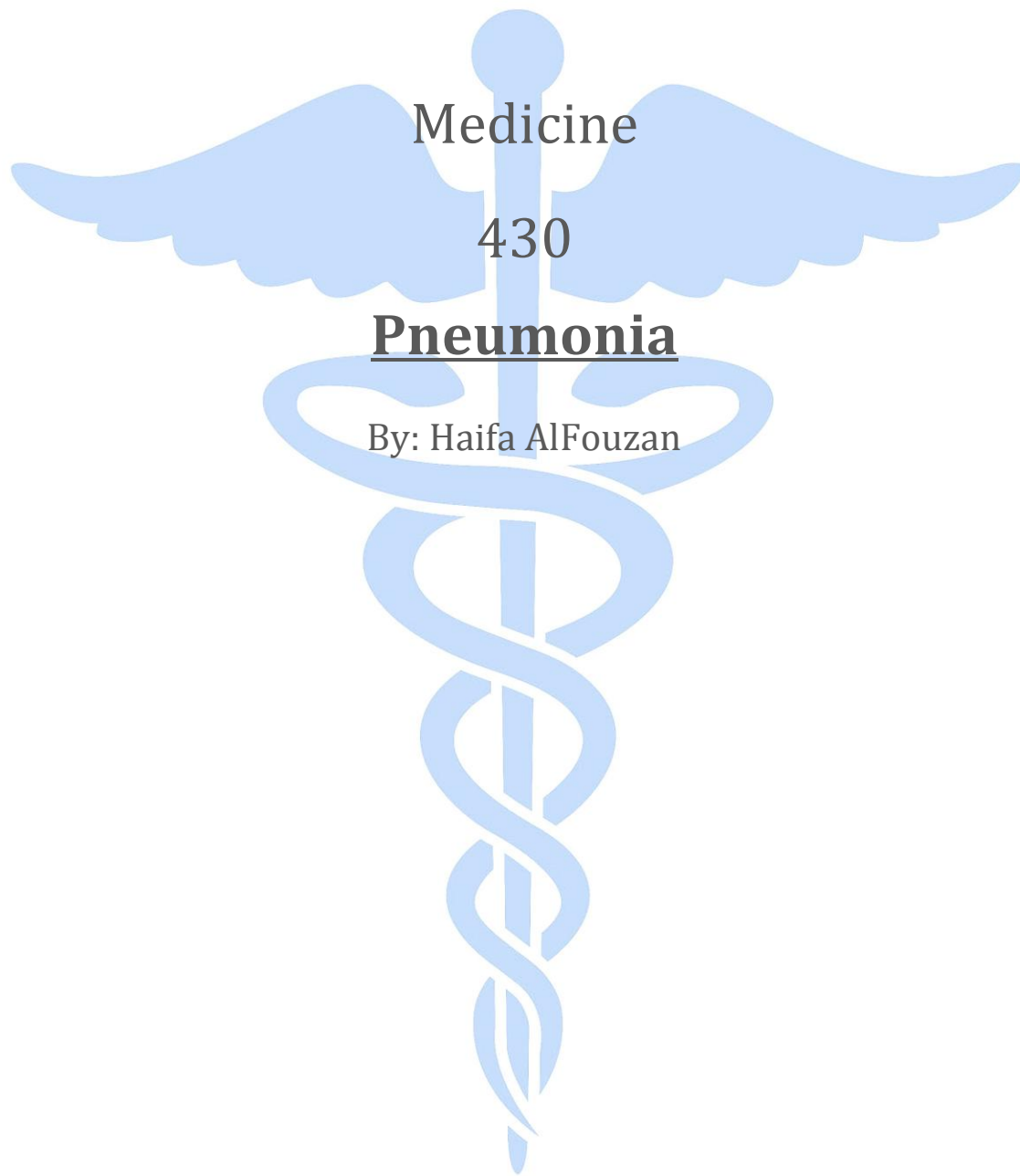


"He who studies medicine without books sails an uncharted sea, but he who studies medicine without patients does not go to sea at all"
William Osler



Medicine

430

Pneumonia

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PNEUMONIA

What is pneumonia?

Pneumonia is defined as an inflammation of the substance of the lungs (parenchyma of the lung “alveoli”) It is usually caused by bacteria.

