROUP E: LABA + LAMA* (consider LABA+LAMA+ICS* if blood eos ≥ 300)	
0 or 1 moderate exacerbations (not leading to hospital admission)	GROUP A: A bronchodilator	GROUP B: LABA + LAMA*
	mMRC 0-1, CAT < 10	mMRC ≥ 2, CAT ≥ 10

*Single inhaler therapy may be more convenient and effective than multiple inhalers; single inhalers improve adherence to treatment

Exacerbations refers to the number of exacerbations per year; eos: blood eosinophil count in cells per microliter; mMRC: modified Medical Research Council dyspnea questionnaire; CAT™: COPD Assessment Test™.

Pharmacological treatement:

- Inhaled B2 agonist(short acting)(SABA)
- Inhaled B2 agonist(long acting)(LABA)
- Inhaled anticholinergic(short acting)(SAMA)
- Inhaled anticholinergic(long acting)(LAMA)
- Inhaled corticosteroid (ICS)
- Combination inhalers
- Methylxanthine
- Phosphodiastrase-4 inhibitor → Mainly for chronic bronchitis

Confounders or Contributors to be Considered in Patients Presenting with Suspected COPD Exacerbation

Figure 4.1

→ Think about DDx like pneumonia to know wether to give ICS or not

Most frequent

Pneumonia
- Chest radiograph

Pulmonary embolism
- Clinical probability assessment (Hemoptysis, surgery, fracture, history of cancer, DVT)
- D-dimer
- CT angiography for pulmonary embolism

Heart failure
- Chest radiograph
- NT Pro-Brain Natriuretic Peptide (Pro-BNP) and BNP
- Echocardiography (For EF)

Less frequent

Pneumothorax, pleural effusion
- Chest radiograph
- Thoracic ultrasound

Myocardial infarction and/or cardic arrhythmias (atrial fibrillation/flutter) (very imp)
- Electrocardiography
- Troponin

Classification of the Severity of COPD Exacerbations

Figure 4.3

COPD Patient with Suspected Exacerbation → Confirm ECOPD Diagnosis and Episode Severity / Consider Differential Diagnosis

Severity	Variable thresholds to determine severity
Mild (default)	• Dyspnea VAS < 5 • RR < 24 breaths/min • HR < 95 bpm • Resting SaO_2 ≥ 92% breathing ambient air (or patient's usual oxygen prescription) AND change ≤ 3% (when known) • CRP < 10 mg/L (if obtained)
Moderate (meets at least three of five*)	• Dyspnea VAS ≥ 5 • RR ≥ 24 breaths/min • HR ≥ 95 bpm • Resting SaO_2 < 92% breathing ambient air (or patient's usual oxygen prescription) AND/OR change > 3% (when known) • CRP ≥ 10 mg/L *If obtained, ABG may show hypoxemia (PaO_2 ≤ 60 mmHg) and/or hypercapnia ($PaCO_2$ > 45 mmHg) but no acidosis
Severe	• Dyspnea, RR, HR, SaO_2 and CRP same as moderate • ABG show new onset/worsening hypercapnia and acidosis ($PaCO_2$ > 45 mmHg and pH <7.35)

Consider Differential Diagnosis:
- Heart failure
- Pneumonia
- Pulmonary embolism

↓
- Appropriate testing and treatment

↓

Determine etiology: viral testing, sputum culture, other

Adapted from: The ROME Proposal, Celli et al. (2021) Am J Respir Crit Care Med. 204(11): 1251-8.

Abbreviations: VAS visual analog dyspnea scale; RR respiratory rate; HR heart rate; SaO_2 oxygen saturation; CRP C-reactive protein; ABG arterial blood gases; PaO_2 Arterial pressure of oxygen.

Key Points for the Management of Stable COPD During COVID-19 Pandemic

Figure 6.1

Protective Strategies	• Follow basic infection control measures • Wear a face covering • Consider shielding/sheltering-in-place • Have the COVID-19 vaccinations in line with national recommendations
Investigations	• Only essential spirometry at times of high prevalence of COVID-19
Pharmacotherapy	• Ensure adequate supplies of medications • Continue unchanged including ICS
Non-Pharmacological Therapy	• Ensure annual influenza vaccination • Maintain physical activity

Diagnosis and Assessment

Figure 4.2

1.	Complete a thorough clinical assessment for evidence of COPD and potential respiratory and non-respiratory concomitant diseases, including consideration of alternative causes for the patient's symptoms and signs: primarily pneumonia, heart failure, and pulmonary embolism.
2.	**Assess:** a. Symptoms, severity of dyspnea that can be determined by using a VAS, and documentation of the presence of cough. b. Signs (tachypnea, tachycardia), sputum volume and color, and respiratory distress (accessory muscle use).
3.	Evaluate severity by using appropriate additional investigations such as pulse oximetry, laboratory assessment, CRP, arterial blood gases.
4.	Establish the cause of the event (viral, bacterial, environmental, other).

Abbreviations: COPD = chronic obstructive pulmonary disease; CRP = C-reactive protein; VAS = visual analog scale.

Potential Indications for Hospitalization Assessment*

Figure 4.4

- Severe symptoms such as sudden worsening of resting dyspnea, high respiratory rate, decreased oxygen saturation, confusion, drowsiness
- Acute respiratory failure
- Onset of new physical signs (e.g., cyanosis, peripheral edema)
- Failure of an exacerbation to respond to initial medical management
- Presence of serious comorbidities (e.g., heart failure, newly occurring arrhythmias, etc.)
- Insufficient home support

*Local resources need to be considered

* Imp notes: • DLCO is decreased in emphysema (normal is 80) • COPD causes respiratory acidosis that is compensated by metabolic alkalosis

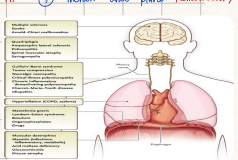
Lecture 3: RS failure

General characteristics:

- Acute RS results when: ① inadequate oxygenation of blood or ② inadequate ventilation or both → ① Hypoxia (paO_2 <60) ② Hypercapnia ($paCO_2$ >50)
- it has 2 types: Type 1: hypoxemic RF → when paO_2 <60 with normal or low $paCO_2$ / Type 2: Hypercapnic RF (Both $paCO_2$ >50 and eventually results in hypoxemia · paO_2 <60)
- Acute VS chronic RF: ① Acute: life threatening changes in ABGs and acid-base status, it develops over minutes to hours so ph is not normal (less or more depending on the type of RF) ② chronic: less dramatic, develops over days, you could see very slight changes to the pH due to body compensations → Such as: ① polycythemia ② cor-pulmonale ③ Renal excretion of bicarbonate * Note: you can't rely on ABGs only to differentiate between acute and chronic RF.

