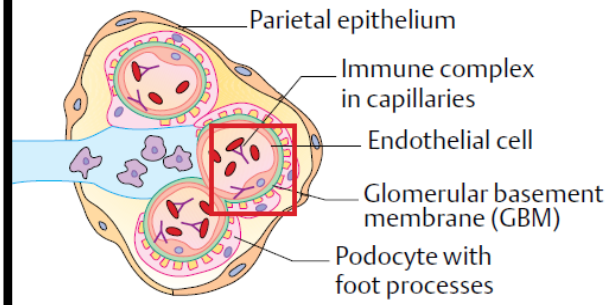
Lecture No. 10-11

Renal diseases

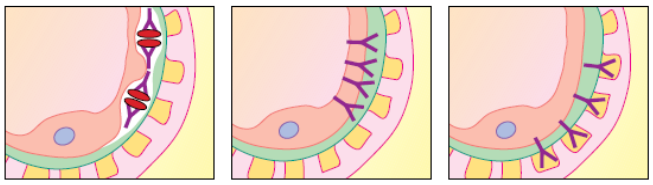
Many renal diseases have underlying immunological mechanisms. Antibody-mediated effects are primarily involved, whereas cellular mechanisms are less important. Immunological diseases of the kidney mainly affect the glomerulus, which is most likely due to its filter function. Circulating antibody-mediated renal diseases are induced in three mechanisms, circulating performed immune complexes accumulate subendothelially on the capillary aspect of the basement membrane, alternatively antibodies may react in situ with the glomerular basement membrane or with antigens of the visceral epithelial cells.

Antibody deposits can cause direct damage to epithelial or endothelial cells of glomerulus due to complement activation and pore formation. On the other hand, the antibodies can also bind to the FC receptors of monocytes, macrophages, granulocytes and platelets. This leads to the activation, or in the case of platelets aggregation of the cells. The glomerular damage can cause two distinct symptom complexes: the nephrotic syndrome and the nephritis syndrome.

Differentiation Between Nephrotic Syndrome and Nephritic Syndrome		
Typical Features	**Nephrotic**	**Nephritic**
Onset	Insidious	Abrupt
Edema	++++	++
Blood pressure	Normal	Raised
Jugular venous pressure	Normal/low	Raised
Proteinuria	++++	++
Hematuria	May/may not occur	+++
Red blood cell casts	Absent	Present
Serum albumin	Low	Normal/slightly reduced