Clinically it usually presents as an acute illness with cough, purulent sputum and fever together with physical signs or radiological changes compatible with consolidation of the lung (Abnormal alveolar filling with fluid causing Air space disease).

Bacterial pneumonia is more frequent in alcoholics and in HIV-infected individuals as compared to the general population. The causative agents are the same as found in community-acquired pneumonia in previously healthy people.

Pneumonia definitions/ General characteristics:

• Community-acquired pneumonia (CAP)

- Cough/fever/sputum production + infiltrate
- Occurs in the community
- Typical or atypical
- Most common organism: **strep pneumoniae**

• Hospital-acquired pneumonia (HAP)

- Pneumonia > 48 hours after admission
- Most common organism: **Gram-negative rods and staph a.**

• Ventilator-associated pneumonia (VAP)

- pneumonia > 48 hours after intubation

• Healthcare-associated pneumonia (HCAP)

- Pneumonia that develops within 48 hours of admission in pts with:
 - Hospitalization in acute care hospital for >2 d in past 90 d
 - Residence in NH or LTC facility
 - Chronic dialysis within 30 days
 - Home IV therapy, home wound care in past 30 days
 - Family member with MDR (multidrug resistance) pathogen

Pathogenesis:

• Inhalation:

- organisms bypass normal respiratory defense mechanisms
- Pt inhales aerobic GN organisms that colonize the upper respiratory tract
- Respiratory support equipment
- TB, viruses, Legionella

• Aspiration:

- occurs when the Pt aspirates colonized upper respiratory tract secretions (usually with old pt present with dysphagia “unable to swallow”)
- Stomach: reservoir of GNR (Gram-negative Rods) that can ascend, colonizing the respiratory tract
- Microaspiration results usually from normal flora in healthy pt, nasopharynx: S. Pneumonia
- Anaerobes

• Hematogenous:

- originate from a distant source and reach the lungs via the blood stream
- Staph endocarditis, septic emboli

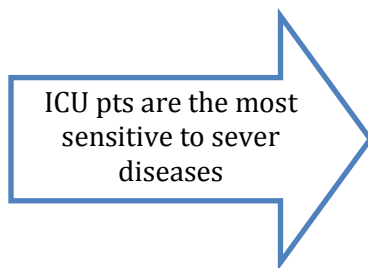
Pathogens involved:

- Community acquired pneumonia usually caused by a single organism.
- Even with extensive diagnostic testing, most investigators cannot identify a specific etiology for CAP in $\geq 50\%$ of patients.
- Caused by a variety of Bacteria, Viruses and Fungi
- **Streptococcus pneumonia is the most common pathogen 60-70% of the time.**
- **The number 1 cause of CAP in all ages: Strep pneumonia.**

- The ordering within each box is from most common to least common, though the order changes depend on which study you look at.

**The sicker the pt is, the more likely they have staph aureus, GNR, or legionella and the less likely they have an atypical infection.

Pathogenic Organisms



Outpatient	<i>Strep pneumo</i> <i>Mycoplasma / Chlamydophila</i> <i>H. influenzae</i> Respiratory viruses
Inpatient, non-ICU	<i>Strep pneumo</i> <i>Mycoplasma / Chlamydophila</i> <i>H. influenzae</i> <u>Legionella</u> Respiratory viruses
ICU	<i>Strep pneumo</i> <u>Staph aureus</u> , <u>Legionella</u> <u>Gram neg bacilli</u> , <i>H. influenzae</i>

Precipitating factors:

- Strep. Pneumoniae - often follows viral infection with influenza or parainfluenza.
- Hospitalized 'ill' patients - often infected with Gram-negative organisms.
- Cigarette smoking (the strongest independent risk factor for invasive pneumococcal disease).
- Alcohol excess.
- Bronchiectasis (e.g. in cystic fibrosis).
- Bronchial obstruction (e.g. carcinoma) - occasionally associated with infection with 'non-pathogenic' organisms (considered to be normal flora).
- Immunosuppression (e.g. AIDS or treatment with cytotoxic agents) - organisms include Pneumocystis jiroveci, Mycobacterium avium-intracellulare, cytomegalovirus.
- Intravenous drug users - frequently associated with Staph. Aureus infection.
- Inhalation from oesophageal obstruction - often associated with infection with anaerobes.