Normal physiology of the respiratory system :

* The respiratory system is not the only determinant of respiration, in fact many systems are involved such as: ① CNS (Brain and spinal cord) → Stroke, drug over dose, trauma could cause RF ② Neuromuscular disease: Myasthenia gravis, GB syndrome, Amyotrophic lateral sclerosis and polio would cause RF ③ upper airway: Stenosis, Spasm or paralysis would cause RF ④ Thorax and plura: Hemothorax, Kyphoscoliosis would cause RF ⑤ CVS: CHF, PE, anemia, valvular disease would cause RF ⑥ lower airways: copD, asthma, pneumonia, ARDS would cause RF

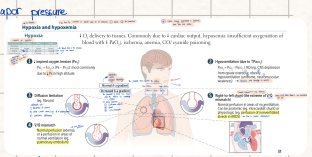


* Normal physiology: normal PAO_2 is around 100 while paO_2 is between 80-100 (90 as an average) → The difference between them is the A-a gradient which is normally around 5-10 mmHg because 2% of the systemic cardiac output passes the pulmonary circulation (physiological shunting), this gradient helps with knowing the cause of the respiratory failure. • How to calculate the PAO_2?

$$PAO_2 = FIO_2 \times (PB - PH_2O) - PACO_2/R$$

(usually 0.8) (usually 47) (mmHg) (0.21) (760 at sea level) (Arterial CO_2)

→ patm is atmosphere pressure, pH2O water vapor pressure.



• $paCO_2$ depends on the ventilation (inversely proportional) while oxygenation depends on O_2 sat

Pathophysiology of RF:

we have 5 mechanisms: causes Type 1 RF: ① V/Q mismatch ② shunting (very severe V/Q) ③ High altitudes · ④ Diffusion impairement; causes type 2 RF: ⑤ Hypoventilation

1 V/Q mismatch: • normal V/Q is 0.8 → Decreased V/Q would be due to a defect in ventilation (Such as pul edema or LD) WHILE increased V/Q is due to decreased perfusion (Such as PE) → if V/Q approaches ① the alveoli will act as a dead space with decreased perfusion and no diffusion of gases. • if the PE was a saddle PE it would cause shunt like V/Q mismatch. * Note: V/Q mismatch typically leads to hypoxia without hypercapnia (Type 1 RF).

2 Shunting: Little or no ventilation in perfused areas due to collapsed alveoli (like atelectasis) or fluid filled alveoli (like pneumonia or pul. edema) or intra-cardiac congenital causes (Tetralogy of Fallot) * Hypoxia due to shunting is not responsive to supplemental O_2 therapy • V/Q ratio is near ZERO

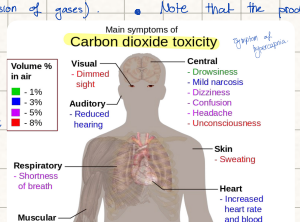
• note that A-a gradient increase here since the problem is in the alveoli (a)

3 Diffusion impairement: Diffusion depends on thickness of alveoli (Fibrosis and RLD) and surface area (emphysema) So it's a structural problem • it causes increased A-a gradient • Note: increasing the inhaled O_2 it will correct the paO_2 but the A-a gradient will remain increased as long as the problem is there.

4 High altitude: the problem is with the PB in which it would decrease leading to decreased PAO_2 then this would lead to paO_2 and hypoxemia and the A-a gradient would remain the same (since there's no problem in the gas exchange process) → Tx: increase the FIO_2 to correct the PAO_2 therefor you correct the hypoxemia

• They found out that sudden ascending to high altitudes would raise the 2,3 DPG = Shift to the right = respiratory alkalosis with chronically staying in the place: ① Polycythemia ② Bicarbonate excretion to correct the pH.

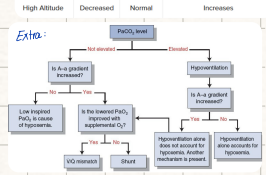
5 Hypoventilation: The ventilation is calculated through: Minute ventilation (6L/min) = Respiratory rate (12 breath/min) x Tidal volume (0.5L), so it occurs when there's a decrease in RR or TV • Hypoventilation leads to high $paCO_2$ • A-a will be normal and less than 10 (since there's no problem in diffusion of gases). • Note that the production of CO_2 in the body in a steady rate • Type 2 RF happens due to a cause that causes hypoventilation



Causes of Hypoxemia

Cause	PaO_2	A-a gradient	PaO_2 response to supplemental oxygen
Hypoventilation	Decreased	Normal (not hypoventilation)	Increases
Diffusion Impairment	Decreased	Increased	Increases
Shunt	Decreased	Increased	Does not increase.
V/Q Mismatch	Decreased	Increased	Usually increases (depends on V/Q mismatch type)
High Altitude	Decreased	Normal	Increases

Extra:



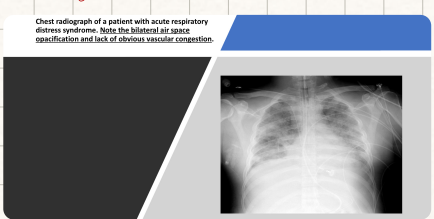
Treatment of RF :

① admit to ICU ② Manage and asses the ABGs ③ correct the hypoxemia by maintaining an arterial O_2 tension (paO_2 >60) or O_2 sat (more than 90%) so provide O_2 and mechanical ventilation by non-invasive (CPAP and BiPAP) or intubate is needed. ④ Specific tx depends on the underlying cause for example: ① asthma: bronchodilators and steroids ② COPD: bronchodilators ③ Abx for pneumonia ④ pul embolism: Heparin.

* Note: SOB or cough are the clinical feeatures that the patient would present with.

ARDS:

- it's a non-cardiogenic pulmonary edema → it follows a criteria : ① Acute onset (<1 week) ② Bilateral infiltration on chest image ③ pul. edema not explained by fluid overload or CHF (the pulmonary capillary wedge pressure is <18 mmHg, if it was larger than that then it's a cardiac cause but it's not)
- clinical features : ① SOB ② Tachycardia ③ Tachypnea ④ progressive hypoxemia (not responsive to supplemental O_2) ⑤ patients are difficult to intubate because of high airway pressure due to stiff noncompliant lung.
- Severity: By the ratio of partial pressure of arterial oxygen (PaO_2) to fraction of inspired O_2 (FiO_2) → ① Mild 200 – 300 mmHg with PEEP ≥ 5 cm H_2O
  ② Moderate: 100 – 200 with PEEP ≥ 5 ③ Severe: <100 with PEEP ≥ 5
- ARDS is responsible for: ① 1/10 ICU ② 1/4 mechanical ventilator ③ Mortality 46 – 60 % ④ Most cases are associated with pneumonia with or without sepsis (60%) or with non pulmonary sepsis (16%)
- Tx: Supportive until you find the underlying cause → Mechanical ventilator (keep low tidal volume and high PEEP) and keep the patient in prone position for some moderate and all severe cases.


Chest radiograph of a patient with acute respiratory distress syndrome. Note the bilateral air space opacification and lack of obvious vascular congestion.

Lecture 4 : ILD

General characteristics:

- Inflammatory process involving the alveolar wall (Reducing in a widespread fibroelastic proliferation and collagen deposition that can lead to irreversible fibrosis, impaired gas exchange and pul. HTN Sometimes and radiologically diffused (mostly on CT scan).

Pathophysiology:

Tissue modeling of Lung fibrosis: Fibroblasts in lung interstetium increases in number & they change into myofibroblasts (they represents a cancer like cell) → Significant Secretions of Growth Factors which are : ① TGF ② VEGF ③ PDGF → more Secretions of cytokines → more collagen deposition and secretions → Architecture damage and abnormal gas exchange.