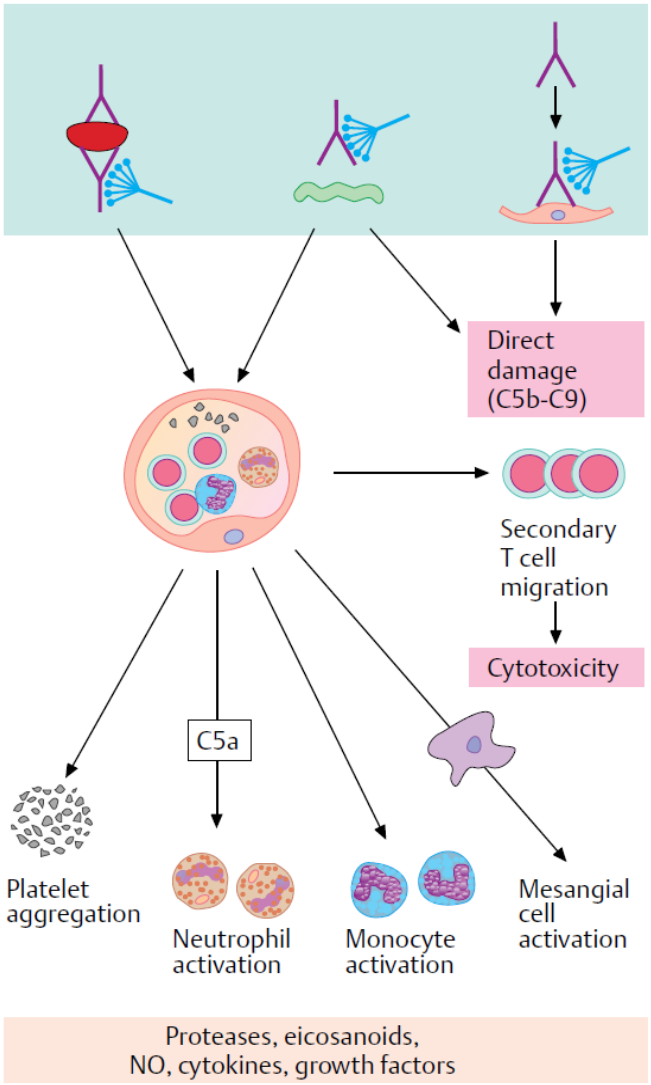
1. Anatomy



2a. Immune complex deposition

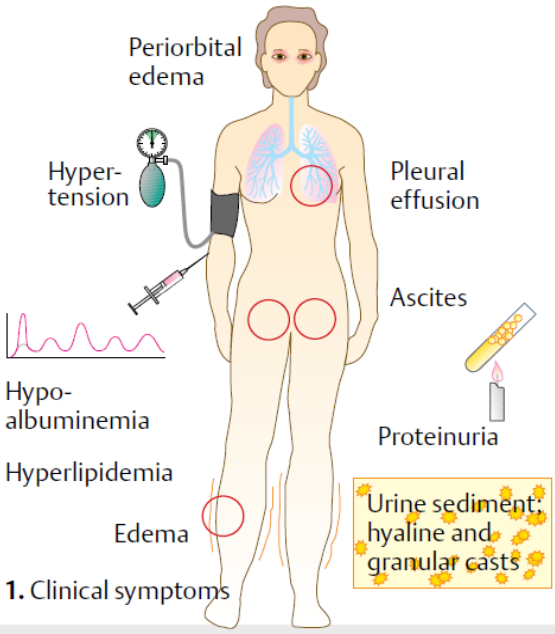
2b. Anti-GBM Ab

2c. Anti-epithelial cell Ab



3. Mediators of glomerular damage

A. Mechanisms

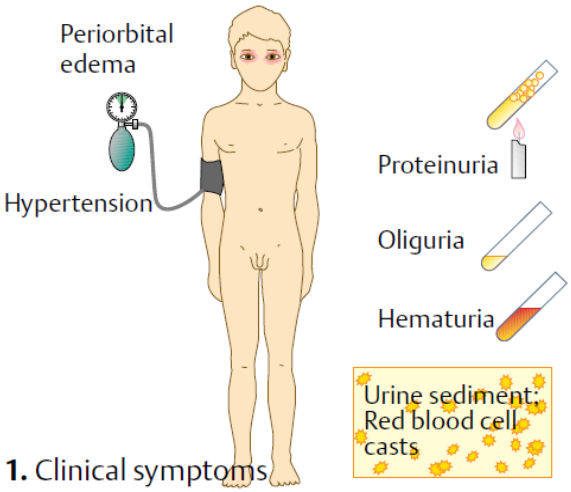


1. Clinical symptoms

	Children	Adults
Membranous glomerulonephritis	5%	20%
Lipoid nephrosis minimal change GN	60%	10%
Focal segmental glomerulosclerosis	10%	10%
Membranoproliferative glomerulonephritis	10%	5%
Proliferative GN (focal, IgA....)	10%	15%
Systemic diseases: diabetes, SLE, amyloidosis...	5%	40%

2. Causes of nephrotic syndrome

B. Nephrotic syndrome



1. Clinical symptoms

Postinfectious GN
Rapidly progressive GN
IgA nephropathy

2. Causes of the nephritic syndrome

C. Nephritic syndrome

Antineutrophil cytoplasmic antibody associated glomerulonephritis

Patients with ANCA-associated glomerulonephritis are usually aged from 40 to70 years and most have had a flu-like illness with arthralgia and myalgia a few days or weeks prior to the onset of renal disease or vasculitis. A spectrum of vasculitis is seen, ranging from disease limited to the kidneys in about a quarter of cases to a systemic vasculitic process with pulmonary involvement in about half the patients. ANCA-associated glomerulonephritis is now the commonest form of crescentic or rapidly progressive glomerulonephritis.

The renal lesion is characterized by few or no deposits of immunoglobulin or complement in the kidney **(so-called pauci-immune glomerulonephritis)** and by necrosis and crescent formation

Two pattern of antineutrophil cytoplasmic antibody (ANCA) reactivity are important clinically: generalized cytoplasmic staining **(cANCA)** and a perinuclear pattern **(pANCA)**. Most cANCA sera react with a serine proteinase called proteinase 3 (PR3), while most pANCA sera react with myeloperoxidase (MPO). A further pattern is associated with inflammatory bowel disease, particularly ulcerative colitis, some cANCA/ Panca positive sera react with neutrophil antigens other than PR3/MPO.

Raised ANCA titres are generally detectable during active granulomatosis with polyangiitis, and rising titres may herald a relapse. There has been debate whether ANCAs are pathogenic in vasculitis or simply a marker, but there is mounting evidence that they are pathogenic. The exact pathogenesis of granulomatosis with polyangiitis is not completely understood, but T cells, B cells, neutrophils and endothelial cells have all been implicated in the process.

Lecture No. 12-13

Membranous glomerulonephritis

Membranous glomerulonephritis can occur at any age, with the peak incidence in adults aged between 30-50 years and is characterized by the formation of immune complexes on the subepithelial surface of the basement membrane. The antibodies react in situ with endogenous podocyte antigens. The majority (70-80%) of patients with primary MN have circulating autoantibodies to **M-type phospholipase A2 receptor (PLA2R),** a transmembrane receptor that is expressed in glomerular podocytes. Antibodies to thrombospondin type-1 domain containing 7A protein (THSDA7A) and neutral endopeptidase have been identified in smaller subsets of patients.

Typical features include diffuse thickening of the basement membrane with fusion of the foot processes. The inhomogeneous distribution of the IgG and C3 deposits results in

granular pattern upon immunofluorescence. Glomerular sclerosis may occur in the latter stage of the disease. Clinically, membranous glomerulonephritis appears as a relatively mild nephrotic syndrome. Around 40% of the patients gradually develop progressive renal failure. The response to corticosteroid is poor.

Etiology

The disease is idiopathic or primary in 80% of cases; the causal antigen is never found. The remaining 20%, however, are secondary to another disease or to drugs. The most important causes are drugs (gold, penicillamine, captopril), infections (hepatitis B or C), systemic lupus erthymatosus, or carcinoma of bronchus, breast, colon or kidney.

Diagnosis

1. Renal biopsy is usually required to establish the diagnosis,
2. Serological testing for relevant autoantibodies (*i.e.*,anti–PLA2R) may be informative if renal biopsy is contraindicated.
3. Identification of PLA2R in glomerular immune deposits (by immunofluorescence or immunohistochemistry) favors the diagnosis of primary MN; mesangial deposits are often present in secondary MN.

Lecture No. 14

Postinfectious glomerulonephritis

Acute poststreptococcal glomerulonephritis is the prototype postinfectious glomerulonephritis, it is a disease of children and adolescents, but adults may be affected. Over 90% of cases are preceded by streptococcal infection of the throat or skin. Patients typically present with acute nephritis 7-12 days sfter a throat infection or about 3 weeks after a skin infection.

Etiology and pathogenesis

Glomerular injury results from passive glomerular trapping of circulating immune complexes composed of nephritogenic bacterial antigens and IgG antibody or by the *in situ* formation of immune complexes. This is followed by immune cell recruitment, production of chemical mediators and cytokines, and local activation of the complement and coagulation cascades that drive an inflammatory response

Diagnosis

1. Increasing titres of streptococcal antibodies and a low serum C3 level. Laboratories can often test for a range of antistreptococcal antibodies including antistreptolysin (ASO), antihyaluronidase (AHase), antistreptokinase (ASKase),antinicotinamide-adenine dinucleotidase (anti-NAD) and anti-DNAse B antibodies. These antibodies

are useful in approx.95% of cases following pharyngitis and 80% in those following pyoderma.

2. Poststreptococcal glomerulonephritis is characterized by a nephritic syndrome consisting of smoky or rust-colored urine, generalized edema, hypertension, and nephritic urine sediment. Proteinuria is typically mild.
3. Patients have rising titers of anti-streptolysin and depressed C3 levels early in nephritis but normal or minimally depressed C4 levels, indicating activation of the alternative complement pathway.
4. Proliferative glomerulonephritis with polymorphonuclear leukocyte and monocyte infiltration, granular immune deposits of IgG and C3, and dome-shaped electron-dense subepithelial deposits (humps) are characteristic.
5. Kidney biopsy is rarely needed in the child but may be warranted if there is an atypical presentation or evolution.