Clinical features:

The clinical presentation varies according to the immune state of the patient and the infecting agent. In the most common type of pneumonia (caused by Strep. Pneumoniae) there is often a preceding history of a viral infection. With Strep. Pneumoniae infection the patient rapidly becomes more ill with a **high temperature** (up to 39.5°C), **pleuritic pain and a dry cough**. A day or two later, **rusty-colored sputum** is produced and at about the same time the patient may develop labial herpes simplex.

The patient **breathes rapidly and shallowly (always check the O₂ saturation)**, the affected side of the chest **moves less**, and signs of **consolidation** may be present **together with a pleural rub**.

- If the pt has positive LR he'll be more susceptible to have pneumonia.
- **Aegophony** : ask the patient to say "BEE" it'll sounds like "BAY" at the area of consolidation

Sign	Positive LR	Negative LR
General appearance		
Cachexia	4.0	NS
Abnormal mental status	2.2	NS
Vital signs		
Temp >37.9 C	2.2	0.7
RR > 28/min	2.2	0.8
HR >100 bpm	1.6	0.7
Lung findings		
Percussion dullness	3.0	NS
Reduced breath sounds	2.3	0.8
Bronchial breath sounds	3.3	NS
Aegophony	4.1	NS
Crackles	2.0	0.8
Wheezes	NS	NS

NS= not significant. LR= Likelihood Ratio

From McGee S, *Evidence-based physical diagnosis*, 2nd edition. St Louis: Saunders, 2007.

Investigations:

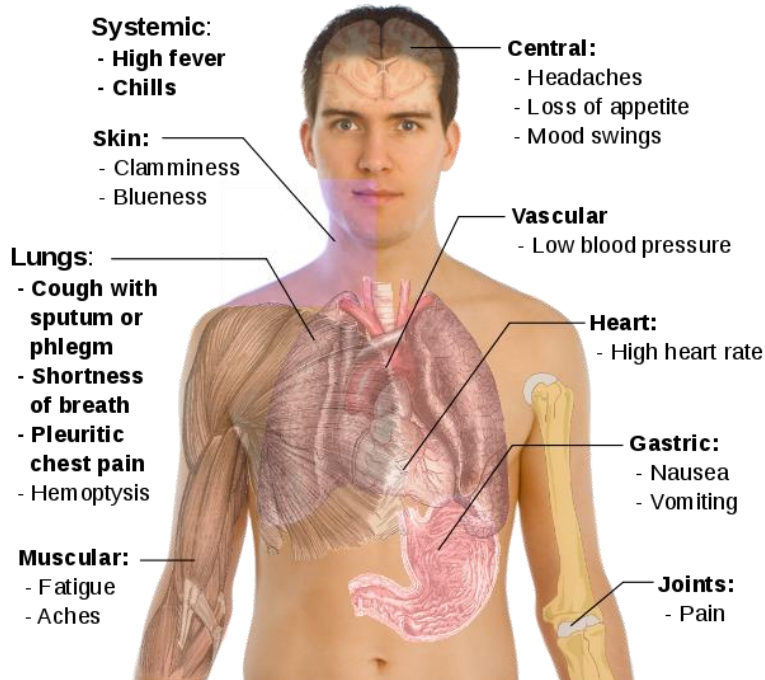
- **Chest X-ray** confirms the area of consolidation, but radiological changes lag behind the clinical course so that X-ray changes may be minimal at the start of the illness.
 - Demonstrable infiltrate by CXR or other imaging technique
 - Establish Dx and presence of complications (pleural effusion, multilobar disease)
 - May not be possible in some outpatient settings
 - CXR: classically thought of as the gold standard
 - CT scan is not always used unless the pt has lung abscess or the X-rays had negative results.
- **Gram stain and culture**: (low sensitivity and specificity) but still worthwhile test because antimicrobial resistance is an increasing problem.
- **CBC (complete blood count)**: In Strep. pneumoniae pneumonia, there is often a white blood cell count that is greater than $15 \times 10^9/L$
- **Blood culture** (always do it with patients suffering from fever)
 - Sputum culture
 - special stain (acid fast: TB, silver stain: pneumocystis carinii in HIV patients)
- **Arterial blood gas** (ABG)
- **Urinary antigen assay** : (for legionella in selected pt)
 - This test is very sensitive
 - The antigen persists in the urine even after treatment has been started.