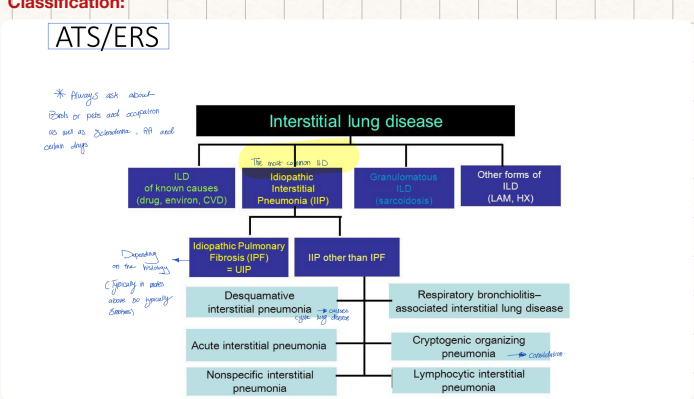
✳ Note: This whole cascade needs environmental factors such as: 1) Smoking 2) Microaspiration 3) occupational exposures 4) viral infx 5) Mechanical stress 6) Air pollution ⊕ Genetic predisposition

Clinical features and physical :

- 1) SOB (at first with exertion and late on rest) 2) cough (non productive) 3) Fatigue 4) Secondary symptoms related to CT diseases like RA, etc..
- PE: 1) Dry velcro-like crackles (End end insp) 2) Digital clubbing 3) Signs of pul. HTN and cyanosis in advanced stages.

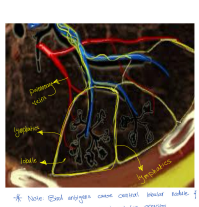
Classification:

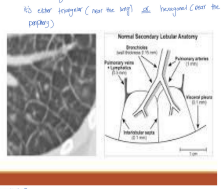
ATS/ERS



✳ Note & Secondary pulmonary lobule :

Secondary pulmonary lobule

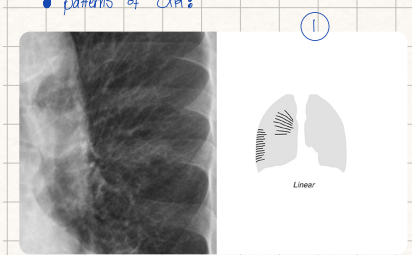


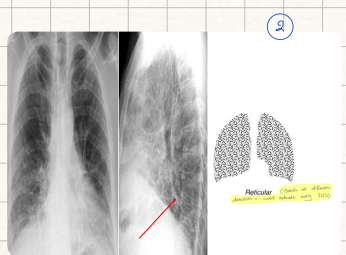


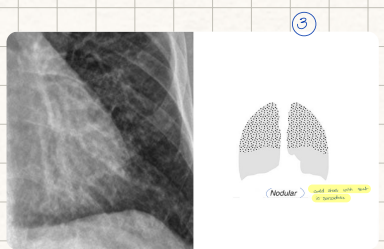
Diagnosis:

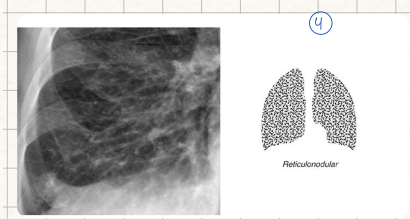
- 1) CXR: Most of ILD are hard to recognise on CXR (other than reducible lung volume) that's why we need HRCT 2) HRCT GOLD STANDARD for ILD (Extra: it shows the extent of fibrosis) 3) PFT } • FEV1/FVC: is normal or increased • Both FEV1 and FVC are both reduced • low DLCO • low TLC and RV } 4) Blood tests (ANA, RF, Anti-scleroderma) 5) Lung Biopsy (Rare not used as frequently in the past) 6) MDT (you do this step before lung biopsy) → we need 4 members of the team: A. pulmonologist B. pathologist C. Radiologist D. Rheumatologist

- patterns of CXR:

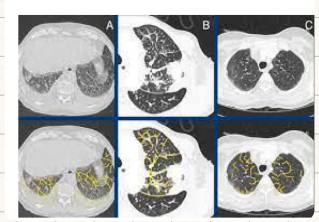








Interlobular septal thickening → On HRCT

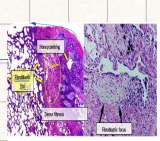


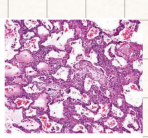
IPF:

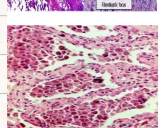
Extra info: Etiology is unknown, usually the patient is a Smoker male and 50 years old. presents with gradual onset of SOB and non-productive cough. Mean Survival is 3-7 years after first diagnosis. • Definition: a chronic fibrosing interstitial pneumonia • Associated with usual interstitial pneumonia (UIP)

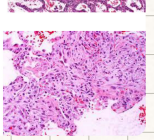
→ UIP is either presented on histology or on HRCT

This pattern is called usual interstitial pneumonia (UIP) also this pattern is found in idiopathic pulmonary fibrosis } Most common disease }









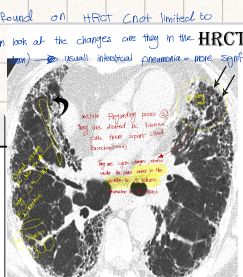
- Note: more pinkish color = more fibrosis while more purple = more inflammation

- in UIP we find heterogeneity (variability between completely normal lung and fibrosed lung)

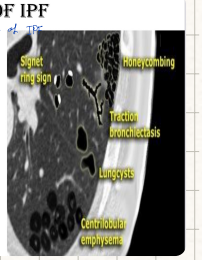
* UIP could also be found on HRCT (not limited to histology): points 1+2+3 then look at the changes are they in the base (apicobasal gradient: upzones) → usually interstitial pneumonia → more significant of IPF

So no need for biopsy

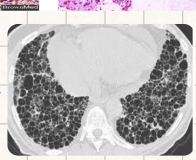
UIP
- Subpleural and basal predominant; distribution is often heterogeneous*
- Honeycombing with or without peripheral traction bronchiectasis or bronchiolectasis¶



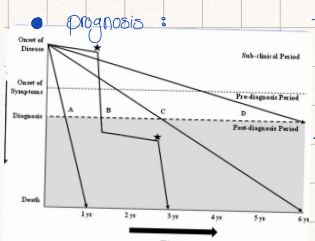
HRCT OF IPF



- Honey combing IPF:



- prognosis:



* Before Antifibrotic agents patients used to die within 2 years of diagnosis (Delayed presentation)

* Patients either die quickly, relapses, or die slowly (due to Anti-fibrotic agents)

- investigations: Same as above

- Tx: (1) Non pharmacological → Nonpharmacologic Management
  - Smoking cessation .
  - Influenza, pneumococcal, and other age-appropriate vaccines should be administered.
  - Supplemental Oxygen.
  - Pulmonary Rehabilitation .
  - Lung Transplantation .
  - Lung Cancer identification.

(2) Pharmacological:

→ A. nintedanib B. pirfenidone (Only FDA approved for IPF)

(Could be used for IPF and others).