IgA nephropathy

IgA nephropathy (mesangial IgA deposition or Bergers disease) is the most common form of primary glomerulonephritis in the world. It affects mainly older children or young adults, and present typically as recurrent episodes of macroscopic haematuria occuring after an upper respiratory tract infection or, less frequently, a gastrointestinal or urinary tract infection, or strenuous exercise. Presentation with acute nephritis, hypertension, the nephrotic syndrome or as a chance finding of microscopic haematuria is less frequent. In contrast to poststreptococcal glomeruonephritis, the period between infection and haematuria is short, ranging from hours to a few days.

Etiology and Pathogenesis

IgA nephropathy can be considered a type of renal limited vasculitis caused by an innate defect in IgA mucosal immunity in the gut or lung: repeated exposure to a variety of environmental antigens results in an abnormal IgA response, namely the generation of nephritogenic polymeric IgA antibodies with defective galactosylation of the IgA hinge region resulting in deposition in the mesangium and the induction of inflammation in genetically susceptible individual.

Diagnosis

1. On light microscopy, the glomeruli show focal and segmental mesangial proliferation and, prominent deposite of IgA are found in the mesangium of every glomerulus, together with complement components of the alternative pathway.
2. Serum IgA levels are variable but may be significantly elevated. However, this is not a specific test, as liver disease and infections may also lead to persistent elevation of IgA.

Lecture No. 15

Lupus nephritis

Lupus nephritis is glomerulonephritis caused by (SLE) Although only 25% of patients with SLE present with renal disease as the first manifestation of lupus . clinical glomerulonephritis occurs in about 50% of cases of SLE at some time, and evidence of renal involvement can be detected in most patients, even in the absence of proteinuria.

Clinical Features

Asymptomatic hematuria or proteinuria may be the presenting features, but they often progress to nephritic and/or nephrotic syndrome. Hypertension, azotemia, nephritic urine sediment (with hematuria and cellular casts), hypocomplementemia and high anti–double-stranded DNA (dsDNA) titers are more commonly found in patients with proliferative lupus nephritis.

Pathophysiology of lupus nephritis

Pathophysiology involves immune complex deposition with development of glomerulonephritis. The immune complexes consist of

- Nuclear antigens (especially DNA)
- High-affinity complement-fixing IgG antinuclear antibodies
- Antibodies to DNA

Deposition of immune complexes from the circulation into the kidney appears to be the initiating event in proliferative lupus nephritis; however, only a subset of immune complexes appears to be nephritogenic.

DNA and anti-DNA antibodies are known to be concentrated in glomerular deposits in the subendothelial location and are likely to play a central role in the pathogenesis of proliferative lupus nephritis.

Classification of lupus nephritis is based on histologic finding

Class I. Minimal mesangial lupus nephritis: normal glomeruli under light microscope, but with minimal mesangial deposits in immunofluorescence. (**Normal serum creatinine and urine laboratory results. Incidental finding**)

Class II. Proliferative mesangial lupus nephritis: hypercellularity and mild mesangial expansion under light microscope, with mesangial deposits evident in immunofluorescence; there may be subepithelial or subendothelial deposits visible in an electron microscope or with immunofluorescence.

Class III. Focal lupus nephritis :lesions present in less than 50% of glomeruli with diffuse subendothelial deposits, with or without mesangial alterations. (Proteinuria and haematuria)

Class IV. Diffuse lupus nephritis : Damage that amounts to more than 50% (Haematuria, proteinuria, nephrotic syndrome, renal failure, arterial hypertension. Associated with elevated anti-nDNA titre and hypocomplementaemia May evolve towards renal failure)

Class V. **Membranous lupus nephritis**: thickening of the basal glomerular membrane with global or segmental immune deposits on the subepithelial wall of the basal membrane; may be associated with mesangial expansion.

Class VI. Sclerosing lupus nephritis, with involvement of over 90% of glomeruli, with no residual activity.

Diagnosis

1. Urinalysis and serum creatinine (all patients with SLE)
2. Renal biopsy
3. Diagnosis is suspected in all patients with SLE, particularly in patients who have proteinuria, microscopic hematuria, red blood cell (RBC) casts, or hypertension. Diagnosis is also suspected in patients with unexplained hypertension, elevated serum creatinine levels, or abnormalities on urinalysis who have clinical features suggesting SLE.
4. Elevated anti–double-stranded-DNA (anti-dsDNA) antibody titers and low complement (C3 and C4) levels often indicate active lupus nephritis and support the diagnosis.
5. If the aforementioned studies are abnormal, **renal biopsy** is usually done to confirm the diagnosis and classify the disorder histologically.
6. Histologic classification helps determine prognosis and direct treatment.

Henoch-Schonlein nephritis

Henoch–Schonlein nephritis (Henoch–Schonlein purpura or anaphylactoid purpura) is a common form of systemic vasculitis in which small blood vessels in a number of organs are involved.

It is usually a disease of children, with a peak age of onset between 4 and 10 years. The syndrome is characterized by nonthrombocytopenic purpura of the skin (particularly around joints) arthralgia, gastrointestinal pain and glomerulonephritis. Kidney disease is the most important manifestation of HSP as renal failure is the main cause of death.

The **prevalence of renal disease** varies from 40% to 100% but in most patients this is mild; progression to renal failure occurs in fewer than 10%. Those with the most severe clinical presentation have the worst outcome: about 40% of those with nephritic or nephrotic syndromes at onset show long-term impairment of renal function.

Immunohistology of the renal biopsy shows irregular,granular deposits of IgA, C3 and fibrin in the glomeruli. Deposits of IgA and C3 are also found in the skin, even in non-affected areas, and are diagnostic of the condition.
As in IgA nephropathy, the available evidence suggests an IgA dominant immune-complex pathogenesis with complement activation occurring via the alternative pathway. A variety of bacterial or viral antigens could be involved, as there is an association with preceding upper respiratory tract infection. In addition, HSN is a seasonal disease: most patients present during the winter. The clinical and immunological similarity between HSN and IgA nephropathy suggests that IgA nephropathy is a renal limited form of HSN.