Management

Types of patients	Organisms	Management	If the patient was on antibiotics
out Previously Healthy Pt	. pneumo, Mycoplasma, viral, Chlamydia pneumo, H. flu (rare nowadays)	Advanced generation macrolide (azithro or clarithro) or doxycycline	within the past 3 months we give them : <ul style="list-style-type: none"> – Respiratory quinolone (moxi-, levo-, gemi-), OR – Advanced macrolide + amoxicillin, OR – Advanced macrolide + amoxicillin-clavulanate
out Pt with comorbidities (cardiopulmonary disease or immunocompromised state)	S. pneumo, viral, H. flu, aerobic GN rods, S. aureus	Respiratory quinolone , OR advanced macrolide	Recent take of antibiotics : <ul style="list-style-type: none"> – Respiratory quinolone OR – Advanced macrolide + beta-lactam
Inpatient (Medical Ward)	all of the above plus polymicrobial infections (+/- anaerobes), Legionella	Respiratory fluoroquinolone, OR Advanced macrolide plus a beta-lactam	Recent take of antibiotics : Regimen selected will depend on nature of recent antibiotic therapy.

Main symptoms of infectious

Pneumonia



Causative Organisms:

	Streptococcus pneumonia	Haemophilus influenzae
Features	<ul style="list-style-type: none"> • Most common cause of CAP • Gram positive diplococci • Lobar infiltrate on CXR • 25% bacteremic 	<ul style="list-style-type: none"> • Nonmotile, Gram negative rod • Encapsulated type b (Hib) <ul style="list-style-type: none"> – The capsule allows them to resist phagocytosis and complement-mediated lysis in the nonimmune host
Symptoms	malaise, shaking chills, fever, rusty sputum, pleuritic chest pain and cough	
Risk factors	<ul style="list-style-type: none"> • Splenectomy (Asplenia) • Sick cell disease, hematologic diseases • Smoking • Bronchial Asthma and COPD • HIV • ETOH (alcoholism) 	<ul style="list-style-type: none"> • Secondary infection on top of viral disease. • Immunosuppression. • splenectomy patients
Prevention	<ul style="list-style-type: none"> • Pneumococcal conjugate vaccine (PCV-13) is a vaccine used to protect infants and young children <ul style="list-style-type: none"> – 13 serotypes of <i>Streptococcus</i> • Pneumococcal polysaccharide vaccine (PPSV-23) <ul style="list-style-type: none"> – 23 serotypes of <i>Streptococcus</i> • PPSV is recommended (routine vaccination) for those over the age of 65 • For both children and adults in special risk categories: <ul style="list-style-type: none"> – Serious pulmonary problems e.g. Asthma, COPD – Serious cardiac conditions, e.g., CHF – Severe Renal problems – Long term liver disease – DM requiring medication – Immunosuppression due to disease (e.g. HIV or SLE) or treatment (e.g. chemotherapy or radiotherapy, long-term steroid use – Asplenia 	<ul style="list-style-type: none"> • Hib conjugate vaccine
Specific Treatment	<ul style="list-style-type: none"> • β-lactams Cephalosporins, eg Ceftriaxone, PenicillinG • Macrolides eg. Azithromycin • Fluoroquinolone (FQ) eg. levofloxacin • Highly Penicillin Resistant: Vancomycin 	<ul style="list-style-type: none"> • Ceftriaxone, Amoxicillin/Clavulanic Acid (Augmentin), FQ, TMP-SMX


Complications of Pneumonia:

- Bacteremia
- Respiratory and circulatory failure
- Pleural effusion (Parapneumonic effusion), empyema, and abscess
 - Pleural fluid always needs analysis in setting of pneumonia (order a thoracentesis)
 - Always needs drainage: Chest tube, surgical

Atypical CAP: (15% of all CAP):

Organisms:

- *Mycoplasma pneumoniae*
- *Chlamydophila pneumoniae*
- *Legionella*
- *Coxiella burnetii* (Q fever)
- *Francisella tularensis* (tularemia)
- *Chlamydia psittaci* (psittacosis)
- Viruses



Zoonotic infection – ask about pets

**** ‘Atypical’: not detectable on gram stain; won’t grow on standard media**

Unlike bacterial CAP, often extra pulmonary manifestations:

- *Mycoplasma*: otitis, nonexudative pharyngitis, watery diarrhea, erythema multiforme, increased cold agglutinin titre
- *Chlamydophila*: laryngitis

****Most don’t have a bacterial cell wall (Don’t respond to β -lactams)**

Therapy:

Macrolides, tetracyclines, quinolones → (intracellular penetration, interfere with bacterial protein synthesis)

Important associations: (VERY IMPORTANT!)