- Nintedanib: at 2014 it was FDA approved for IPF and others, it decreases the progression of lung disease, the mechanism of action is clear: which is Tyrosine kinase inhibitor → other indications: 1) Scleroderm (initial tx for pulmonary symptoms) 2) RA (Secondary after using immune suppresion → [illegible]) 3) Hypersensitivity pneumonia

✳ Note: the patient would relapse but slower

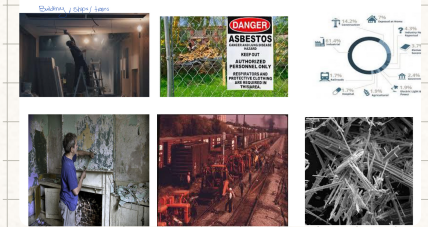
- Pirfenidone: not FDA approved for anything except for IPF.
- PAN Study: prednisone + Azathioprine + N-acetylcystine

they used it on patients on a long term and they found significant deaths so they had to stop it.

✳ Note: you should not use immune supressors for IPF unless it's acute exacerbations.

Other ILD :

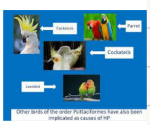
✳ Asbestos no tx



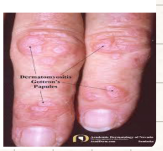
Hypersensitivity pneumonitis (HP)

Bird Antigens + cotton

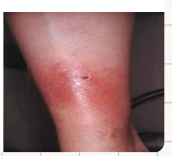




Dermatomyositis/Polymyositis

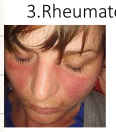
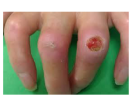
Sarcoidosis

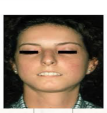
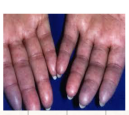



Connective tissue related ILD
1. Systemic lupus erythematosus
2 ,4,5 Scleroderma
3.Rheumatoid arthritis .

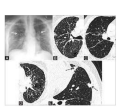
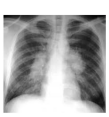
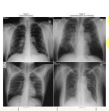
CT- ILD

Tx: immune suppresion then nintedanib

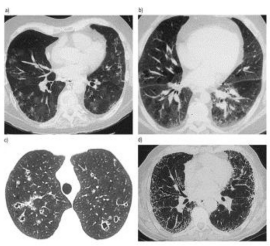



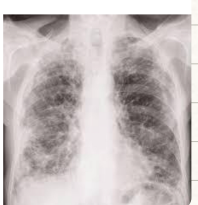
Sarcoidosis

Smoking related interstitial lung disease



Drug induced
Radiation induced



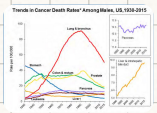
Extra: Drugs Examples:

1) chemotherapeutic agents
2) Amiodarone
3) nitrofurantoin
4) penicillamine

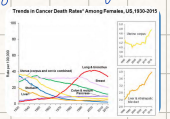
Lecture 5 : lung cancer

General characteristics:

- MC cause of cancer deaths in females and males . However, Breast ca is the most common in females vs prostate cancer in males (incidence wise) • 1.8m new lung cases (14%) vs 1.6m deaths (25%)
- Mortality decreased in 1990s due to targeted therapy (chemo didn't change but targeted therapy did) Moreover in 2014 mortality droped with 30% due to screening (CT scan).



- Mortality rates are higher in males



- Pathological types are divided into : (1) Small cell carcinoma (25%) (2) non-small cell carcinoma (75%) includes: 1) Adenocarcinoma (32%) 2) Squamous cell carcinoma (29%) 3) large cell carcinoma (9%) 4) unclassified / undifferentiated (12%)
- Etiology or risk factors of lung cancer: (1) Smoking (accounts for 80-90%) while passive smoking accounts for 25% → Direct association between pack-year and risk of smoking

* Note: cancers in non smokers is 25-5% of all (2) Radon (present in soil and presents in the basement) (3) Asbestos (4) COPD (independent of smoking) → 3-6 times more than smoking alone) (5) Age (Average dx is 70 years old)

↳ Extra note: 2nd most frequent cause in US

Clinical features:

- it has non specific features but most frequently : (1) Cough (75%) (2) SOB (3) chest pain (4) Hemoptysis (15%) → This is a bad sign bc it shows invading of endo-bronchili
- less frequently : (1) clubbing (2) Hoarseness (3) wheeze (15%) (4) Dysphagia (5) pleal effusion (very poor prognosis = equivalent to distant mets) • (5-15%) are asymptomatic • 15% would have extra-pul. Symptom • 5% would have paraneoplastic syndrome.

* Note : patients would presents as recurrent pneumonia of the same Anatomical area.

- Local invasion Signs: (1) SVC syndrome : Most commonly associated with Small cell carcinoma , you could see facial fullness and arm edema, dilated veins over the anterior chest and face with jugular venous distention → it may be the primary presentation of the disease , the chest radiograph will show widening of mediastinum or right hilar mass (2) phrenic nerve palsy : Results in hemidiaphragm paralysis diagnosed by Sniff test (Extra point) (3) Horner syndrome : due to invasion of cervical sympathetic chain by apical tumor (Extra) (4) pancost tumors : Superior Sulcus tumor (C8-T2) causing Shoulder pain radiating down to the arm and association of Horner syndrome in 60% of the time , it's a unique tumor of stage 2 but it's usually diagnosed at a higher stage (2B or 3A) → Tx : neoadjuvant chemo (etoposide and cisplatin) and concurrent radio followed by surgical resection , overall survival is (44-54%) depending on (1) post surgery presence or absence of microscopic disease in the resected specimen.

↳ initial symptom.

- paraneoplastic syndrome :

Association with

SCLC

(1) Syndrome of inappropriate ADH (Hyponatremia)

(2) cushing syndrome ectopic ACTH

(3) neurological such as: Eaton lambert syndrome (Extra: antibiotic against pre-synaptic voltage gated calcium channels = Block of Ach release = muscle weakness) , cerebral ataxia, autonomic neuropathy , limbic encephalitis , sensory neuropathy

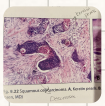
Squammous cell carcinoma

(1) PTH-like hormone secretions = Hypercalcemia } * Note: Hypercalcemia could be due to this OR extensive bony mets } → patients present with anorexia, n, constipation , lethargy (poor prognosis and association with advanced disease)

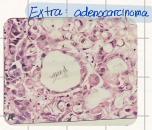
(2) Hypertrophic pulmonary osteoarthropathy : Mostly in the tibia , consists with digital clubbing , arthralgia , joint effusion , abnormal proliferation of the skin and soft tissue and osseous tissues in the distal parts of extremities

Squamous cell carcinoma and adenocarcinoma:

→ Adenocarcinoma : • Pathology (Histology characteristic) : 1) neoplastic glandl formation 2) pneumocyte marker expression: TTF-1 (key marker) and Napsin A (sometimes present) 3) Intracytoplasmic Mucin (Mucin inside tumor cells) • Classifications of adenocarcinoma : Based on the architecture: (1) Mucinous (produces a lot of mucin) (2) Non-mucinous : (not much mucin) this includes } Acinar / papillary / Micropapillary / lepidic / Solid } • prognostic significance of subtypes : (1) Solid, micropapillary and cribriform pattern : indicates worse or adverse prognosis (2) Minimally invasive adenocarcinoma : Small solitary tumor (≤3 cm) and minimally invasive (≤5mm) , has a good prognosis (surgical therapy only no need for chemo or radio, it shows a predominant lepidic growth pattern resembling precursor glandular lesions (3) Lepidic predominant adenocarcinoma : The invasion is greater than 5mm , this pathology classification is not related to prognosis.

