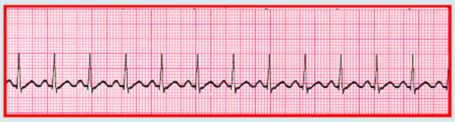
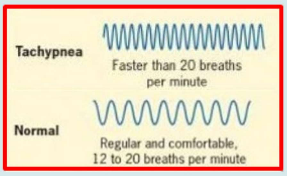
Fever productive cough and confusion

A 67-year-old woman with mild Alzheimer's disease living at home, who has a 2-day history of **productive cough**, **fever**, and **increased confusion,** is transferred to the emergency department. According to the transfer records, she has had **no recent hospitalizations or recent use of antibiotic agents**. Her temperature is **38.4°C**, the blood pressure is **145/85 mm Hg**, the respiratory rate is **28 breaths per minute**, the heart rate is **110 beats per minute**, and the oxygen **saturation is 91% while she is breathing ambient air**. **Crackles** are heard in both lower lung fields. She is oriented to person only. The white-cell count is 4000 per cubic millimeter, the serum sodium level is 130 mmol per liter, and the blood urea nitrogen is 25 mg per deciliter (9.0 mmol per liter). A radiograph of the chest shows infiltrates in both lower lobes.

What is the most likely diagnosis?

How and where should this patient be treated?





Bilateral lower lobe infiltrates with predominant right-sided pneumo and parapneumonic effusion

N Engl J Med 2014;370:543-51.

A 67-year-old woman with mild Alzheimer's disease living at home, who has a 2-day history of **productive cough**, **fever**, and **increased confusion**, is transferred to the emergency department. According to the transfer records, she has had **no recent hospitalizations or recent use of antibiotic agents**. Her temperature is **38.4°C**, the blood pressure is **145/85 mm Hg**, the respiratory rate is **28 breaths per minute**, the heart rate is **110 beats per minute**, and the oxygen **saturation is 91% while she is breathing ambient air**. **Crackles** are heard in both lower lung fields. She is oriented to person only. The white-cell count is 4000 per cubic millimeter, the serum sodium level is 130 mmol per liter, and the blood urea nitrogen is 25 mg per deciliter (9.0 mmol per liter). A radiograph of the chest shows infiltrates in both lower lobes.

What is the most likely diagnosis?

How and **where**

should this patient be treated?

CURB-65 severity assessment score for pneumonia

- **Confusion: or new AMTS<8**
- **Urea: ≥ 7mmol/l (= 42 mg/dl)**
- **Respiratory Rate: ≥ 30/min**
- **Blood Pressure: Systolic ≤ 90 and/or diastolic ≤60**
- **Age: ≥ 65**

Urea, v.n.15-50 mg/dl

4 factors gives a mortality of **83%**, 3 factors **33%**, 2 factors **23%**, one factor **8%**, no factors **2.4%**

Should not be used as a substitute for clinical judgement – can sometimes over/under-estimate severity

0–1 home; 2 hospital therapy; ≥3 consider ITU.

System	SOFA
Respiration	
Pa_{O_2}/F_{IO_2}, mm Hg (kPa)	
Coagulation	
Platelets, $\times 10^3/\mu L$	
Liver	
Bilirubin, mg/dL (μmol/L)	
Cardiovascular	
Central nervous system	
Glasgow Coma Scale score[c]	
Renal	
Creatinine, mg/dL (μmol/L)	
Urine output, mL/d	

qSOFA

- Respiratory rate ≥22/min
- Altered mentation
- Systolic blood pressure ≤100 mm Hg

SIRS

- Temperature >38°C or <36°C
- Tachycardia >90bpm
- Respiratory rate >20 breaths/min or P_aCO_2 <4.3kPa
- WBC $>12\times10^9$/L or $<4\times10^9$/L, or >10% immature (band) forms

Protocolli di Terapia Antibiotica Empirica Ragionata delle Principali Infezioni

SEPSI NON SEVERA	I° SCELTA	II° SCELTA
COMUNITARIA entro 4 giorni dal ricovero (ospedaliera precoce)	Amoxicillina Clavulanico + Claritromicina	Levofloxacina
ASSOCIATA ASS. SANITARIA	Piperacillina tazobactam+ Claritromicina	Levofloxacina+/- Amikacina
OSPEDALIERA TARDIVA (oltre 5 giorni dal ricovero)	Piperacillina tazobactam+ Amikacina*+/- Vancomicina**	Levofloxacina+Amikacina+/- Linezolid**

SEPSI SEVERA SHOCK SETTICO	I° SCELTA	II° SCELTA
COMUNITARIA entro 4 giorni dal ricovero (ospedaliera precoce)	Amoxicillina clavulanico + Levofloxacina	Levofloxacina+ Gentamicina
ASSOCIATA ASS.SANITARIA	Meropenem+Vancomicina + Amikacina*	Levofloxacina+ Amikacina+Linezolid
OSPEDALIERA TARDIVA (oltre 5 giorni dal ricovero)	Meropenem+Vancomicina + Amikacina*	Levofloxacina+Amikacina+ Linezolid

*se si sospetta polmonite da Legionella associare Levofloxacina al posto di Amikacina

** associare Vancomicina o Linezolid se fattori di rischio per MRSA: recente (< 30 giorni) ospedalizzazione o terapia con fluorochinolonici, colonizzazione nota da MRSA

N Engl J Med 2014;370:543-51.

PNEUMONIA OUTCOMES RESEARCH TRIAL (PORT) SEVERITY INDEX

	POINTS ASSIGNED FOR EACH CRITERION
VITAL SIGNS	
Pulse >125/min	10
Systolic BP <90 mm Hg	20
Temp <35 or >40°C	15
Respiratory rate >30/min	20
HISTORY OF CO-MORBID CONDITIONS	
Neoplasm (active, not skin)	30
Cirrhosis or chronic hepatitis	20
Heart failure, stroke, chronic renal insufficiency	10
Altered mental status	20
DEMOGRAPHY	
Age	age (subtract 10 for women)
Nursing home resident	10
LABORATORY DATA	
Arterial pH <7.35	30
BUN >30 mg/dL	20
Serum sodium <130 mEq/L	20
Glucose >250 mg/dL	10
Hematocrit <30%	10
pO2 <60 mm Hg or O2 saturation <90%	10
Pleural effusion on chest radiograph	10

CURB-65 severity assessment score for pneumonia

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- Urea: ≥ 7mmol/l (= 42 mg/dl)
- Respiratory Rate: ≥ 30/min
- Blood Pressure:Systolic ≤ 90 and/or diastolic ≤60
- Age: ≥ 65

4 factors gives a mortality of 83%, 3 factors 33%, 2 factors 23%, one factor 8%, no factors 2.4%

Should not be used as a substitute for clinical judgement – can sometimes over/under-estimate severity

0–1 home; 2 hospital therapy; ≥3 consider ITU.

MORTALITY AT 30 DAYS

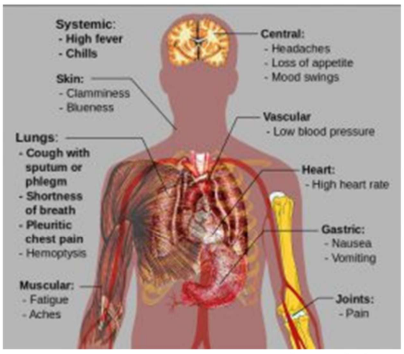
		MORTALITY		
POINT SCORE	CLASS	*Community-Acquired Pneumonia**	*Community-Acquired Pneumonia*†	*S. pneumoniae*‡
≤70	II	<1%	3%	—
71-90	III	3%	4%	3%
91-130	IV	8%	8%	21%
>130	V	29%	22%	35%

*Original calculation in patients with community-acquired pneumonia report of PORT score (Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med.* 1997;336:243-250.)

†Mortality in patients admitted for pneumonia during a 1-year period, Veterans Affairs Medical Center, Houston (patients with noninfectious causes were excluded) (Musher DM, Roig IL, Cazares G, et al. Can an etiologic agent be identified in adults who are hospitalized for community-acquired pneumonia: results of a one-year study. *J Infect.* 2013;67:11-18.)