Lecture No. 16

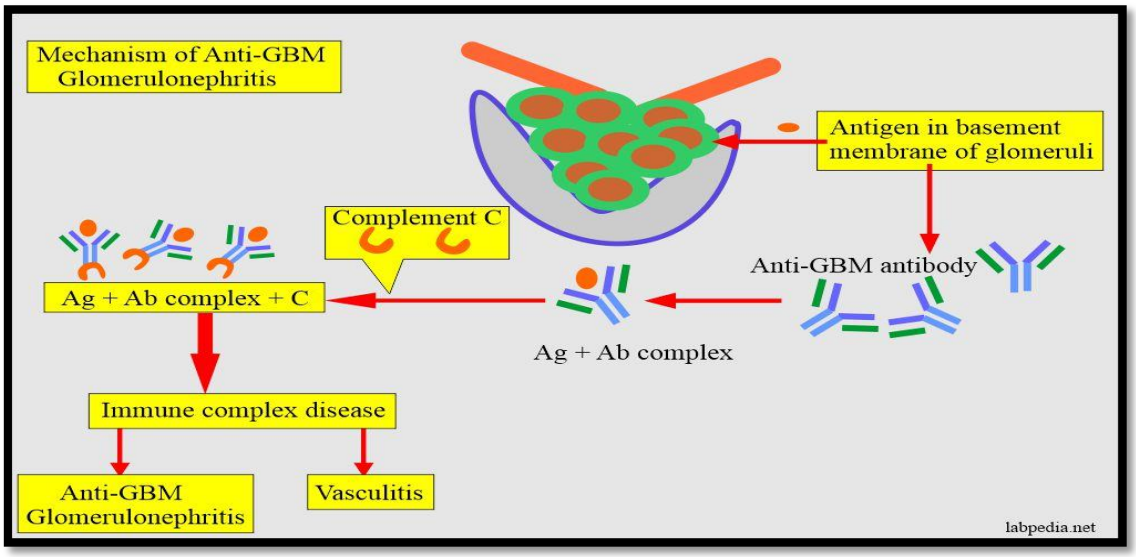
Anti-glomerular basement membrane disease

Acute glomerulonephritis mediated by anti-glomerular basement membrane (anti-GBM) antibody account for about 1-2% of all cases of glomerulonephritis. Anti-CBM nephritis is more common in men and in those who possess HLA-DR2. Patients present with nephritis alone or, more commonly, with glomerulonephritis and lung haemorrhage, a combination termed Goodpasture's syndrome. However, rapidly progressive nephritis and pulmonary haemorrhage can occur in other multisystem disorders such as SLE or Wegener's granulomatosis so the combination of renal and lung involvement is not synonymous with anti-GBM disease.

The target antigen is the α3 chain of type IV collagen, a major constituent of the GBM. Lung damage results from antibodies to antigens common to both alveolar and glomerular basement membranes. In Goodpasture's syndrome, respiratory symptoms often precede renal disease by 1 year or longer. Haemoptysis, usually leading to anemia, is a prominent feature and the sputum typically contains haemosiderin-laden macrophages. Lung biopsies show intra-alveolar haemorrhage and necrotizing alveolitis.

Etiology

Although the cause is unknown, anti-GBM disease follows upper respiratory tract infections in 20-60% 0f patients, or exposure to certain hydrocarbons. These agents may damage alveolar basement membrane, generating new and potent antigens able to stimulate autoantibody production. Alternatively, the agent responsible (e.g. a virus may cross-react with basement membrane antigens. Pulmonary haemorrhage in anti-GBM disease is strongly associated with cigarette smoking.



Figure(1):Mechanism of Anti-GBM glomerulonephritis

Diagnosis

1. **Renal involvement includes**
   - **a)** Gross or microscopic hematuria, proteinuria, a decreased 24-hour creatinine clearance, and elevated blood urea and serum creatinine levels.
   - **b)** Abnormally shaped RBCs and casts can be found in the urine sediment.
2. **In those patients with pulmonary involvement,** decreased total lung capacity and increased uptake of carbon monoxide is evident. An iron deficiency anemia with decreased hemoglobin and hematocrit can develop if pulmonary hemorrhage is severe.
3. The ESR and CRP level may be normal or increased.
4. Circulating antibodies to the GBM (anti - GBM) glomerular basement membrane can be detected in about 87% of patients. These antibodies can be identified by IIF, ELISA, or Western blot.

Lecture No. 17

Respiratory disease

Drug-Induced Pulmonary Disease

Drug-induced pulmonary disease is lung disease brought on by a bad reaction to a medicine. Pulmonary means related to the lungs.

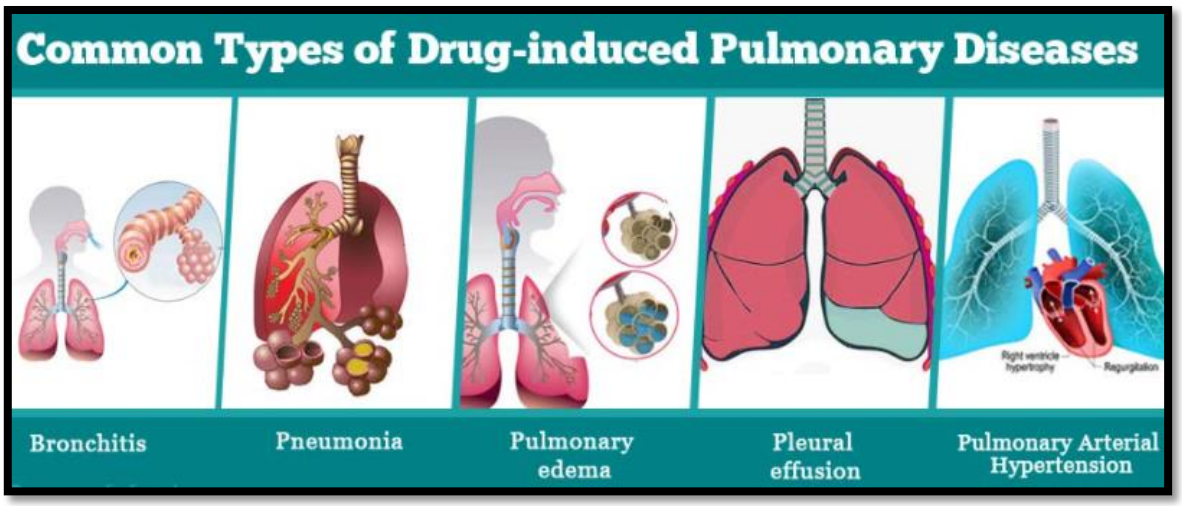
What is the most common drug-induced respiratory problem?