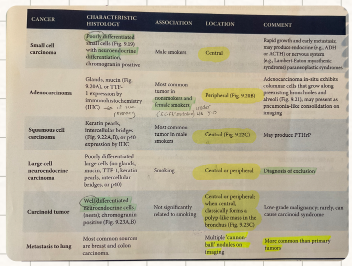


→ Extra: SCC



Extra : adenocarcinoma

→ Squamous cell carcinoma: • pathology (Histology characteristic): 1) Keratin pearls and intracellular desmosome (on immuno-histo chemistry) 2) IHC markers: p40, p63, CK5.6, Desmoglein. • Subtypes: ① Nonkeratinizing (no production of keratin) ② Keratinizing ③ Basaloid (more aggressive and poorly differentiated subtype • Features of SCC: 1) Extensive central necrosis (causing cavitation: hallow spaces inside the tumor) 2) Hypercalcemia 3) pancoast tumors.



CANCER	CHARACTERISTIC HISTOLOGY	ASSOCIATION	LOCATION	COMMENT
Small cell carcinoma	Poorly differentiated small cells (Fig. 9.19) with neuroendocrine differentiation, chromogranin positive	Male smokers	Central	Rapid growth and early metastasis; may produce endocrine (e.g., ADH or ACTH) or nervous system (e.g., Lambert-Eaton myasthenic syndrome) paraneoplastic syndromes
Adenocarcinoma	Glands, mucin (Fig. 9.20A), or TTF-1 expression by immunohistochemistry (IHC) → if the primary	Most common tumor in nonsmokers and female smokers (EGFR mutation) under 45 Y.O	Peripheral (Fig. 9.20B)	Adenocarcinoma in-situ exhibits columnar cells that grow along preexisting bronchioles and alveoli (Fig. 9.21); may present as pneumonia-like consolidation on imaging
Squamous cell carcinoma	Keratin pearls, intercellular bridges (Fig. 9.22A,B), or p40 expression by IHC	Most common tumor in male smokers	Central (Fig. 9.22C)	May produce PTHrP
Large cell neuroendocrine carcinoma	Poorly differentiated large cells (no glands, mucin, TTF-1, keratin pearls, intercellular bridges, or p40)	Smoking	Central or peripheral	Diagnosis of exclusion
Carcinoid tumor	Well differentiated neuroendocrine cells (nests); chromogranin positive (Fig. 9.23A,B)	Not significantly related to smoking	Central or peripheral; when central, classically forms a polyp-like mass in the bronchus (Fig. 9.23C)	Low-grade malignancy; rarely, can cause carcinoid syndrome
Metastasis to lung	Most common sources are breast and colon carcinoma.		Multiple 'cannon-ball' nodules on imaging	More common than primary tumors

Diagnosis:

① CXR (imp for Dx but not for screening) ② CT scan with IV contrast (imp for staging)

* Note: consider CT for abdomen for adrenal gland and liver mets) ③ PET : Directed at sites of potential mets when 1) focal findings are present 2) when CT shows evidence of advanced disease ④ MRI brain for tumors larger than 5cm. & Invasive staging:

1) Bronchoscopic endobrachial ultrasound - transbronchial needle aspiration (TBNA) 2) Endoscopic-TBNA 3) Mediastinoscopy 4) Thoracoscopy or videoassisted thoracoscopy (VATS)

* you should take biopsy after the radiological investigations (if it's central : Bronchoscopy / if it's periphral : CT guided biopsy)

* Note: you have to diagnose and evaluate the patient within 6 weeks → only (8-26%) are diagnosed at stages 1+2 while (28% — 38%) at stage 3 and 4

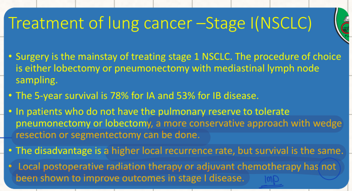
Treatment:

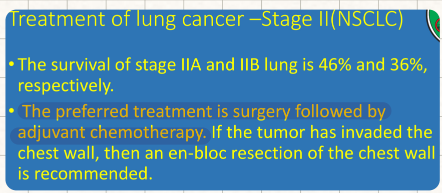
1 SCLC: very sensitive to chemo but high recurrence rate (it depends on the stage) → 1) Limited (chest LN involvement without axillary and cervical) : lobectomy then adjuvant chemo {if peripheral nodule without mediastinal or hilar lymphadenopathy} BUT {if medistinal or hilar : you need 4-6 chemo cycles then radiation therapy} * Note: Radiation is imp to prevent recurrance and we should do prophylactic whole brain radiation.

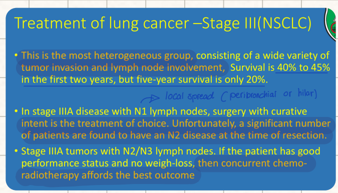
2) Extensive (the opposite of limited) → chemo (platinum based) → (50-60%) should be offered radiation therapy followed by brain prophylactic radiation * Note: for extensive type (Mean survival is 8-13%) and only 5% survive up to 2 years.

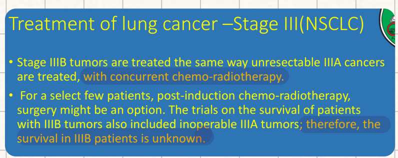
2 NSCLC:

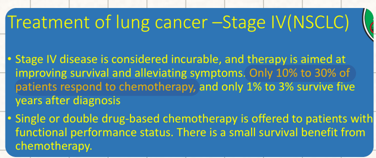
Preserves lung function.


Treatment of lung cancer –Stage I(NSCLC)
Surgery is the mainstay of treating stage 1 NSCLC. The procedure of choice is either lobectomy or pneumonectomy with mediastinal lymph node sampling.
The 5-year survival is 78% for IA and 53% for IB disease.
In patients who do not have the pulmonary reserve to tolerate pneumonectomy or lobectomy, a more conservative approach with wedge resection or segmentectomy can be done.
The disadvantage is a higher local recurrence rate, but survival is the same.
Local postoperative radiation therapy or adjuvant chemotherapy has not been shown to improve outcomes in stage I disease.
imp


Treatment of lung cancer –Stage II(NSCLC)
The survival of stage IIA and IIB lung is 46% and 36%, respectively.
The preferred treatment is surgery followed by adjuvant chemotherapy. If the tumor has invaded the chest wall, then an en-bloc resection of the chest wall is recommended.


Treatment of lung cancer –Stage III(NSCLC)
This is the most heterogeneous group, consisting of a wide variety of tumor invasion and lymph node involvement, Survival is 40% to 45% in the first two years, but five-year survival is only 20%.
→ local spread (peribronchial or hilar)
In stage IIIA disease with N1 lymph nodes, surgery with curative intent is the treatment of choice. Unfortunately, a significant number of patients are found to have an N2 disease at the time of resection.
Stage IIIA tumors with N2/N3 lymph nodes. If the patient has good performance status and no weigh-loss, then concurrent chemo-radiotherapy affords the best outcome


Treatment of lung cancer –Stage III(NSCLC)
Stage IIIB tumors are treated the same way unresectable IIIA cancers are treated, with concurrent chemo-radiotherapy.
For a select few patients, post-induction chemo-radiotherapy, surgery might be an option. The trials on the survival of patients with IIIB tumors also included inoperable IIIA tumors; therefore, the survival in IIIB patients is unknown.