‡Results in patients with proven pneumococcal pneumonia (Musher DM, Alexandraki I, Graviss EA, et al. Bacteremic and nonbacteremic pneumococcal pneumonia. A prospective study. *Medicine [Baltimore].* 2000;79:210-221.)

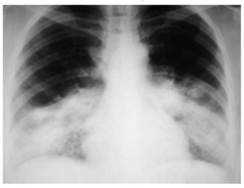
Clinical features *Symptoms:* Fever, rigors, malaise, anorexia, dyspnoea, cough, purulent sputum, haemoptysis, and pleuritic pain. *Signs:* Pyrexia, cyanosis, confusion (can be the only sign in the elderly—may also be hypothermic), tachypnoea, tachycardia, hypotension, signs of consolidation (diminished expansion, dull percussion note, ↑tactile vocal fremitus/vocal resonance, bronchial breathing), and a pleural rub.



42 mg/dl (v.n. TS, 15-50 mg/dl)

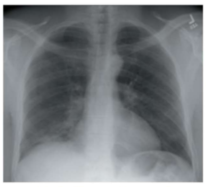
Severity 'CURB-65' is a simple, validated scoring system.[6,7] 1 point for each of: **C**onfusion (abbreviated mental test ≤8); **U**rea >7mmol/L; **R**espiratory rate ≥30/min; **B**P <90 systolic and/or 60mmHg diastolic); age ≥**65**. 0–1 home Rx possible; 2 hospital therapy; ≥3 severe pneumonia indicates mortality 15–40%—consider ITU. It may 'underscore' the young—use clinical judgement. Other features increasing the risk of death are: co-existing disease; bilateral/multilobar involvement; P_aO_2 <8kPa/S_aO_2 <92%.

Tests aim to establish diagnosis, identify pathogen, and assess severity (see below). *CXR* (fig 1, p737): lobar or multilobar infiltrates, cavitation or pleural effusion. *Assess oxygenation:* oxygen saturation, p156 (ABGs if S_aO_2 <92% or severe pneumonia) and BP. *Blood tests:* FBC, U&E, LFT, CRP, blood cultures. *Sputum* for microscopy and culture. In severe cases, check for *Legionella* (sputum culture, urine antigen), atypical organism/viral serology (PCR sputum/BAL, complement fixation tests acutely, paired serology) and check for pneumococcal antigen in urine. *Pleural fluid* may be aspirated for culture. Consider *bronchoscopy* and *bronchoalveolar lavage* if patient is immunocompromised or on ITU.



A 53-year-old patient with severe legionella pneumonia. Chest radiograph shows dense consolidation in both lower lobes.

A 38-year-old patient with Mycoplasma pneumonia. Chest radiograph shows a vague, ill-defined opacity in the left lower lobe.



Patchy infiltrates in the right middle lobe

Fig 1. PA chest radiograph showing multiple rounded ring lesions of differing sizes in the right lower zone, at the right apex and in the left lower zone. The lesions are largest in the right lower zone, where they can be seen to contain air-fluid levels, typical appearance of infection in a pneumatocele (=air cyst) or cavitating lesion. A moderate right-sided hydropneumothorax can also be seen, suggesting that one of these lesions may have ruptured into the pleural cavity. The patient also has a right subclavian central venous catheter for the administration of antibiotics. The diagnosis in this case was that of multiple pulmonary abscesses in a patient who was an intravenous drug user.

Pneumonia[5]

An acute lower respiratory tract illness associated with fever, symptoms and signs in the chest, and abnormalities on the chest x-ray—fig 1, p737. Incidence: 5-11/1000, ↑ if very young or old (30% are under 65yrs). Mortality: ~21% in hospital.

1. Community-Acquired Pneumonia

- Fever or hypothermia, tachypnea, cough with or without sputum, dyspnea, chest discomfort, sweats or rigors (or both).
- Bronchial breath sounds or inspiratory crackles on chest auscultation.
- Parenchymal opacity on chest radiograph.
- Occurs outside of the hospital or within 48 hours of hospital admission in a patient not residing in a long-term care facility.

HEALTH CARE–ASSOCIATED PNEUMONIA

- Hospitalization for ≥48 h
- Hospitalization for ≥2 days in prior 3 months
- Nursing home or extended-care-facility residence
- Antibiotic therapy in preceding 3 months
- Chronic dialysis
- Home infusion therapy
- Home wound care
- Family member with MDR infection

MDR, multidrug-resistant

2. Nosocomial Pneumonia (Hospital-Acquired, Ventilator-Associated, and Health Care–Associated)

- **Hospital-acquired pneumonia (HAP)** occurs > 48 hours after admission to the hospital or other health care facility and excludes any infection present at the time of admission.
- **Health care–associated pneumonia (HCAP)** occurs in community members whose extensive contact with healthcare has changed their risk for virulent and drug resistant organisms.
- **Ventilator-associated pneumonia (VAP)** develops following endotracheal intubation and mechanical ventilation.
- At least two of the following: fever, leukocytosis, purulent sputum.
- New or progressive parenchymal opacity on chest radiograph.
- Especially common in patients requiring intensive care or mechanical ventilation.

Classification and causes

Community-acquired pneumonia (CAP) may be primary or secondary to underlying disease. *Streptococcus pneumoniae* is the commonest cause, followed by *Haemophilus influenzae* and *Mycoplasma pneumoniae*. *Staphylococcus aureus*, *Legionella* species, *Moraxella catarrhalis*, and *Chlamydia* account for most of the remainder. Gram negative bacilli, *Coxiella burnetii* and anaerobes are rarer. Viruses account for up to 15%. Flu may be complicated by community-acquired MRSA pneumonia (CA-MRSA).

Hospital-acquired (*nosocomial*; >48h after hospital admission). Most commonly Gram negative enterobacteria or *Staph. aureus*. Also *Pseudomonas*, *Klebsiella*, *Bacteroides*, and *Clostridia*.

Aspiration Those with stroke, myasthenia, bulbar palsies, ↓consciousness (eg post-ictal or drunk), oesophageal disease (achalasia, reflux), or with poor dental hygiene risk aspirating oropharyngeal anaerobes.

Immunocompromised patient: Strep. pneumoniae, H. influenzae, Staph. aureus, M. catarrhalis, M. pneumoniae, Gram -ve bacilli and *Pneumocystis jiroveci* (formerly named *P. carinii*, p410–p411). Other fungi, viruses (CMV, HSV), and mycobacteria.

Management ►► p826. Antibiotics (p161): orally if not severe and not vomiting; severe give by IV. Oxygen: keep P_aO_2 >8.0 and/or saturation ≥94%. IV fluids (anorexia, dehydration, shock) and VTE prophylaxis. Analgesia if pleurisy—eg paracetamol 1g/6h. Consider ITU if shock, hypercapnia, or uncorrected hypoxia. If failure to improve, or CRP remains high, repeat CXR and look for progression/complications. Follow-up: at 6 weeks (±CXR).

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PROTOCOLLI DI TERAPIA ANTIBIOTICA
EMPIRICA - RAGIONATA
DELLE PRINCIPALI INFEZIONI

Comitato Infezioni Ospedaliere
Azienda Ospedaliero-Universitaria "Ospedali Riuniti" di Trieste

2015/2016

MICROBIAL CAUSES OF COMMUNITY-ACQUIRED PNEUMONIA, BY SITE OF CARE

	Hospitalized Patients	
Outpatients	Non-ICU	ICU
Streptococcus pneumoniae	*S. pneumoniae*	*S. pneumoniae*
Mycoplasma pneumoniae	*M. pneumoniae*	*Staphylococcus aureus*
Haemophilus influenzae	*Chlamydia pneumoniae*	*Legionella* spp.
C. pneumoniae	*H. influenzae*	Gram-negative bacilli
Respiratory viruses[a]	*Legionella* spp.	*H. influenzae*
	Respiratory viruses[a]	

[a]Influenza A and B viruses, human metapneumovirus, adenoviruses, respiratory syncytial viruses, parainfluenza viruses.

Note: Pathogens are listed in descending order of frequency. ICU, intensive care unit.