Interstitial pneumonitis (ie, inflammation of the lung interstitium, such as the alveolar septa) is the most common manifestation of drug-induced lung disease.

The Common Types of Drug-induced Pulmonary Diseases

There are different types of lung or pulmonary diseases caused by drugs are:

1. **Allergic reactions** like asthma, hypersensitivity pneumonitis, or eosinophilic pneumoni
2. **-Lymph node swelling**
3. **Alveolar haemorrhage**, i.e. bleeding into lung sacs .
4. **Bronchitis,** i.e., inflammation of the airways .
5. **Pneumonia**
6. **Pulmonary edema**, i.e., fluid accumulation in the lungs .
7. **Pleural effusion** i.e., fluid accumulation around the lungs .
8. **Pulmonary fibrosis i**.e., formation of scar tissue in the lungs .
9. **Pulmonary arterial hypertension**i.e defined as a mean pulmonary arterial pressure greater than 25 mm Hg at rest or greater than 30 mm Hg during exercise .
10. **Lung failure.**



Many medicines and substances are known to cause lung disease in some people. These include:

- Antibiotics, such as nitrofurantoin and sulfa drugs
- Heart medicines, such as amiodarone
- Chemotherapy drugs such as bleomycin, cyclophosphamide, and methotrexate
- Street drugs

Symptoms

Symptoms may include any of the following:

- Bloody sputum
- Chest pain
- Cough
- Fever
- Shortness of breath

- Wheezing

Diagnosis of Drug-induced Pulmonary Diseases

It has always been a challenge for pulmonologists to diagnose drug-induced pulmonary disease. The medications can cause reactions in varied forms, which makes it difficult for pulmonologists to identify the drug or its reaction.

Tests that could detect changes in the lungs include the following:

1. **Imaging tests like chest x-ray and chest CT scan .**
2. **Lung function tests :** The primary purpose of pulmonary function testing is to identify the severity of pulmonary impairment**.** The tests measure lung volume, capacity, rates of flow, and gas exchange.
3. **Bronchoscopy** : is a procedure to look directly at the airways in the lungs using a thin, lighted tube (bronchoscope). The bronchoscope is put in the nose or mouth. It is moved down the throat and windpipe (trachea), and into the airways **.**
4. **Blood tests to rule out SLE-like reactions as a cause of the lung disease**
5. Lung Biopsy, in rare cases

Lecture No. 18

Eosinophilic Pneumonia

Chronic eosinophilic pneumonia (CEP) is an idiopathic disorder characterized by an abnormal and marked accumulation of eosinophils in the interstitium and alveolar spaces of the lung causing inflammation and damage. Causes include smoking, allergic reactions and parasitic infections. EP may occur suddenly or worsen slowly.

What are the types of eosinophilic pneumonia?

There are three main types of eosinophilic pneumonia. They include:

- **Acute eosinophilic pneumonia:** This type worsens quickly as your blood oxygen level falls. Most patients with AEP completely recover with treatment.
- **Chronic eosinophilic pneumonia:** This type worsens slowly, over days or weeks. If untreated, it may persist over weeks or months and result in severe symptoms.
- **Löffler syndrome (simple pulmonary eosinophilic, or SPE):** This form of eosinophilic pneumonia may cause no symptoms or only mild symptoms such as a dry cough. Löffler syndrome occurs due to a parasitic infection (roundworms). With treatment, the condition typically resolves within one month.

Causes of Eosinophilic pneumonia

Eosinophilic pneumonia has many causes, both infectious and noninfectious. But healthcare providers don't always know the exact cause.

Common noninfectious triggers include:

- Allergic reactions.
- Fungus (usually aspergillosis).
- Inhaled toxins, such as chemical fumes or particulate metals (found in the air) or dust.
- Medication, including commonly used antibiotics, nonsteroidal anti-inflammatory drugs (NSAIDs) or selective serotonin reuptake inhibitors (SSRIs).
- Smoking, especially if you've had a change in cigarette smoking habits (starting smoking for the first time or smoking more often).
- Underlying conditions, including cancer, autoimmune disease or inflammatory disease.

The symptoms of eosinophilic pneumonia

Signs of eosinophilic pneumonia vary, depending on the type and cause. Common symptoms include:

- Cough.
- Fever.
- Shortness of breath (dyspnea).

Acute eosinophilic pneumonia can worsen quickly, often within two weeks. Symptoms are usually more severe in people who smoke and may include:

- Chest pain.
- Chills.
- Fatigue.
- Muscle aches or muscle pain (myalgia).

Without prompt diagnosis and treatment, the oxygen in your blood may fall to dangerously low levels. This can lead to acute respiratory failure in a few hours, requiring emergency treatment.

Common symptoms include:

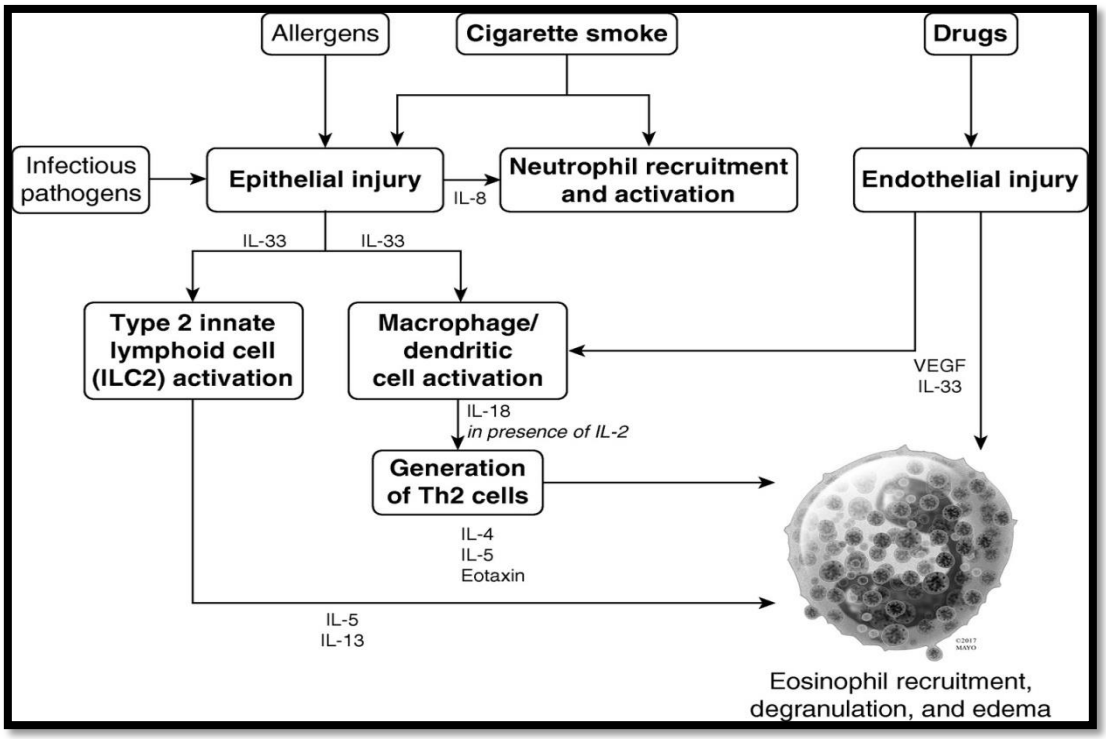
- Shortness of breath that worsens.
- Night sweats.
- Unexplained weight loss.
- Wheezing.

Pathogenicity of Chronic Eosinophilic Pneumonia

The pathophysiological role of eosinophils in autoimmune diseases is not well defined; however, it has been shown that the production of pro-inflammatory cytokines stimulates and activates different cell groups, and can simultaneously induce autoantibodies and/or increased infiltration of eosinophils in various tissues, without an underlying autoimmune disease.

A proposed model for the pathogenesis of acute eosinophilic pneumonia. IL-33 may be released by damaged epithelial cells responding to noxious stimulants such as allergens,

infectious pathogens, and other inhalational toxins, including cigarette smoke. IL-33 and vascular endothelial grow factor (VEGF) may also be released by endothelial cells after drug-induced injury. In addition to IL-33, acute exposure to cigarette smoking induces epithelial cell release of IL-8, which mediates recruitment and activation of neutrophils. An additional source of IL-33 in the lung may be the activation of innate type 2 lymphoid cells, which have the capacity to rapidly generate IL-33 in response to certain stimuli. Subsequent generation and binding of IL-33 to cells expressing its receptor (ST2), including macrophages and dendritic cells, may lead to recruitment and activation of T-helper cell type 2 (Th2)-polarized T lymphocytes and production of cytokines like IL-5, which further promote recruitment and activation of eosinophils in the lung tissue. Eosinophils may also migrate into the lung because of chemokine gradients and increased permeability in the context of endothelial injury.



Diagnosis of Eosinophilic pneumonia

- medical history and travel.
- physical exam.
- Blood tests, including a complete blood count, to detect abnormalities.
- Broncho alveolar lavage (BAL) is the most important test to diagnose EP. Uses a flexible tube (bronchoscope) to collect fluid from your lungs to look for signs of disease.
- Chest x-ray and CT scan.
- Peripheral blood eosinophilia count , peripheral eosinophilia is often present in chronic eosinophilic pneumonia.
- Sedimentation rate (ESR)

Occupational lung diseases

Occupational or work-related lung diseases are lung conditions that have been caused or made worse by long-term exposure to certain irritants in the workplace. Dust particles, chemicals, fungal spores, and certain animal droppings are examples of exposures that may increase your risk of developing occupational lung disease.

There is no cure for occupational lung diseases. Controlling your exposure to lung irritants and treatment can help slow the disease progression, lessen symptoms, and improve your quality of life. If you smoke, quit. Smoking can cause or worsen lung disease.

The symptoms of an occupational lung disease

- Coughing
- Shortness of breath
- Chest pain
- Chest tightness
- Abnormal breathing pattern .

Types of occupational lung diseases

- Asthma.
- Bronchiolitis obliterans.
- COPD.(Chronic obstructive pulmonary disease)
- Hypersensitivity pneumonitis.
- Lung cancer.
- Mesothelioma.
- Pneumoconiosis.

The difference between inorganic and organic dust

Inorganic refers to any substances that do not contain carbon, excluding certain simple carbon oxides, such as carbon monoxide and carbon dioxide.

Organic refers to any substances that do contain carbon, excluding simple carbon oxides, sulfides, and metal carbonates .

Exposure to environmental and occupational lung irritants may put you at risk of developing chronic lung disease, including:

1. **Silicosis** is caused by breathing in tiny bits of silica, a mineral found in sand, quartz, and many other types of rock. Silicosis mainly affects workers exposed to silica dust in jobs such as construction and mining.
2. **Coccidioidomycosis or Valley fever** is an infection caused by breathing in the spores of the fungus Coccidioides found in the soil. Valley fever mainly affects workers exposed to dust storms or areas where contaminated soil is being disturbed, in jobs like construction or farming.

3. **Hypersensitive pneumonitis** is caused when you breathe in a specific substance (allergen) that triggers an allergic reaction in the body.
4. **Histoplasmosis** is caused by breathing fungal spores from soil that has been contaminated by bird or bat droppings. Some occupations that may expose workers to spores are farmers, pest control workers, poultry keepers, construction workers and landscapers.
5. **Asbestosis** is a naturally occurring mineral used as an insulation material and as a fire retardant. The main group at risk for asbestosis is people who worked in mining, milling, manufacturing, installation, or removal of asbestos products .
6. **Coal workers pneumoconiosis**, commonly known as black lung disease, occurs when coal dust is inhaled. Continued exposure to coal dust causes scarring in the lungs.
7. **Mesothelioma** is a rare type of cancer that occurs in the lining of the lungs and less commonly the lining of the abdomen. Asbestos exposure is the primary risk factor for mesothelioma. Occupations such as mining or milling, electricians, plumbers, pipe-fitters, insulators, or even remodelers of older homes still have a high risk of exposure.
8. **Work-related asthma:-** Men working in forestry and minerals and women working in service industries (waitresses, cleaners, and dental workers) are most likely to develop occupational asthma.