Treatment of lung cancer –Stage IV(NSCLC)
Stage IV disease is considered incurable, and therapy is aimed at improving survival and alleviating symptoms. Only 10% to 30% of patients respond to chemotherapy, and only 1% to 3% survive five years after diagnosis
Single or double drug-based chemotherapy is offered to patients with functional performance status. There is a small survival benefit from chemotherapy.

* Targeted therapy:

① EGFR → treated with TKIs : Erlotinib, Gefitinib, Afatinib ② ALK → treated with ALK inhibitors : Crizotinib, ceritinib, Alecitinib * Note: ROS-1 mutation can also be treated with crizotinib (since it's structurally similar to ALK)

* Immunotherapy : if no ALK or EGFR mutation or if it failed — use immunotherapy

• How does PD-1 work in cancer? PD-1 is a checkpoint protien that normally helps to regulate the immune system by inactivating T-cells (to prevent autoimmunity) However some tumor exploit PD-1 by producing PD-L1 or PD-L2 which turns off T cells allowing tumors to be unchecked and grow

- Drugs of PD-1 inhibitors: (1) Nivolumab: it's IgG4 against PD-L1, approved for NSCLC that has progressed after chemo (2) pembrolizumab: also IgG4, approved for metastatic NSCLC with high PD-L1 expressing (50%), cannot be used if the tumor has EGFR or ALK mutations (But Nivolumab can be used).

* other treatements: VEGF-A inhibitor (Bevacizumab): not immuno-therapy it's an anti-angiogenesis antibody that inhibits vascular endothelial growth factor to prevent tumor blood vessel formation, used in non-Squammous NSCLC with platinum based chemo (contraindicated in SCC due to risk of fatal hemoptysis), Also could be used in breast, renal, colon and brain cancers.

➡ In Summary:

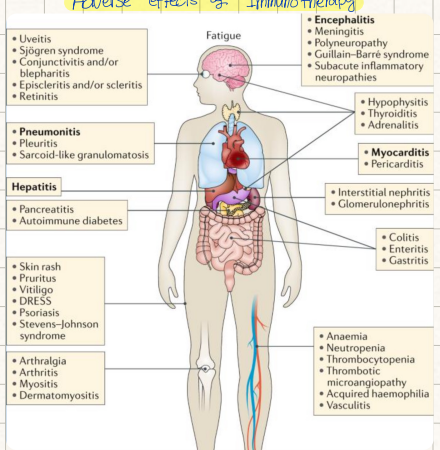
Stage I (Early-Stage Tumor, No Lymph Node Involvement)
Surgery (lobectomy or wedge resection) is the main treatment.
Radiation therapy may be used if surgery is not possible.

Stage II (Larger Tumor or Spread to Nearby Lymph Nodes)
Surgery with adjuvant chemotherapy (to reduce recurrence).

Stage III (Locally Advanced Tumor, Spread to Mediastinal Nodes)
Radiation + Chemotherapy
Adjuvant immunotherapy (after chemoradiation in some cases).

Stage IV (Metastatic NSCLC or Recurrent Disease)
Chemotherapy (platinum-based).
Targeted therapy (if EGFR, ALK, or ROS-1 mutation present).
Immunotherapy (if no targetable mutations).

Adverse effects of Immunotherapy



National Lung Screening Trial

- 53,454 participants
- Age 55-74 (Medicare covers until 77)
- Current or former smokers – 30 pack years. If quit, had to quit within 15 years.
- Randomized to Low Dose CT (LDCT) vs CXR
- Scanned for 3 years followed for 3.5 years
- 20% reduction in lung cancer mortality
- 7% reduction in overall mortality

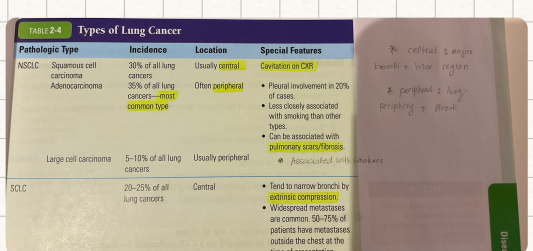


TABLE 2-4 Types of Lung Cancer

Pathologic Type	Incidence	Location	Special Features
NSCLC: Squamous cell carcinoma, Adenocarcinoma	30% of all lung cancers; 35% of all lung cancers—most common type	Usually central; Often peripheral	Cavitation on CXR; • Pleural involvement in 20% of cases. • Less closely associated with smoking than other types. • Can be associated with pulmonary scars/fibrosis.
Large cell carcinoma	5–10% of all lung cancers	Usually peripheral	
SCLC	20–25% of all lung cancers	Central	• Tend to narrow bronchi by extrinsic compression. • Widespread metastases are common. 50–75% of patients have metastases outside the chest at the time of presentation.

Lecture 6: pneumonia

General characteristics

- 8th leading cause of death • 2-3 mil cases/year ⇝ 500,000 hospitalized ⇝ >60,000 deaths • ICU ~ 30-40% deaths vs inpatients 10% vs outpatients 1% • It's An acute RS disease with symptoms of SOB, cough (productive yellow to greenish sputum), sometimes severe (septic shock to RS failure) • On PE: (1) crackles and bronchial sounds (2) Dull percussion (3) Decreased breathing sounds (4) Tachypnea (5) Tachycardia • on X-Ray: infiltrates (lobar or bronchial or interstetial) • For Dx: clinical and chest imagining, labs are not useful but you could ask for CBC, KFT, Blood and sputum cultures. * Note: CRP and procalcitonine are useful for follow ups but not diagnosis.
- There are 2 types: (1) CAP: outside the hospital (Extra note: most commonly associated with S. pneumonia) (2) HAP: Hospital acquired after 48 hours or more (Extra: mostly MRSA and pseudomonas) or VAP: after 48 or more of endotracheal intubation.
- DDx of pneumonia: (1) Exacerbation of COPD, CHF, bronchiectasis (but they are associated with chronic hx) (2) PE (3) Acute bronchitis (4) ILD (5) Hypersensitivity pneumonitis.

Testing:

- Note: 50% of the time you'll get a negative test due to our immune system
  1. Blood and sputum culture : depends (60-70%) on timing / use of Ab / type of organism → (1) Fast grow (Staph and GNB) (2) Slow grow (Influenza and strep pneumonia)
  2. Urine pneumococcal Ag (sensitivity of 70%) → not affected by Ab use
  3. urine legionella Ag (Detects only serotype 1)
  4. viral PCR (covid, influenza)
- procalcitonin : used to know when to stop Ab use and if you need to change the Ab. depending on it's value in serum (should be 0.25 or less) → Mechanism? it's a prohormone that is secreted from thyroid neuroendocrine cells (should be undetectable in serum), now if there's an infection : IL1, 6, TNF produce procalcitonin synthesis and increase it's levels it starts to rise in 2-4h with peak in 24h (levels correlates with severity) * Note: levels decrease quickly once infection is under control * Note: procalcitonin could increase in case of medullary carcinoma.
  * Imp note: you should not wait for procalcitonin levels to start Ab → you should start it depending on the clinical picture.
  * Note: in ICU patients stop Ab on procalcitonin (0.50), it's elevated in CKD, in ESRD bacterial infection levels are mildely elevated due to reduced clearance, post HD → Drop by 30% (harder to catch)