Table 9–10. Organisms prevalent in nosocomial pneumonias.[1]

- *Streptococcus pneumonia,* often drug-resistant, in HCAP
- *Staphylococcus aureus,* methicillin-sensitive (MSSA)
- *S aureus,* methicillin-resistant (MRSA)
- Gram-negative rods, non-ESBL
- ESBL-producing gram-negative rods including *Klebsiella pneumonia, Escherichia coli* and *Enterobacter* species
- *Pseudomonas aeruginosa*
- Acinetobacter species

ESBL, extended spectrum beta-lactamase.
[1]Nosocomial pneumonias include hospital-associated pneumonia (HAP), ventilator-associated pneumonia (VAP), and health care–associated pneumonia (HCAP).

SPETTRO ANTIBATTERICO

Lo spettro antibatterico esprime l'insieme delle specie batteriche sulle quali l'antibiotico è abitualmente attivo. Esistono delle specie costantemente sensibili, delle specie che possono acquisire una resistenza e altre naturalmente resistenti a un dato antibiotico. Esempi di **resistenza naturale** sono rappresentati dalla resistenza degli anaerobi agli aminosidi, dei batteri Gram-negativi ai glicopeptidi, alla daptomicina e al linezolid, degli enterococchi alle cefalosporine di 3° generazione. Al contrario, per quanto riguarda le **resistenze acquisite**, si tratta di batteri abitualmente sensibili che divengono resistenti per diverse cause quali la **pressione selettiva degli antibiotici** che si realizza soprattutto in ambiti quali gli ospedali, le lungodegenze per anziani, nonché la possibilità di interscambio di resistenze da una specie a un'altra. Le resistenze, purtroppo, sono in costante incremento soprattutto a livello ospedaliero e nelle lungodegenze; anche in comunità si stanno verificando fenomeni di resistenza. Fra i batteri **Gram-positivi** un problema rilevante è rappresentato dagli **stafilococchi meticillinoresistenti** (MRSA), dagli **enterococchi resistenti alla vancomicina e agli aminoglicosidi**, dagli **pneumococchi resistenti alla penicillina e ai macrolidi**. Le problematiche di resistenza di maggiore impatto clinico-terapeutico sono fra i batteri **Gram-negativi**, in particolare fra gli **enterobatteri** (Escherichia coli, Proteus spp., Klebsiella pneumoniae ecc.) fra gli **Acinetobacter spp**. e **Pseudomonas aeruginosa** per produzione di enzimi quali le **β-lattamasi,** le **β-lattamasi a spettro esteso (ESBL)** e le **carbapenemasi** (es. KPC [Klebsiella Pneumoniae Carbapenemase] e altre). La resistenza può essere cromosomica, e in questo caso riguarda soprattutto alcuni antibiotici, quali la rifampicina, e i fluorochinoloni (la resistenza è specifica e riguarda una singola famiglia), o plasmidica. Quest'ultimo tipo di resistenza è trasmissibile e molto frequente e interessa la gran parte degli antibiotici: β-lattamine, aminosidi, tetracicline, sulfamidici. La trasmissione può avvenire fra diversi batteri della stessa specie o fra specie differenti. I meccanismi di resistenza sono molteplici: produzione di enzimi inattivanti, modificazioni del sito bersaglio, riduzione della permeabilità di membrana, aumento delle pompe di efflusso, acquisizione di una via metabolica alternativa.

Common multidrug-resistant (MDR) organisms

- **Gram+**
  - Vancomycin-Resistant Enterococci (VRE)
  - Methicillin-Resistant Staphylococcus aureus (MRSA)
  - Multidrug-Resistant Streptococcus Pneumoniae
- **Gram-**
  - Extended-spectrum β-lactamase (ESBLs) producing Gram-negative bacteria, i.e., ESBL Klebsiella Pneuminiae or ESBL Escherichia Coli.
  - Carbapenemase-producing Enterobacteriaceae (CPE), i.e., Klebsella Pneumoniae Carbapenemase (KPC)
  - Multidrug-Resistant gram negative bacteria (MDR-GNB)
    - Enterobacteriaceae
    - Escherichia coli
    - Klebsiella pneumoniae
    - Acinetobacter baumannii
    - Pseudomonas aeruginosa

MANAGEMENT OF HEALTHCARE-ASSOCIATED PNEUMONIA — Healthcare-associated pneumonia (HCAP) was included in prior hospital-acquired pneumonia (HAP) guidelines (but not current HAP guidelines) to **identify patients thought to be at increased risk for multidrug-resistant (MDR) pathogens coming from community settings.** HCAP referred to pneumonia acquired in healthcare facilities such as **nursing homes**, **hemodialysis centers**, and **outpatient clinics** or during a **hospitalization within the past three months**. The rationale for the separate designation of HCAP (and its association with HAP) was that patients with HCAP were thought to be at higher risk for MDR organisms. However, several studies have shown that many patients defined as having HCAP are not at high risk for MDR pathogens and that this designation is not a good predictor of who will have an infection with an MDR organism. Furthermore, although interaction with the healthcare system is potentially a risk for MDR pathogens**, underlying patient characteristics (recent receipt of antimicrobials, comorbidities, functional status, and severity of illness) are important independent determinants of risk for MDR pathogens.** In addition, there is no evidence to indicate that treating patients with HCAP according to the recommendations in HAP guidelines improves outcomes. We feel that patients previously classified as having HCAP should be managed in a similar way to those with CAP (assessing risks for MDR organisms) because patients with HCAP frequently present from the community and are initially cared for in emergency departments.

UpToDate 2017

CAP - risk factors for drug-resistant pathogens

Gram-negative bacilli (including Pseudomonas) — Risk factors for CAP due to gram-negative bacilli include previous antibiotic therapy, recent hospitalization, immunosuppression, pulmonary comorbidity (eg, cystic fibrosis, bronchiectasis, or repeated exacerbations of chronic obstructive pulmonary disease that require frequent glucocorticoid and/or antibiotic use), probable aspiration, and multiple medical comorbidities (eg, diabetes mellitus, alcoholism).

Methicillin-resistant Staphylococcus aureus — Risk factors for MRSA include gram-positive cocci in clusters seen on sputum Gram stain, known colonization with MRSA, risk factors for colonization with MRSA (eg, end-stage renal disease, contact sport participants, injection drug users, those living in crowded conditions, men who have sex with men, prisoners), recent influenza-like illness, antimicrobial therapy (particularly with a fluoroquinolone) in the prior three months, necrotizing or cavitary pneumonia, and presence of empyema.

Drug-resistant S. pneumoniae — Age >65 years; Beta-lactam, macrolide, or fluoroquinolone therapy within the past three to six months. Alcoholism. Medical comorbidities. Immunosuppressive illness or therapy. Exposure to a child in a daycare center. Prior exposure to the healthcare setting such as from prior hospitalization or from residence in a long-term care facility. Recent therapy or a repeated course of therapy with beta-lactams, macrolides, or fluoroquinolones are risk factors for pneumococcal resistance to the same class of antibiotic. Thus, an antimicrobial agent from an alternative class is preferred for a patient who has recently received one of these agents

CLINICAL CONDITIONS ASSOCIATED WITH AND LIKELY PATHOGENS IN HEALTH CARE–ASSOCIATED PNEUMONIA

	Pathogen			
Condition	**MRSA**	***Pseudomonas aeruginosa***	***Acinetobacter* spp.**	**MDR Enterobacteriaceae**
Hospitalization for ≥48 h	√	√	√	√
Hospitalization for ≥2 days in prior 3 months	√	√	√	√
Nursing home or extended-care-facility residence	√	√	√	√
Antibiotic therapy in preceding 3 months		√		√
Chronic dialysis	√			
Home infusion therapy	√			
Home wound care	√			
Family member with MDR infection	√			√

Abbreviations: MDR, multidrug-resistant; MRSA, methicillin-resistant *Staphylococcus aureus*.

A flu-like illness with mild hypoxia

Mr Jones is a 54 year old male who reports that he has had a **"flu-like" illness for 2 days** with symptoms of "feeling hot and aching all over". Symptom-based questioning provided no clues as to the focus of the infection, although a risk assessment revealed that he had been to **a spa hotel** during the previous week. He was normally fit and well and had no previous medical history of note. His observations showed a *regular pulse of 110*, *BP of 130/90*, *respiratory rate of 20* and a *temperature of 38.6°c*. His ***SpO2 was 92***, however. *Clinical examination of his chest was unremarkable*. *He denied having any respiratory symptoms*, in terms of a cough, chest pain, or dyspnoea.