Diagnose of an occupational lung disease

- **Pulmonary function tests**: diagnostic tests that help to measure the lungs' ability to move air into and out of the lungs effectively. The tests are usually performed with special machines into which the person must breathe.
- **Microscopic examination** from biopsy or autopsy of tissue, cells, and fluids from the lungs
- **Measurement of respiratory or gas exchange functions**
- **Examination of airway or bronchial activity**

How can occupational lung diseases be prevented?

The best prevention for occupational lung diseases is avoidance of the inhaled substances that cause lung diseases and Do not smoke. Smoking can actually increase the risk for occupational lung disease.

Lecture No. 19

Asthma

A chronic disease in which the bronchial airways in the lungs become narrowed and swollen, making it difficult to breathe. Symptoms include wheezing, coughing, tightness in the chest, shortness of breath, and rapid breathing. An asthma attack may be brought on by pet hair, dust, smoke, pollen, mold, exercise, cold air, or stress.

Asthma signs and symptoms include:

1. Shortness of breath
2. Chest tightness or pain
3. Wheezing when exhaling, which is a common sign of asthma in children
4. Trouble sleeping caused by shortness of breath, coughing or wheezing
5. Coughing or wheezing attacks that are worsened by a respiratory virus, such as a cold or the flu

Types of asthma

1. Allergic asthma
2. Seasonal asthma
3. Non allergic asthma
4. Exercise induced asthma
5. Difficult asthma
6. Childhood asthma

Causes

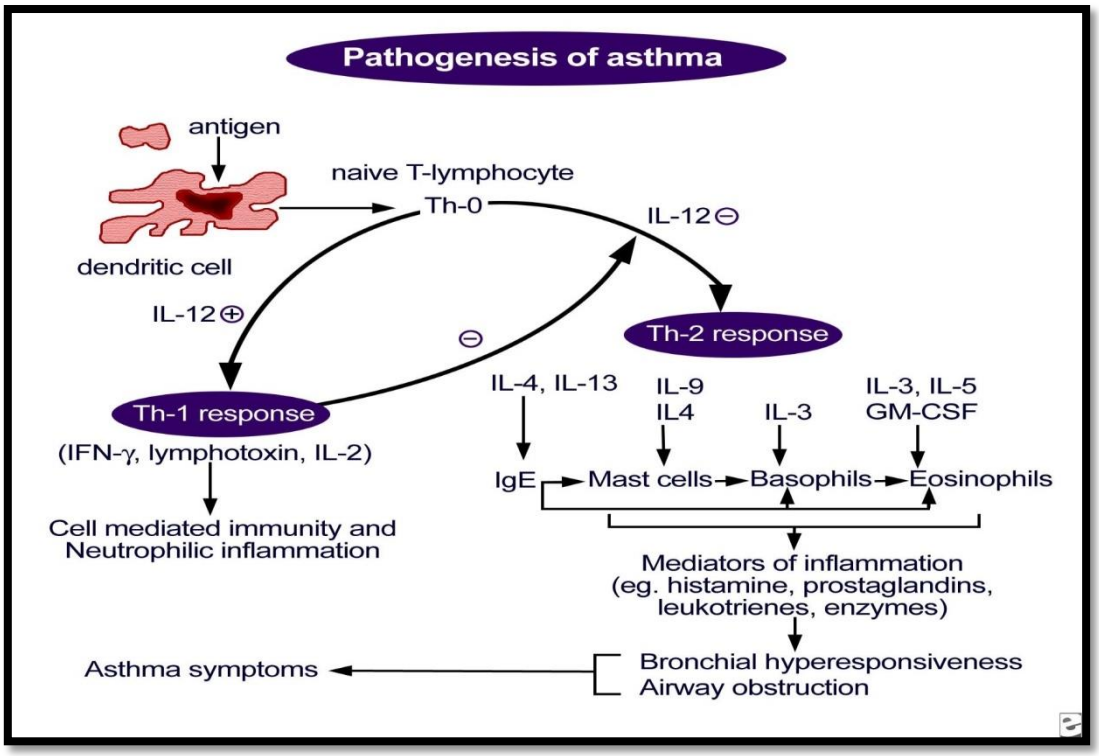
It isn't clear why some people get asthma and others don't, but it's probably due to a combination of environmental and inherited (genetic) factors. Exposure to various irritants and substances that trigger allergies (allergens) can trigger signs and symptoms of asthma. Asthma triggers are different from person to person and can include:

1. Airborne allergens, such as pollen, dust mites, mold spores, pet dander or particles of cockroach waste
2. Respiratory infections, such as the common cold
3. Physical activity
4. Cold air
5. Air pollutants and irritants, such as smoke
6. Certain medications, including beta blockers, aspirin, and nonsteroidal anti-inflammatory drugs, such as ibuprofen (Advil, Motrin IB, others) and naproxen sodium (Aleve)
7. Strong emotions and stress
8. Sulfites and preservatives added to some types of foods and beverages, including shrimp, dried fruit, processed potatoes .
9. Gastroesophageal reflux disease (GERD), a condition in which stomach acids back up into your throat

Pathophysiology

There are two phases of an asthma exacerbation, which include the early phase and late phase. The early phase is initiated by IgE antibodies that are sensitized and released by plasma cells. These antibodies respond to certain triggers in the environment, such as the risk factors listed above. IgE antibodies then bind to high-affinity mast cells and basophils. When a pollutant or risk factor gets inhaled, the mast cells release cytokines and eventually de-granulate. Released from mast cells are histamine, prostaglandins, and leukotrienes.
Simultaneously, cytokines derived from the mast cell will signal other inflammatory cells and their mediators to the lung. The result is airway inflammation, increased vascular permeability, mucus secretion, bronchospasm, and wheezing. These events are referred to as the *early asthmatic response* because they occur within minutes. A major component of the early response is bronchospasm.

The *late asthmatic response* is delayed by hours. It is caused by a multitude of inflammatory cells continuing the inflammatory process. Of the inflammatory cells, the T cells play an important role. Antigen presenting cells may present a variety of allergenic antigens to chronically activated T helper cells. These cells then secrete multiple cytokines that maintain and intensify the local inflammatory response. Many other inflammatory cells, including mast cells and eosinophils, will respond to the T cells' cytokines. These inflammatory cells will produce cytokines, which amplify the cellular response and the inflammatory reaction. There is a migration of inflammatory cells from the circulation into the pulmonary vasculature and the airway submucosa. A central component to the inflammatory process as well as treatment is the arachidonic acid pathway, which leads to the generation of leukotrienes.