- **Splenectomised patients** → *Strep pneumoniae*, *H. influenzae*
- **Alcoholism** → *Strep pneumoniae*, *Klebsiella*, oral anaerobes, *Acinetobacter*, TB
- **Aspiration** → *Klebsiella*, *E. Coli*, oral anaerobes
- **COPD/smoking** → *H. influenzae*, *Pseudomonas*, *Legionella*, *Strep pneumo.*, *Moraxella catarrhalis*, *Chlamydophila pneumoniae*
- **HIV** → *S. pneumo*, PCP (*pneumocystis carinii*), *H. influenzae*, *P. aeruginosa*, MTB, *Crypto*, *Histo*, *Aspergillus*, atypical mycobacteria
- **Recent hotel, cruise ship** → *Legionella* (MCQ)
- **Structural lung disease (bronchiectasis)** → *Pseudomonas*, *Burkholderia cepacia*, *Staph. Aureus*
- **ICU, Ventilation** → *Pseudomonas*, *Acinetobacter*

CAP: influenza

- More common cause in children :
 - RSV, influenza, parainfluenza
- Influenza most important viral cause in adults, especially during winter months :
 - Inhale small aerosolized particles from coughing, sneezing → 1-4 day incubation
 - 'uncomplicated influenza' (fever, myalgia, malaise, rhinitis) → Pneumonia
- Adults > 65 account for 63% of annual influenza-associated hospitalizations and 85% of influenza-related deaths
- Recent worldwide pandemic of H1N1 Influenza A (2009-2010) and Current epidemic in Saudi Arabia (2010-2011)
- H1N1 risk factors:
 - **Pregnancy, obesity, cardiopulmonary disease, chronic renal disease, chronic liver disease**
- CXR findings often subtle, to full blown ARDS (Adult Respiratory Distress Syndrome)
- Respiratory (or Droplet) isolation for suspected or documented influenza (Wear mask and gloves) NP swab for, Rapid Ag test Infl A,B, H1N1 PCR RNA
- Current Seasonal Influenza Vaccine prevents disease (given every season)
- Bacterial pneumonia (S. pneumo, S. aureus) may follow viral pneumonia
- Treatment:
 - Adamantanes
 - Influenza A
 - **Amantadine / Symmetrel 100mg orally twice daily**
 - **Rimantadine / Flumadine 100mg orally 4 times daily**
 - Not effective on H1N1 (its resistant)
 - Neuraminidase inhibitors
 - Influenza A and B
 - 70-90% effective for prophylaxis
 - Give within 48h of symptom onset to reduce duration/severity of illness, and viral shedding
 - **Oseltamivir / Tamiflu 75gm oral twice daily**
 - **Zanamivir / Relenza 10gm (inhalation) twice daily**
 - Osteltamivir dose in severe disease 150mg bid

How to treat a pneumonia patient?

1. First we decide if he should be treated as an outpatient or an inpatient (most important decision), 2 methods:

- **CURB-65** (1st Method)
 - Confusion of new onset
 - blood Urea greater than 7 mmol/l (19 mg/dL)
 - Respiratory rate of 30 breaths per minute or greater
 - Blood pressure less than 90 mmHg systolic or diastolic blood pressure 60 mmHg or less
 - age 65 or older
 - Every one of these is scored with 1 point
 - If the score was from 0-1 → outpatient ... 2 → inpatient ... 3 or more → ICU
 - Mortality: 2 factors→9% ... 3 factors→15% ... 5 factors→57%

Pneumonia Severity Index (PSI) (2nd Method)

- 20 variables including underlying diseases; stratifies pts into 5 classes based on Mortality risk

No RCTs comparing CURB-65 and PSI!!