The presence of a fever with a low SpO2 should always raise the possibility that the patient has an atypical pneumonia, regardless of the absence of respiratory symptoms and positive findings in the chest examination. The history of a spa holiday raises the question of hot tub usage, which is associated with the potential for **Legionnaire's disease** (*transmission: breathing contaminated droplets of water in the air, Legionella bacteria grows best in warm water, risk factors: hot tubs, whirlpool spas, swimming pools, cooling systems or air-conditioning units for large buildings such as hospitals, public showers, humidifiers*). He was referred to the Emergency Assessment Unit and a ***CXR revealed an area of consolidation***, with ***Legionnaire's antigen testing positive in his urine***. His ***liver function tests were also noted to be grossly deranged***. Within hours of arriving in hospital, the patient became increasingly unwell from ***multi-organ failure***, requiring transfer to the ***intensive care unit***. With intravenous antibiotics and supportive care, the patient made a full recovery. All patients with a pyrexia of unknown origin should have pulse oximetry performed, as this may indicate the presence of an atypical pneumonia.

Geky Medics

- **Typical bacterial pathogens:** S. pneumoniae, Haemophilus influenzae, S. aureus and gram-negative bacilli such as Klebsiella pneumoniae and Pseudomonas aeruginosa.

- **Atypical organisms:** Mycoplasma pneumoniae, Chlamydia pneumoniae, Legionella species, respiratory viruses such as influenza viruses, adenoviruses, human metapneumovirus, and respiratory syncytial viruses.

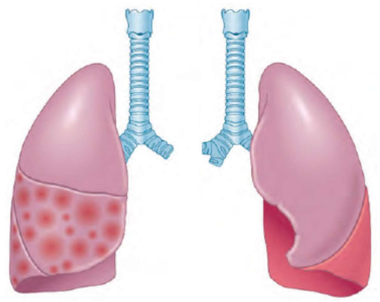
Atypical organisms cannot be cultured on standard media or seen on Gram's stain.

Radiological pattern is often worse than signs suggest (clinical-radiological dissociation) (i.e., Mycoplasma pneumoniae)

Atypical pathogens are intrinsically resistant to all β-lactam agents and must be treated with a macrolide, a fluoroquinolone, or a tetracycline.

Differentiation between typical and atypical pneumonia on the basis of patient history and chest radiograph is not reliable in guidance of antibiotic treatment.

Bacterial pneumonia has two patterns of anatomic distribution: **lobular bronchopneumonia** and **lobar pneumonia**. **Patchy consolidation** of the lung is the dominant characteristic of bronchopneumonia, while **consolidation of a large portion of a lobe** or of an entire lobe defines lobar pneumonia. These anatomic categorizations may be difficult to apply in individual cases because patterns overlap. The same organisms may produce either pattern depending on patient susceptibility.



Bronchopneumonia Lobar pneumonia

Foci of bronchopneumonia are consolidated areas of acute suppurative inflammation. The consolidation may be confined to **one lobe** but is more often **multilobar** and frequently **bilateral** and **basal** because of the tendency of secretions to gravitate to the lower lobes. Well-developed lesions are slightly elevated, dry, granular, gray-red to yellow, and poorly delimited at their margins. Histologically, the reaction usually elicits a neutrophil-rich exudate that fills the bronchi, bronchioles, and adjacent alveolar spaces.

In **lobar pneumonia,** four stages of the inflammatory response have classically been described: congestion, red hepatization, gray hepatization, and resolution. In the first stage of **congestion** the lung is heavy, boggy, and red. It is characterized by vascular engorgement, intra-alveolar fluid with few neutrophils, and often the presence of numerous bacteria. The stage of **red hepatization** that follows is characterized by massive confluent exudation, as neutrophils, red cells, and fibrin fill the alveolar spaces. On gross examination, the lobe is red, firm, and airless, with a liver-like consistency, hence the term hepatization. The stage of **gray hepatization** that follows is marked by progressive disintegration of red cells and the persistence of a fibrinosuppurative exudates, resulting in a color change to grayish-brown. In the final stage of **resolution** the exudate within the alveolar spaces is broken down by enzymatic digestion to produce granular, semifluid debris that is resorbed, ingested by macrophages, expectorated, or organized by fibroblasts growing into it. Pleural fibrinous reaction to the underlying inflammation, often present in the early stages if the consolidation extends to the surface (pleuritis), may similarly resolve. More often it undergoes organization, leaving fibrous thickening or permanent adhesions.

Complications of pneumonia include (1) tissue destruction and necrosis, causing **abscess** formation (particularly common with type 3 pneumococci or Klebsiella infections); (2) spread of infection to the pleural cavity, causing the intrapleural fibrinosuppurative reaction known as **empyema**; and (3) **bacteremic dissemination** to the heart valves, pericardium, brain, kidneys, spleen, or joints, causing metastatic abscesses, endocarditis, meningitis, or suppurative arthritis.

Specific pneumonias

Pneumococcal pneumonia is the commonest bacterial pneumonia. It affects all ages, but is commoner in the elderly, alcoholics, post-splenectomy, immuno-suppressed, and patients with chronic heart failure or pre-existing lung disease. Clinical features: fever, pleurisy, herpes labialis. CXR shows lobar consolidation. If mod/severe check for urinary antigen. Treatment: amoxicillin, benzylpenicillin, or cephalosporin.

Staphylococcal pneumonia may complicate influenza infection or occur in the young, elderly, intravenous drug users, or patients with underlying disease, eg leukaemia, lymphoma, cystic fibrosis (CF). It causes a bilateral cavitating bronchopneumonia. Treatment: flucloxacillin± rifampicin, MRSA: contact lab; consider vancomycin.

Klebsiella pneumonia is rare. Occurs in elderly, diabetics and alcoholics. Causes a cavitating pneumonia, particularly of the upper lobes, often drug resistant. Treatment: cefotaxime or imipenem.

Pseudomonas is a common pathogen in bronchiectasis and CF. It also causes hospital-acquired infections, particularly on ITU or after surgery. Treatment: anti-pseudomonal penicillin, ceftazidime, meropenem, or ciprofloxacin + aminoglycoside. Consider dual therapy to minimize resistance.

Mycoplasma pneumoniae occurs in epidemics about every 4yrs. It presents insidiously with flu-like symptoms (headache, myalgia, arthralgia) followed by a dry cough. CXR: reticular-nodular shadowing or patchy consolidation often of 1 lower lobe, and worse than signs suggest. Diagnosis: PCR sputum or serology. Cold agglutinins may cause an autoimmune haemolytic anaemia. Complications: skin rash (erythema multiforme, fig 3, p564), Stevens-Johnson syndrome, meningoencephalitis or myelitis; Guillain-Barré syndrome. Treatment: clarithromycin (500mg/12h) or doxycycline (200mg loading then 100mg od) or a fluroquinolone (eg ciprofloxacin or norfloxacin).

Clinical-radiological dissociation

Legionella pneumophilia colonizes water tanks kept at <60°C (eg hotel air-conditioning and hot water systems) causing outbreaks of Legionnaire's disease. Flu-like symptoms (fever, malaise, myalgia) precede a dry cough and dyspnoea. Extra-pulmonary features include anorexia, D&V, hepatitis, renal failure, confusion, and coma. CXR shows bi-basal consolidation. Blood tests may show lymphopenia, hyponatraemia, and deranged LFTs. Urinalysis may show haematuria. Diagnosis: *Legionella* urine antigen/culture. Treatment: fluoroquinolone for 2-3wks or clarithromycin (p380). 10% mortality.

Chlamydophila pneumoniae is the commonest chlamydial infection. Person-to-person spread occurs causing a biphasic illness: pharyngitis, hoarseness, otitis, followed by pneumonia. Diagnosis: *Chlamydophila* complement fixation test, PCR invasive samples.[8] Treatment: doxycycline or clarithromycin.