Diagnosis

1- Physical exam

2-**Lung function tests :-** These are also called (pulmonary function tests.) Lung function tests detect how well you inhale (breathe in) and exhale (breathe out) air from your lungs. These tests measure breathing.

Lung function tests are often done before and after inhaling a medication known as a bronchodilator. This medicine opens the airways. If lung function improves a lot with a bronchodilator, the patient likely has asthma.

Common Lung function tests used to assess airways include:

a. **Spirometry:** A type of lung function test that measures how much you breathe in and out and how fast you breathe out.

b. **FeNO test (exhaled nitric oxide):** A test that helps assess inflammation in the airways.

c. **Bronchial provocation or "trigger" tests:** Tests that measure if lungs are sensitive to certain irritants or triggers such as methacholine or histamine.

d. **Diffusion Capacity:** Diffusion capacity measures how well oxygen flows from the lungs into your blood. Poor diffusion indicates damage to the lung where the oxygen and blood meet in the lungs. Diffusion capacity is usually normal in asthmatics.

3- Allergy tests

4- Blood tests: measured the levels of immunoglobulin E (IgE) and Eosinophil . If the levels are high, this could be a sign of severe asthma.

5-**Chest X-Ray:-**in asthma, the chest X-ray is likely to show air trapping or hyperexpansion.

Lecture No. 20

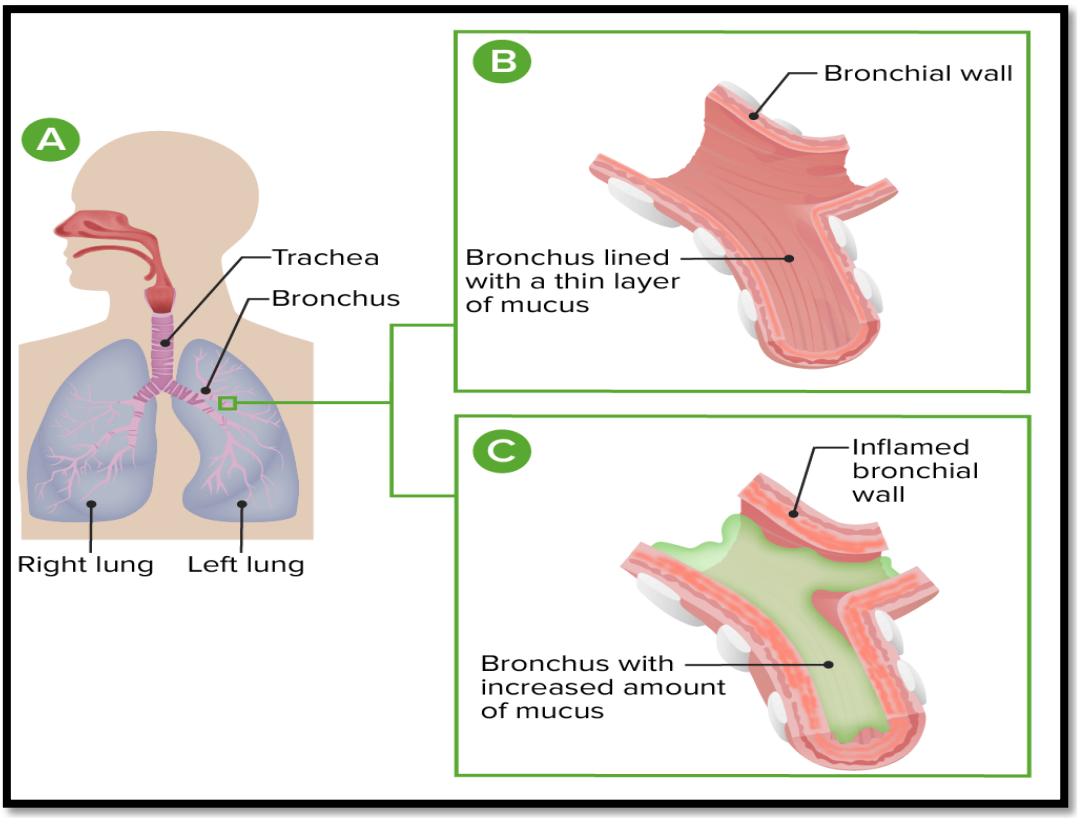
Non-allergic bronchitis

It is a form of lower respiratory tract infection occurs due to a viral or bacterial infection. Some people develop non-allergic bronchitis after a cold, for instance. Bronchitis can be acute or chronic. Acute form leads to cough, which may contain mucus, while in case of chronic bronchitis, cough last for more than a few months. Air pollution and smoking are some major causes of bronchitis.

Symptoms of Acute Bronchitis

Each person is different, and symptoms will vary depending on the cause of inflammation. The symptoms associated with acute bronchitis are similar to those of the cold and flu and last less than 3 weeks .

- Coughing with or without mucus
  - A runny nose
  - A sore throat
  - Sneezing
  - Fever & chills
  - Breathing difficulties
  - Extreme fatigue
- Mild headache
- Mild body ache



Causes

A virus usually causes acute bronchitis. Bacteria can sometimes cause acute bronchitis. But, even in these cases, taking antibiotics is NOT advised and will not help you get better.

Diagnosis

1. **Spirometry :-** A test that measures lung function as breathe in and out of a mouthpiece that is attached to a device called a spirometer.

2. **Peak expiratory flow :-** A test that measures the force of air breathe out (exhale) into the mouthpiece of a device called a peak expiratory flow meter

3. **Chest X-ray:-** A radiology test that produces images of the chest to look for evidence of other conditions that could be causing your coughand breathing problems.

4. **Complete blood count (CBC) with differential**
5. **Procalcitonin levels** (to distinguish bacterial from nonbacterial infections)
6. **Sputum cytology** (if the cough is persistent)
7. **Blood culture** (if bacterial superinfection is suspected)
8. **Chest radiography** (if the patient is elderly or physical findings suggest pneumonia)
9. **Bronchoscopy** (to exclude foreign body aspiration, tuberculosis, tumors, and other chronic diseases)
10. **Influenza tests**
11. **Laryngoscopy** (to exclude epiglottitis)