effect of microbiologic on prolactin levels

Condition	Rise in PCT (>0.25 ng/mL)	No Rise or Minimal Rise (<0.25 ng/mL)
Bacterial Infections	Typical respiratory bacteria (most common cause)	Chlamydia pneumoniae, Mycoplasma pneumoniae, Mycobacteria spp., Lyme borreliosis
Fungal Infections	Candida spp.	Aspergillosis, Coccidioidomycosis, Mucormycosis
Parasitic Infections	Plasmodium spp. (Malaria)	—
Toxin-Mediated Illnesses	Severe Clostridioides difficile infections, Mushroom poisoning	Clostridioides difficile colonization
Severe Physiologic Stress	Burns, Trauma, Surgery, Bowel ischemia, Pancreatitis, Intracerebral hemorrhage, Shock of any kind (septic, anaphylactic, hemorrhagic, cardiogenic)	— (without infection)
Immune Disorders & Rheumatologic Conditions	Kawasaki disease	Gout, Pseudogout, IBD, SLE, Rheumatoid arthritis, Vasculitis, Sarcoidosis, Still's disease, Temporal arteritis, Relapsing polychondritis
Malignancies	Medullary thyroid cancer, Lung cancers with neuroendocrine components	Lymphoma, Sarcoma, Pancreatic cancer, Renal cell carcinoma
Other Comorbidities	Renal insufficiency (mild elevation but not due to infection) drops after hemodialysis	—
Drugs	Alemtuzumab (CD52 antibody), Interleukin-2, Rituximab (anti-CD20 antibody), Total antibody-based treatments	Glucocorticoids

Condition	Commonly encountered pathogen(s)
Alcoholism	*S. pneumoniae* and anaerobes
COPD and/or smoking	*S. pneumoniae*, *H. influenzae*, *M. catarrhalis*, and *Legionella* species
Nursing home residency	*S. pneumoniae*, gram-negative bacilli, *H. influenzae*, *S. aureus*, anaerobes, and *C. pneumoniae*
Poor dental hygiene	Anaerobes
Epidemic Legionnaires' disease	*Legionella* species
Exposure to bats or soil enriched with bird droppings	*Histoplasma capsulatum*
Exposure to birds	*Chlamydia psittaci*
Exposure to rabbits	*Francisella tularensis*

Interpretation of procalcitonin levels in respiratory tract infections

Level (ng/mL)	Likelihood of bacterial infection*
<0.10	Very unlikely
0.10 to 0.25	Unlikely
0.25 to 0.50	Likely
>0.50	Very likely

* This interpretation assumes a clinically compatible syndrome and the absence of other causes of procalcitonin elevation.

Severity of pneumonia:

- how to know if the patient needs admission? depending on CURB-65
- what is the definition of Severe pneumonia? 3 of minor points or 1 major point:

C: Confusion / U: urea / R: RR / B: BP / 65 age.

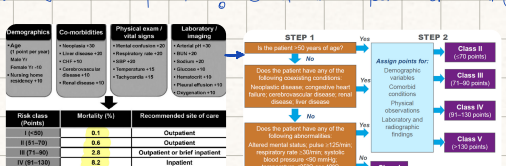
CURB-65 (1 point for each of the below):
1. New onset confusion
2. Urea >7 mmol/l
3. Respiratory rate ≥ 30/min
4. Blood pressure (SBP < 90 mmHg or DBP ≤ 60 mmHg)
5. Age ≥ 65 years

CURB-65: 0 or 1	CURB-65: 2	CURB-65: 3 – 5
< 3% 30-day mortality	9% 30-day mortality	15 – 40% 30-day mortality
Outpatient care	Short inpatient stay	Inpatient care (IV)

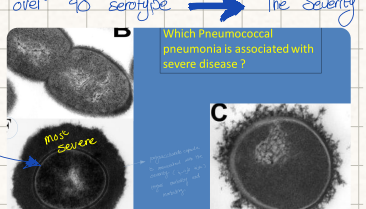
Validated definition includes either one major criterion or three or more minor criteria

Minor criteria
- Respiratory rate ≥ 30 breaths/min
- PaO_2/FiO_2 ratio ≤ 250
- Multilobar infiltrates
- Confusion/disorientation
- Uremia (blood urea nitrogen level ≥ 20 mg/dl)
- Leukopenia* (white blood cell count < 4,000 cells/μl)
- Thrombocytopenia (platelet count < 100,000/μl)
- Hypothermia (core temperature < 36°C)
- Hypotension requiring aggressive fluid resuscitation

Major criteria
- Septic shock with need for vasopressors
- Respiratory failure requiring mechanical ventilation

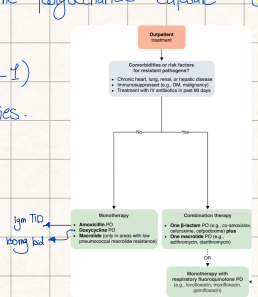


- Note: The most common pathogen of pneumonia is : Strep. pneumonia if CAP → only affects humans (through secretions), naso pharyngeal colonization of young children is the main source of infection in adults, it has over 90 serotype → The severity of these serotypes depends on the polysaccharide capsule (the thicker = the more severe)



Treatment of CAP:

(1) (outpatient) → CURB 65 : (0-1), then if healthy or has comorbidities:



② Inpatients (ICU or non-ICU).

◆ Non-Severe CAP (No Risk Factors for MRSA or P. aeruginosa).

Option 1: Combination Therapy

Beta-lactam (Ampicillin/Sulbactam, Cefotaxime) Ceftriaxone, Ceftaroline) — 1.5-3gm every 6h | 1-2g/8h | 1-2g/day | 600mg/12h

Macrolide (Azithromycin, Clarithromycin) or Doxycycline — 500mg/day | 500mg twice/day

Option 2: Monotherapy

Respiratory Fluoroquinolone (Levofloxacin, Moxifloxacin) — 750mg/day | 400mg/day

◆ Severe CAP (No Risk Factors for MRSA or P. aeruginosa)

Option 1: Beta-lactam + Macrolide

Strong recommendation, moderate evidence

Option 2: Beta-lactam + Respiratory Fluoroquinolone

Strong recommendation, low evidence

➡ Assess Risk Factors for Resistant Pathogens

◆ High Risk for MRSA? ✅ Yes → Treat with Vancomycin, Linezolid, Teicoplanin

◆ High Risk for Pseudomonas? ✅ Yes → Treat with Meropenem, Aztreonam, Piperacillin/Tazobactam, Ceftazidime

* predictors of mortality in patients with CAP

① Decreased consciousness ② O2 Sat <90% ③ Acute renal failure ④ Shock (Sepsis) ⑤ Aspiration ⑥ Adherence to ATS

is NOT significantly associated with reduced mortality

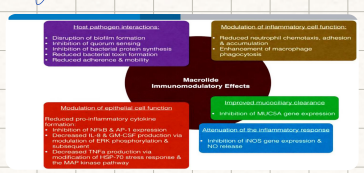
* predictors of length of stay (>4 days) in CAP:

① pneumonia class 5 ② RR> 40 ③ Sodium <130

④ pleural effusion ⑤ Mechanical ventilator ⑥ Active alcohol intake

⑦ adherence of ATS = Shorter stay ⑧ Acute renal failure.