Chlamydiophila psittaci causes psittacosis, an ornithosis acquired from infected birds (typically parrots). Symptoms include headache, fever, dry cough, lethargy, arthralgia, anorexia, and D&V. Extra-pulmonary features are legion but rare, eg meningo-encephalitis, infective endocarditis, hepatitis, nephritis, rash, splenomegaly. CXR shows patchy consolidation. Diagnosis: *Chlamydophila* serology. Treatment: doxycycline or clarithromycin.

Viral pneumonia The commonest cause is influenza (p402 and BOX). Other viruses that can affect the lung are: measles, CMV, and varicella zoster.

Pneumocystis pneumonia (PCP) causes pneumonia in the immunosuppressed (eg HIV). The organism responsible was previously called *Pneumocystis carinii*, and now called *Pneumocystis jiroveci*.[9] It presents with a dry cough, exertional dyspnoea, ↓P_aO_2, fever, bilateral crepitations. CXR may be normal or show bilateral perihilar interstitial shadowing. Diagnosis: visualization of the organism in induced sputum, bronchoalveolar lavage, or in a lung biopsy specimen. Drugs: high-dose co-trimoxazole (p410-p411), or pentamidine by slow IVI for 2-3 weeks (p411). Steroids are beneficial if severe hypoxaemia. Prophylaxis is indicated if the CD4 count is $<200 \times 10^6$/L or after the 1st attack.[10]

Complications of pneumonia

Respiratory failure (See p180.) Type 1 respiratory failure (P_aO_2 <8kPa) is relatively common. Treatment is with high-flow (60%) oxygen. *Transfer the patient to ITU if hypoxia does not improve with O_2 therapy or P_aCO_2 rises to >6kPa.* Be careful with O_2 in COPD patients; check ABGs frequently, and consider elective ventilation if rising P_aCO_2 or worsening acidosis. Aim to keep SaO_2 at 94–98%, P_aO_2 ≥8kPa.

Hypotension may be due to a combination of dehydration and vasodilatation due to sepsis. If systolic BP is <90mmHg, give an intravenous fluid challenge of 250mL colloid/crystalloid over 15min. If BP does not rise, consider a central line and give IV fluids to maintain the systolic BP >90mmHg. If systolic BP remains <90mmHg despite fluid therapy, request ITU assessment for inotropic support (adrenaline, noradrenaline).

Atrial fibrillation (p124) is quite common, particularly in the elderly. It usually resolves with treatment of the pneumonia. β-blocker or digoxin may be required to slow the ventricular response rate in the short term.

Pleural effusion Inflammation of the pleura by adjacent pneumonia may cause fluid exudation into the pleural space. If this accumulates in the pleural space faster than it is reabsorbed, a pleural effusion develops. If this is small it may be of no consequence. If it becomes large and symptomatic, or infected (empyema), drainage is required (p184 & p780).

Empyema is pus in the pleural space. It should be suspected if a patient with a resolving pneumonia develops a recurrent fever. Clinical features: CXR indicates a pleural effusion. The aspirated pleural fluid is typically yellow and turbid with a pH <7.2, glucose↓, and LDH↑. The empyema should be drained using a chest drain, inserted under radiological guidance. Adhesions and loculation can make this difficult.

Lung abscess is a cavitating area of localized, suppurative infection within the lung (see fig 1).

Causes: •Inadequately treated pneumonia •Aspiration (eg alcoholism, oesophageal obstruction, bulbar palsy) •Bronchial obstruction (tumour, foreign body) •Pulmonary infarction •Septic emboli (septicaemia, right heart endocarditis, IV drug use) •Subphrenic or hepatic abscess.

Clinical features: Swinging fever; cough; purulent, foul-smelling sputum; pleuritic chest pain; haemoptysis; malaise; weight loss. Look for: finger clubbing; anaemia; crepitations. Empyema develops in 20–30%.

Tests: Blood: FBC (anaemia, neutrophilia), ESR, CRP, blood cultures. Sputum microscopy, culture, and cytology. *CXR:* walled cavity, often with a fluid level. Consider CT scan to exclude obstruction, and bronchoscopy to obtain diagnostic specimens.

Treatment: Antibiotics as indicated by sensitivities; continue until healed (4–6 wks). Postural drainage. Repeated aspiration, antibiotic instillation, or surgical excision may be required.

Septicaemia may occur as a result of bacterial spread from the lung parenchyma into the bloodstream. This may cause metastatic infection, eg infective endocarditis, meningitis. Treatment with IV antibiotic according to sensitivities.

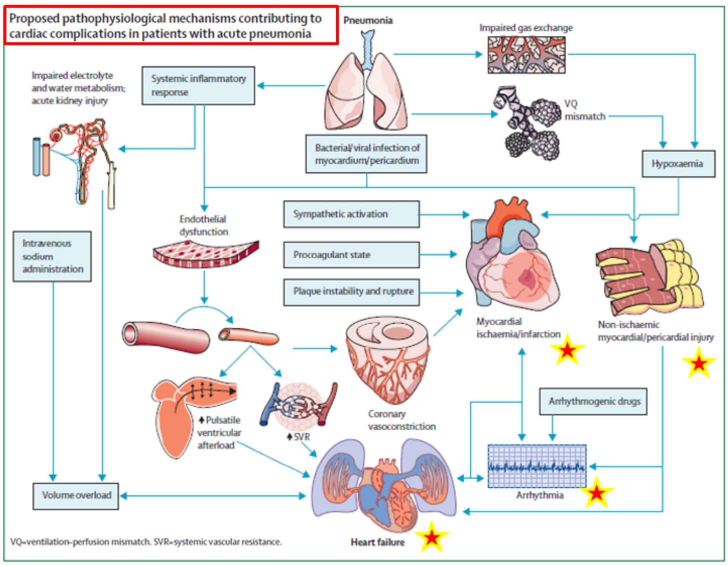
Pericarditis and myocarditis may also complicate pneumonia.

Jaundice This is usually cholestatic, and may be due to sepsis or secondary to antibiotic therapy (particularly flucloxacillin and co-amoxiclav).

Acute pneumonia and the cardiovascular system

Lancet 2013; 381: 496-505

Although traditionally regarded as a disease confined to the lungs, acute pneumonia has important effects on the cardiovascular system at all severities of infection. Pneumonia tends to affect individuals who are also at high cardiovascular risk. Results of recent studies show that about a quarter of adults admitted to hospital with pneumonia develop a major acute cardiac complication during their hospital stay, which is associated with a 60% increase in short-term mortality. These findings suggest that outcomes of patients with pneumonia can be improved by prevention of the development and progression of associated cardiac complications.



Vascular endothelium and peripheral vessels	Impaired reactive hyperaemia response and response to nitric oxide;[35] decreased peripheral vascular resistance in most young adults, but increased peripheral vascular resistance in up to a third of middle-aged adults (no data available for elderly patients);[36–39] increased concentrations of endothelin-1 and adrenomedullin[40,41]
Myocardium	Depression of left ventricular function;[37,38,42] myocarditis;[43] increased concentrations of troponins, BNP, and ANP[44–47]
Cardiac rhythm	Acute cardiac arrhythmias[20,48,49]
Coronary arteries	Possible acute inflammatory changes in atherosclerotic plaques;[50–52] possible coronary vasoconstriction[53]
Pulmonary circulation	Increased pulmonary artery pressures[54]
Cardiac autonomic function	Impairment of cardiovascular autonomic reflexes[55]
Coagulation	Increased procoagulant activity[56–58]
Renal function and fluid and sodium balance	Increased production of vasopressin;[41,59,60] decreased ACE activity;[61–63] water retention;[59] acute kidney injury[64,65]

BNP=B-type natriuretic peptide. ANP=atrial natriuretic peptide. ACE=angiotensin-converting enzyme.

Table: **Effects of pneumonia on the cardiovascular system**

Lancet 2013; 381: 496–505

Pneumococcal vaccine (eg 23-valent Pneumovax II®, 0.5mL SC) At-risk groups: • ≥65yrs old • Chronic heart, liver (eg cirrhosis), renal (eg renal failure, nephrosis*, post-transplant*) or lung conditions • Diabetes mellitus • Immunosuppression, eg spleen function↓ (eg splenectomy, asplenia*, sickle cell* or coeliac disease), AIDS, or on chemotherapy or prednisolone >20mg/d). CI: pregnancy, lactation, T°↑. (* = ↑risk of fatal pneumococcal infection (above), revaccinate after 6yrs.) Children: *OHCS* p151.