2. Should we admit him to the medical floor or the ICU?

1 major criteria or 3 minor criteria → ICU

• Major criteria:

- Invasive ventilation
- septic shock on pressors

• Minor criteria

- Respiratory Rate more than 30
- Multilobar infiltrates on CXR
- Confusion
- Blood Urea Nitrogen >20
- WBC <4,000
- Platelets <100,000
- Temp <36,
- hypotension requiring aggressive fluids
- PaO₂/FiO₂ <250

TABLE 239-6 Severity-of-Illness Scoring System Based on Pneumonia Patient Outcomes Research Team (PORT) Cohort Study Data

Patient Characteristic	No. of Points
Age	
Men	Age, years
Women	Age, years -10
Nursing home residents	Age, years +10
Coexisting illnesses	
Neoplastic disease ^a	30
Liver disease ^b	20
Congestive heart failure ^c	10
Cerebrovascular disease ^d	10
Renal disease ^e	10
Physical examination findings	
Altered mental status ^f	20
Respiratory rate >30/min	20
Systolic blood pressure <90 mmHg	20
Temperature <35°C (<95°F) or >40°C (>104°F)	15
Pulse rate >125/min	10
Laboratory and radiographic findings	
Arterial pH < 7.35	30
Blood urea nitrogen >30 mg/dL (>11 mmol/L)	20
Sodium <130 mmol/L	20
Glucose >250 mg/dL (>14 mmol/L)	10
Hematocrit <30%	10
Partial pressure of arterial oxygen <60 mmHg	10
Pleural effusion	10

PSI (Harrison's internal medicine 16th edition)

3. CAP inpatient therapy :

Medical floor:

- Respiratory quinolone OR
- IV β-lactam PLUS macrolide (IV or PO)
 - β-lactams: cefotaxime, ceftriaxone, ampicillin; ertapenem
 - May substitute doxycycline for macrolide (level 3)

All of these regimens cover strep pneumonia and cover atypicals

ICU:

- β-lactam (ceftriaxone, cefotaxime, Amox-clav) **PLUS EITHER** quinolone **OR** azithromycin
- Penicillin-allergic: respiratory quinolone **PLUS** aztreonam

Pseudomonal coverage:

- Antipneumococcal, antipseudomonal: β-lactam (pip-tazo, cefepime, imi, mero) **PLUS EITHER**:
 - (cipro or levo) **OR**
 - (Aminoglycoside AND Azithromycin) **OR**
 - (aminoglycoside AND respiratory quinolone)

CA-MRSA(Methicillin-resistant Staphylococcus aureus) coverage:

- Vancomycin or Linezolid

4. Pearls of treatment:

- **Give 1st dose Antibiotics in ER (no specified time frame)**
- **Switch from IV to oral when pts are hemodynamically stable and clinically improving**
- **Discharge from hospital:**
 - As soon as clinically stable, off oxygen therapy, no active medical problems
- **Duration of therapy is usually 7-10 days:**
 - Treat for a minimum of 5 days
 - Before stopping therapy:
 - afebrile for 48-72 hours,
 - hemodynamically stable,
 - RR <24,
 - O2 sat >90%,
 - normal mental status
 - Treat longer if initial therapy wasn't active against identified pathogen; or if complications (lung abscess, empyema)

Other:

The disease	Q fever	Psittacosis	Tularemia
Causative organism	Coxiella burnetti	Chlamydophila psittac	Francisella tularensis
Carrier (Exposure)	Exposure to farm animals or parturient cats	Exposure to birds	Rabbits, squirrels, rodents
Susceptibility	Epidemic in Middle east, recent large outbreaks in Iraq	Bird owners, pet shop employees, vets	Landscapers, Hunters
Leads to	Acute Pneumonia, severe headache, hepatitis	Severe pneumonia. It presents chiefly as an atypical pneumonia, it mimic typhoid fever	fever, lethargy, anorexia, signs of septicemia
Diagnosis	complement fixation, new NAAT	Blood analysis, microbiological cultures or serology	microbiological cultures or serology
Chronic conditions	endocarditis, FUO, granuloma in liver	endocarditis, hepatitis, myocarditis, arthritis	The liver and spleen may become enlarged. Pneumonia may occur at presentation or may be a late complication
Treatment	Doxycycline, Rifampin, hydroxychloroquine	1st: Tetracycline Alternative : Macrolide	streptomycin

References:

- Harrison's internal medicine (16th edition)
- Step-Up to Medicine
- Kumar & Clark's Clinical Medicine (7th Edition)