- Macrolide effects:



- Note: Azithromycin is better than clarithromycin regarding GI side effects AND Macrolides is better than quanlones.
- Drug resistance S. pneumonia in CAP:
- Corticosteroids: Only used in ICU patients on high flow O_2: Decreases the risk of mortality and less vasopressors use? but net effect is zero with side effects (hyperglycemia + risk of infection)

markers of resistance

β-lactams
- MIC of ≥4
- 2nd-generation cephalosporins

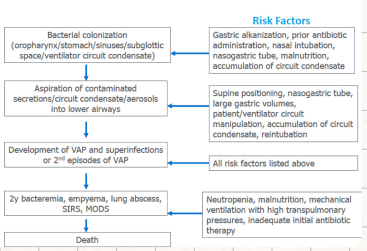
Macrolides
- Number of cases continues to grow
- Low-level (*mef*) and high-level (*erm*) resistance are relevant

Fluoroquinolones
- Small number of cases
- Judicious use

* Note: Blood and Sputum cultures are recommended for Severe cases.

Treatment of HAP

Pathogenesis



causes: ① MRSA ② pseudomonas.

MRSA risk factors

- The commonly associated risk factors for MRSA infection are
  - prolonged hospitalization,
  - intensive care admission
  - recent hospitalization
  - recent antibiotic use
  - MRSA colonization
  - invasive procedures
  - HIV infection
  - admission to nursing homes
  - open wounds
  - hemodialysis
  - discharge with long-term central venous access

Psuedomans risk factors

- A compromised immune system (eg, patients with HIV, solid organ or hematopoietic cell transplant recipients, neutropenic hosts, and those on immunosuppressive or immunomodulatory agents such as TNF-alfa inhibitors)
- Recent prior antibiotic use
- Structural lung abnormalities such as cystic fibrosis or bronchiectasis
- Repeated exacerbations of chronic obstructive pulmonary disease requiring frequent glucocorticoid and/or antibiotic use

ATS-IDSA Guidelines

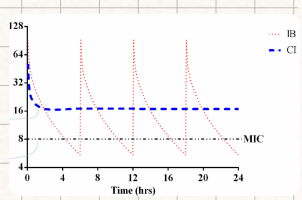
- **Use noninvasive sampling with semiquantitative cultures** to diagnose VAP, rather than invasive sampling with quantitative cultures and rather than noninvasive sampling with quantitative cultures
- **Use clinical criteria alone, rather than using serum PCT + clinical criteria**, to decide whether or not to initiate antibiotic therapy
- **Use clinical criteria alone rather than using CRP + clinical criteria**, to decide whether or not to initiate antibiotic therapy
- **Use clinical criteria alone, rather than using CPIS + clinical criteria**, to decide whether or not to initiate antibiotic therapy

ATS-IDSA Guidelines

- **Use 2 antipseudomonal antibiotics** from different classes for the empiric treatment of suspected VAP only in patients with any of the following:
  - a risk factor for antimicrobial resistance
  - pts in an ICU where >10% of Gm -ve isolates are resistant to an agent being considered for monotherapy
  - pts in an ICU where local antimicrobial susceptibility rates are not available
  - high risk of mortality
- All other pts with HAP who are being treated empirically may be prescribed **a single antibiotic** with activity against *P. aeruginosa*

ATS-IDSA Guideline

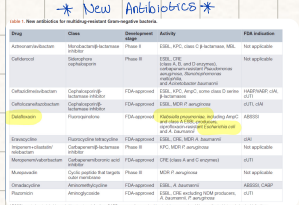
- **7-8 days** (Minimum) of antimicrobial therapy is recommended
- No differences in mortality, clinical cure, and recurrent pneumonia compared to longer courses
- Should decrease antibiotic exposure with decreased costs and undesirable side effects
- Applies to all organisms including non-glucose-fermenting gram-negative bacilli



continuous tx causes less resistance because it stays above the MIC vs intermittent cause more resistance bc it's below the MIC

- **Risk factors for MDR VAP**
  - Prior IV antibiotic use within 90 days
  - Septic shock at time of VAP
  - ARDS preceding VAP
  - Five or more days of hospitalization prior to the occurrence of VAP
  - Acute renal replacement therapy prior to VAP onset

* New Antibiotics *



Bronchoectasis

- Abnormal brochial dilation (shaped as cylindrical, Saccular, varicose) . could be confused by chronic bronchitis
- Incidence declining since preantibiotic era
- Causes : ① cystic fibrosis ② TB, fungi ③ ciliary disorders (immotile cilia syndrome) ④ immune deficiency (IgG, IgA) ⑤ post necrotizing infection (pneumonia → especially in childhood) , (Measles, influenza, pertussis) ⑥ CT disease (RA, sjogren) ⑦ HIV ⑧ IBD ⑨ Alpha 1 AT deficiency (emphysema with recurrent pulmonary infections) ⑩ Reflux ⑪ Bronchial obstruct ⑫ Allergic bronchopulmonary Aspergillosis
- pathophysiology :

- Bronchiectasis occurs as a result of a vicious circle consisting of an impaired mucociliary transport system, inflammation, infection and repair of the airways with peribronchial fibrosis
- Damage to the mucociliary system prevents secretion elimination and facilitates bacterial growth and bronchial inflammation.

- Expectorated sputum has increased concentrations of elastase and the chemoattractants ,interleukin-8, tumor necrosis factor (TNFα) ,prostanoids.
- Localized vs. diffuse

- Clinical features + PE :

- Symptoms
  - Chronic cough
  - dyspnea
  - Sputum production
  - Hemoptysis
- Signs
  - Wheezes and crackles
  - Bronchial breathing
  - Clubbing

- Diagnostic testing :

TABLE 3. DIAGNOSTIC TESTING FOR BRONCHIECTASIS.*

LEVEL OF TESTING	APPROPRIATE TESTS		
	BLOOD	IMAGING	OTHER
Primary	Complete and differential blood count, IgG, IgA, IgM	High-resolution CT	Spirometry or bronchodilator test
Secondary	Rheumatoid factor; IgE, aspergillus precipitins (ABPA); IgG subclasses; alpha, -antitrypsin level	Sinus CT	Sputum bacterial, mycobacterial, fungal culture and sensitivity; bronchoscopy with mucosal biopsy, cultures (for focal obstruction, infection, primary ciliary dyskinesia); sweat chloride test analysis (for cystic fibrosis)

- Tx :

Treatment

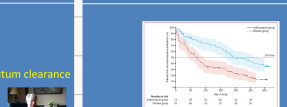
- Antibiotics for exacerbations
  - Bacterial colonization increases risk of exacerbation
  - Inhaled vs oral vs parenteral
- Bronchodilators for reversible airflow limitation.
- Surgery in cases of medical failure and localized disease (rare)
- Treatment of hemoptysis

Nebulized Hypertonic saline

- Improvement of mucociliary clearance
- Decreases mucus viscosity
- Stimulates cough
- Enhances the effectiveness of respiratory physiotherapy
- Inhibits epithelial sodium channels (ENaC)

Treatment

- Bronchopulmonary hygiene
  - Physical measures to promote sputum clearance
  - DNAase
  - NAC
- Treatment of underlying cause



- azithromycin treatment for 6 months in patients with non-cystic fibrosis bronchiectasis significantly decreases the rate of event-base exacerbations and increases the time to the first event-based exacerbation compared with placebo

Lecture 7: plural diseases