Community-acquired pneumonia

Lancet 2015; 386: 1097–108

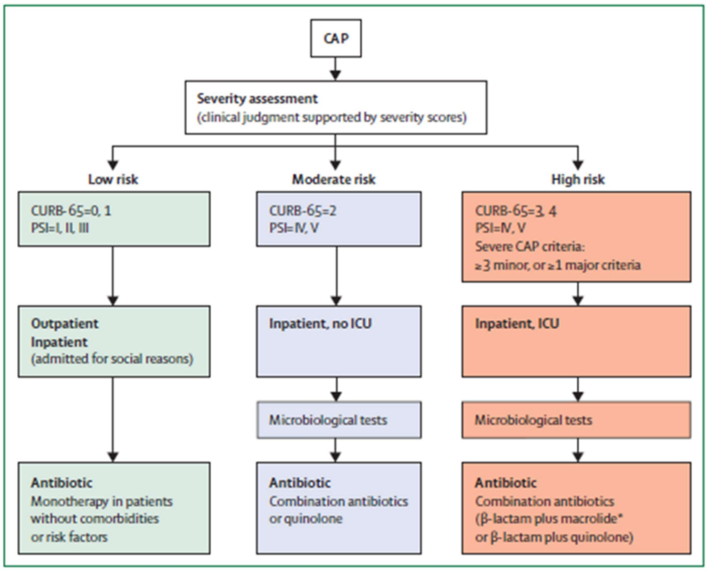


***Figure 2:* Acute management of the community-acquired pneumonia**
CAP=community-acquired pneumonia. CURB-65=Confusion Urea Respiratory rate Blood pressure and age ≥65 year old score. PSI=Pneumonia Severity Index. ICU=intensive care unit. *Combination with macrolide is preferred.

Community-acquired pneumonia

Lancet 2015; 386: 1097–108

	Outpatient	Inpatient, low severity	Inpatient, no ICU, moderate severity	Inpatient, ICU, high severity
Sputum culture	None routinely	Yes	Yes	Yes
Blood culture	None routinely	None routinely	Yes	Yes
Legionella urinary antigen	None routinely	None routinely	Yes	Yes
Pneumococcal urinary antigen	None routinely	None routinely	Yes	Yes
Invasive respiratory tract sample culture	None routinely	None routinely	None routinely	Yes
Others	None routinely	None routinely	None routinely	Yes*

***Figure 1*: Microbiological investigations**
ICU=intensive care unit. *Others indicates fungal, tuberculosis cultures, PCR, specific serology, lung biopsy.

Community-acquired pneumonia

Lancet 2015; 386: 1097–108

	American (IDSA/ATS)		British (NICE/BTS)		European	
	Preferred	Alternative	Preferred	Alternative	Preferred	Alternative
Outpatient without comorbidities; low severity	Macrolide	Doxycycline	Amoxicillin	Macrolide or tetracycline	Amoxicillin or tetracycline	Macrolide
Outpatient with comorbidities or high rate bacterial resistance	β-lactam plus macrolide	Respiratory fluoroquinolone			Respiratory fluoroquinolone	
Inpatient not in ICU; moderate severity	β-lactam* plus macrolide	Respiratory fluoroquinolone	Amoxicillin plus macrolide	Respiratory fluoroquinolone†	Aminopenicillin with or without macrolide	Respiratory fluoroquinolone
Inpatient in ICU; high severity	β-lactam‡ plus macrolide	β-lactam‡ plus respiratory fluoroquinolone	β-lactamase stable β-lactams¶ plus macrolide	Respiratory fluoroquinolone†	Third-generation cephalosporin§ plus macrolide	Respiratory fluoroquinolone with or without a third-generation cephalosporin§

Local or adapted guidelines should be used to adapt for different epidemiology. IDS=Infectious Diseases Society of America. ATS=American Thoracic Society. NICE=National Institute for Health and Care Excellence. BTS=British Thoracic Society. ICU=intensive care unit. *Preferred β-lactam drugs include cefotaxime, ceftriaxone, and ampicillin. †Respiratory fluoroquinolone limited to situations in which other options cannot be prescribed or are ineffective (eg, hepatotoxicity, skin reactions, cardiac arrhythmias, and tendon rupture). ‡Preferred β-lactam drugs include cefotaxime, ceftriaxone, or ampicillin-sulbactam. ¶β-lactamase-stable β-lactams include co-amoxiclav, cefotaxime, ceftaroline fosamil, ceftriaxone, cefuroxime, and piperacillin-tazobactam. §Third-generation cephalosporin (eg, cefotaxime, ceftriaxone).

***Table*: Empirical antibiotics suggested for community-acquired pneumonia**

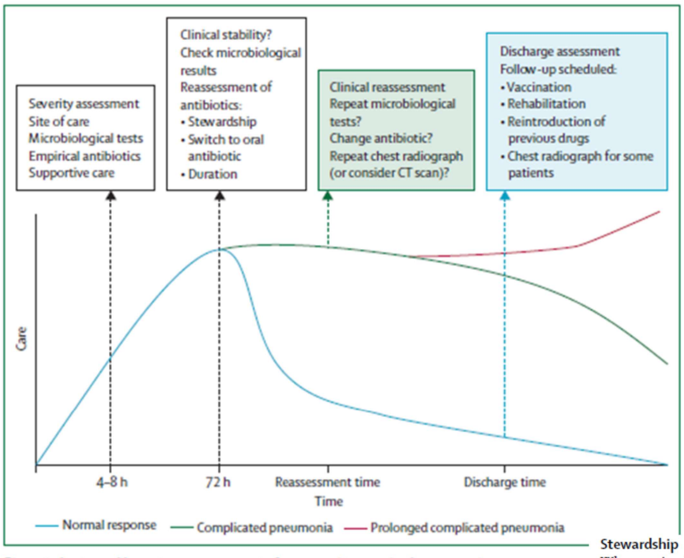


Figure 3: **Acute and long-term assessment of community-acquired pneumonia**

Community-acquired pneumonia

Lancet 2015; 386: 1097–108

Stewardship

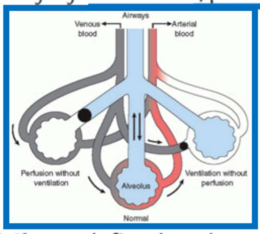
When microbiological tests become available, it is important to re-evaluate antibiotic treatment. Antibiotics should be adapted according to antibiogram results, narrowed according to the identified pathogen, and discontinued when a diagnosis of pneumonia is unlikely.[25] Stewardship is fundamental to avoid the continuation of unnecessary treatment, increasing the selective pressure for resistance, and reducing the risks of unnecessary complications (eg, *Clostridium difficile* infection).[125]

Respiratory failure

Respiratory failure occurs when gas exchange is inadequate, resulting in hypoxia. It is defined as a P_aO_2 <8kPa and subdivided into 2 types according to P_aCO_2 level.

Type I respiratory failure: defined as hypoxia (P_aO_2 <8kPa) with a normal or low P_aCO_2. It is caused primarily by ventilation/perfusion (V/Q) mismatch, eg:

- Pneumonia
- Pulmonary oedema
- PE
- Asthma
- Emphysema
- Pulmonary fibrosis
- ARDS (p178)



P_aO_2 < 60 mm Hg
P_aCO_2 < 45 mm Hg

P_aO_2 < 60 mm Hg
P_aCO_2 > 45 mm Hg

Type II respiratory failure: defined as hypoxia (P_aO_2 <8kPa) with hypercapnia (P_aCO_2 >6.0kPa). This is caused by alveolar hypoventilation, with or without V/Q mismatch. Causes include:

- *Pulmonary disease*: asthma, COPD, pneumonia, end-stage pulmonary fibrosis, obstructive sleep apnoea (OSA, p194).
- *Reduced respiratory drive*: sedative drugs, CNS tumour or trauma.
- *Neuromuscular disease*: cervical cord lesion, diaphragmatic paralysis, poliomyelitis, myasthenia gravis, Guillain-Barré syndrome.
- *Thoracic wall disease*: flail chest, kyphoscoliosis.

Hypoxemia results from any combination of five mechanisms:

1. ***Hypoventilation.*** Hypoxemia from hypoventilation alone has an increased Paco2.

2. ***Right-to-left shunt.*** Right-to-left shunting occurs when blood enters the systemic circulation without traversing ventilated lung (e.g., congenital cardiac malformation, pulmonary consolidation or atelectasis). A hallmark of significant right-to-left shunting is the failure of arterial oxygen levels to increase in response to supplemental oxygen.

3. ***Ventilation-perfusion (V . /Q.) mismatch.*** Ideal pulmonary gas exchange depends on a balance of ventilation and perfusion. Any abnormality resulting in a regional alteration of either ventilation or perfusion can adversely affect pulmonary gas exchange, resulting in hypoxemia. (e.g., pulmonary emboli, pneumonia, asthma, chronic obstructive pulmonary disease). Hypoxemia improves with supplemental oxygen.

4. ***Diffusion impairment.*** Pulmonary gas exchange requires diffusion across the alveolar–blood barrier. Regardless of the specific cause of the diffusion impairment (alveolar or interstitial disease, e.g., edema or fibrosis). Hypoxemia improves with supplemental oxygen.

5. ***Low inspired oxygen.*** Decreased ambient oxygen pressure results in hypoxemia. This is commonly seen at high altitude. Hypoxemia improves with supplemental oxygen.

Acute compensatory mechanisms for hypoxemia:

•Increased minute ventilation increases;

•pulmonary arterial vasoconstriction to decrease perfusion to hypoxic alveoli;

•Increased sympathetic tone to improve oxygen delivery by increasing cardiac output, usually with an increased heart rate.

Chronic compensatory mechanisms for hypoxemia:

•increased red blood cell mass

•decreased tissue oxygen demands.

CO_2 REMOVAL

Depends on

- Partial pressure gradient across alveolar-capillary membrane
- CO_2 has 200 times higher than O_2 diffusion coefficient and 20 times higher diffusion ability therefore alveolar surface area, wall thickness and exposure time are less relevant

The *thickness of the respiratory*)1 *membrane*

- the rate of diffusion through the membrane is inversely proportional to the thickness of the membrane,
- any factor that increases the thickness to more than two to three times normal can interfere with normal respiratory exchange of gases.
- Examples:

1. some pulmonary diseases: which cause fibrosis of the lungs, which can increase the thickness of some portions of the respiratory membrane.
2. edema:

Which is fluid in the interstitial space of the membrane and in the alveoli-so the respiratory gases must then diffuse not only through the membrane but also through this fluid.

CATEGORIES OF RESPIRATORY DISEASE

Category	Examples
Obstructive lung disease	Asthma Chronic obstructive pulmonary disease (COPD) Bronchiectasis Bronchiolitis
Restrictive pathophysiology—parenchymal disease	Idiopathic pulmonary fibrosis (IPF) Asbestosis Desquamative interstitial pneumonitis (DIP) Sarcoidosis
Restrictive pathophysiology—neuromuscular weakness	Amyotrophic lateral sclerosis (ALS) Guillain-Barré syndrome
Restrictive pathophysiology—chest wall/pleural disease	Kyphoscoliosis Ankylosing spondylitis Chronic pleural effusions
Pulmonary vascular disease	Pulmonary embolism Pulmonary arterial hypertension (PAH)
Malignancy	Bronchogenic carcinoma (non-small-cell and small-cell) Metastatic disease
Infectious diseases	Pneumonia Bronchitis Tracheitis

A. Respiratory Support

Respiratory support has both nonventilatory and ventilatory aspects.

1. Nonventilatory aspects—The main therapeutic goal in acute hypoxemic respiratory failure is to ensure adequate oxygenation of vital organs. Inspired oxygen concentration should be the lowest value that results in an arterial hemoglobin saturation of 90% or more (Po_2 60 mm Hg or more [7.8 kPa or more]). Higher arterial oxygen tensions are of no proven benefit. Restoration of normoxia may rarely cause hypoventilation in patients with chronic hypercapnia; however, **oxygen therapy should not be withheld for fear of causing progressive respiratory acidemia.** Hypoxemia in patients with obstructive airway disease is usually easily corrected by administering low-flow oxygen by nasal cannula (1–3 L/min) or Venturi mask (24–40%). Higher concentrations of oxygen are necessary to correct hypoxemia in patients with ARDS, pneumonia, and other parenchymal lung diseases.

2. Ventilatory aspects—Ventilatory support consists of maintaining patency of the airway and ensuring adequate alveolar ventilation. Mechanical ventilation may be provided via face mask (noninvasive) or through tracheal intubation.

A. Noninvasive positive-pressure ventilation—NPPV delivered via a full face mask or nasal mask is first-line therapy in COPD patients with hypercapnic respiratory failure who can protect and maintain the patency of their airway, handle their own secretions, and tolerate the mask apparatus. Several studies have demonstrated the effectiveness of this therapy in reducing intubation rates and ICU stays in patients with ventilatory failure. A bilevel positive-pressure ventilation mode (BiPAP) is preferred for most patients. Patients with acute lung injury or ARDS or those who suffer from severely impaired oxygenation do not benefit and should be intubated if they require mechanical ventilation.

B. Tracheal intubation—Indications for tracheal intubation include: (1) hypoxemia despite supplemental oxygen, (2) upper airway obstruction, (3) impaired airway protection, (4) inability to clear secretions, (5) respiratory acidosis, (6) progressive general fatigue, tachypnea, use of accessory respiratory muscles, or mental status deterioration, and (7) apnea. In general, orotracheal intubation is preferred to nasotracheal intubation in urgent or emergency situations because it is easier, faster, and less traumatic. The tip of the endotracheal tube should be positioned 2–4 cm above the carina and be verified by chest radiograph immediately following intubation; auscultation should be performed to verify that both lungs are being inflated. Only tracheal tubes with high-volume, low-pressure air-filled cuffs should be used. Cuff inflation pressure should be kept below 20 mm Hg if possible to minimize tracheal mucosal injury.

C. Mechanical ventilation—Indications for mechanical ventilation include: (1) apnea, (2) acute hypercapnia that is not quickly reversed by appropriate specific therapy, (3) severe hypoxemia, and (4) progressive patient fatigue despite appropriate treatment.

Several modes of positive-pressure ventilation are available. Controlled mechanical ventilation (CMV; also known as assist-control or A-C) and synchronized intermittent mandatory ventilation (SIMV) are ventilatory modes in which the ventilator delivers a minimum number of breaths of a specified tidal volume each minute. In both CMV and SIMV, the patient may trigger the ventilator to deliver additional breaths. In CMV, the ventilator responds to breaths initiated by the patient above the set rate by delivering additional full tidal volume breaths. In SIMV, additional breaths are not supported by the ventilator unless the pressure support mode is added. Numerous alternative modes of mechanical ventilation now exist, the most popular being pressure support ventilation (PSV), pressure control ventilation (PCV), and CPAP.

PEEP is useful in improving oxygenation in patients with diffuse parenchymal lung disease, such as ARDS. It should be used cautiously in patients with localized parenchymal disease, hyperinflation, or very high airway pressure requirements during mechanical ventilation.

D. Complications of mechanical ventilation—Potential complications of mechanical ventilation are numerous. Migration of the tip of the endotracheal tube into a main bronchus can cause atelectasis of the contralateral lung and overdistention of the intubated lung. Barotrauma refers to rupture and loss of integrity of the alveolar space secondary to high transmural pressures applied during positive pressure ventilation. Barotrauma is manifested by subcutaneous emphysema, pneumomediastinum, subpleural air cysts, pneumothorax, or systemic gas embolism. Volutrauma is sometimes used to refer to subtle parenchymal injury due to overdistention of alveoli from excessive tidal volumes without alveolar rupture, mediated through inflammatory rather than physical mechanisms. The principal strategy to avoid volutrauma is the use of low tidal volume ventilation.

Acute respiratory alkalosis caused by overventilation is common. Hypotension induced by elevated intrathoracic pressure that results in decreased return of systemic venous blood to the heart may occur in patients treated with PEEP, those with severe airflow obstruction, and those with intravascular volume depletion. Ventilator-associated pneumonia is another serious complication of mechanical ventilation.

Noninvasive positive pressure ventilation in acute respiratory failure in adults

INTRODUCTION — Noninvasive positive pressure ventilation (NPPV) refers to positive pressure ventilation delivered through a noninvasive interface (nasal mask, facemask, or nasal plugs), rather than an invasive interface (endotracheal tube, tracheostomy). Its use has become more common as its benefits are increasingly recognized [1,2]. (See "Overview of mechanical ventilation", section on 'Types

Indications — A trial of NPPV is worthwhile in most patients who do not require emergent intubation and have a disease known to respond to NPPV, assuming that they lack contraindications [3]. This is especially true for patients who have features that predict success using NPPV (table 1).

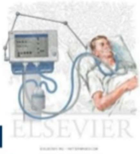
Conditions known to respond to NPPV include (see 'Benefits' below):

- Exacerbations of chronic obstructive pulmonary disease (COPD) that are complicated by hypercapnic acidosis ($PaCO_2$ >45 mmHg or pH <7.30)
- Cardiogenic pulmonary edema
- Acute hypoxemic respiratory failure.

Contraindications — The need for emergent intubation is an absolute contraindication to NPPV. In addition, there are numerous relative contraindications to NPPV (table 2) [8]:

- Cardiac or respiratory arrest
- Inability to cooperate, protect the airway, or clear secretions
- Severely impaired consciousness
- Nonrespiratory organ failure
- Facial surgery, trauma, or deformity
- High aspiration risk
- Prolonged duration of mechanical ventilation anticipated
- Recent esophageal anastomosis

Positive pressure ventilation



Method of NIV	CPAP	BiPAP
Name	Continuous Positive Airway Pressure	Bilevel Positive Airway Pressure
Descriptions	Preset ePAP (PEEP) Pt initiate breathing **ePAP (4 to 20 cmH2O)** Open more alveoli (recruitment)	Preset iPAP/ ePAP Pt initiate breathing Can set backup RR **iPAP (8 – 20 cmH2O)** **ePAP (4 – 10 cm H2O)**
Indications	COPD – APE(decrease venous return) – sleep apnea	Acute hypercapnia – cardiogenic APE – resp muscle fatigue/paralysis

By Dr. Fekri Eltahir Abdalla

Noninvasive positive pressure ventilation (NPPV) refers to positive pressure ventilation delivered through a noninvasive interface (nasal mask, facemask, nasal plugs, or helmet).
A trial of NPPV is worthwhile for a variety of patients. The following recommendations pertain to patients who do not require emergent intubation and lack contraindications to NPPV:
For patients with an exacerbation of chronic obstructive pulmonary disease (COPD) complicated by hypercapnic acidosis (PaCO >45 mmHg or pH <7.30) who do not require emergent intubation and lack contraindications to NPPV, we recommend a trial of NPPV (Grade 1A).
For patients with acute cardiogenic pulmonary edema, we recommend a trial of NPPV (Grade 1A).
For patients with hypoxemic respiratory failure due to causes other than cardiogenic pulmonary edema, we suggest a trial of NPPV (Grade 2B).
For patients with an asthma exacerbation who continue to have severe symptoms despite initial bronchodilator therapy, we suggest a trial of NPPV (Grade 2B).
NPPV may be beneficial in preventing recurrent respiratory failure following extubation if employed early.

- Pneumonia – Difficulty managing secretions is an accepted contraindication to NPPV (table 1). However, NPPV may be beneficial in patients with pneumonia if they are able to manage their secretions [87]. In one trial, 105 patients with acute hypoxemic respiratory failure of varying etiologies were randomly assigned to receive standard medical therapy alone or NPPV plus standard medical therapy [36]. NPPV decreased ICU mortality (18 versus 39 percent) and the intubation rate (25 versus 52 percent). These effects were particularly strong in the subgroup of patients with hypoxemic respiratory failure due to pneumonia. The outcomes of decreased ICU mortality [88], a decreased intubation rate [88,89], and improved oxygenation [90] were also reported in separate randomized trials that enrolled patients with community-acquired pneumonia or immunosuppressed patients with pulmonary infiltrates and fever.

Potential indicators of success in noninvasive positive pressure ventilation

Younger age
Lower acuity of illness (APACHE score)
Able to cooperate, better neurologic score
Less air leaking, intact dentition
Moderate hypercarbia ($PaCO_2$ >45 mmHG, <92 mmHG)
Moderate acidemia (pH <7.35, >7.10)
Improvements in gas exchange and heart respiratory rates within first two hours

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Contraindications to noninvasive positive pressure ventilation

Cardiac or respiratory arrest
Nonrespiratory organ failure
Severe encephalopathy (eg, GCS <10)
Severe upper gastrointestinal bleeding
Hemodynamic instability or unstable cardiac arrhythmia
Facial or neurological surgery, trauma, or deformity
Upper airway obstruction
Inability to cooperate/protect airway
Inability to clear secretions
High risk for aspiration

GCS: Glasgow Coma Score.

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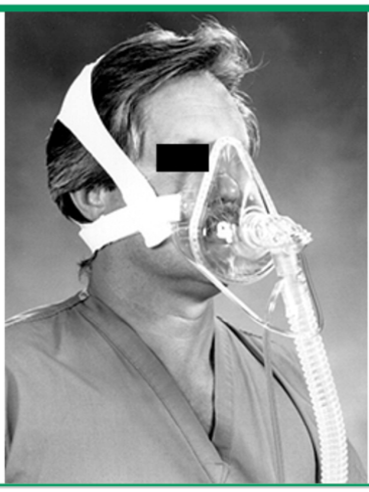
Alternative interfaces

A) Nasal pillows (prongs). B) Hybrid pillows/oral interface. C) Total face mask. D) Mouthpiece. E) Helmet.

Oronasal mask



Oronasal mask (Spectrum, Respironics, Inc) adapted for use with noninvasive positive pressure ventilation. To prevent rebreathing in the case of ventilator failure, the mask incorporates an "anti-asphyxia" valve and a quick-release strap.

Bedside tests in chest medicine

Sputum examination Collect a good sample; if necessary ask a physiotherapist to help. Note the appearance: clear and colourless (chronic bronchitis), yellow-green (pulmonary infection), red (haemoptysis), black (smoke, coal dust), or frothy white-pink (pulmonary oedema). Send the sample to the laboratory for microscopy (Gram stain and auramine/ZN stain, if indicated), culture, and cytology.

Peak expiratory flow (PEF) is measured by a maximal forced expiration through a peak flow meter. It correlates well with the forced expiratory volume in 1 second (FEV_1) and is used as an estimate of airway calibre, but is more effort-dependent.

Pulse oximetry allows non-invasive assessment of peripheral O_2 saturation (SpO_2). It provides a useful tool for monitoring those who are acutely ill or at risk of deterioration. An oxygen saturation of ≤80% is clearly abnormal and action is usually required, unless this is usual for the patient, eg in COPD. If a previously healthy person has pneumonia, a saturation of <92% is a serious sign; see p160. Here, check arterial blood gases (ABG) as P_aCO_2 may be rising despite a normal P_aO_2. Causes of erroneous readings: poor perfusion, motion, excess light, skin pigmentation, nail varnish, dyshaemoglobinaemias, and carbon monoxide poisoning. As with any bedside test, be sceptical, and check ABG, whenever indicated (p181).

assessment of the percentage of hemoglobin that is oxygenated

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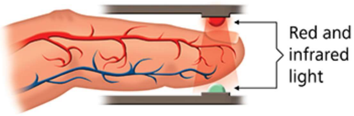
Pulse oximetry measurements may help identify significant drops in Pao2 below 60 to 65 mm Hg but are relatively insensitive to changes in Pao2 from 90 to 65 mm Hg.



Arterial blood gas (ABG) analysis Heparinized blood is usually taken from the radial or femoral artery (see p785), and pH, P_aO_2, and P_aCO_2 are measured using an automated analyser. Remember to note FiO_2 (fraction or percentage of inspired O_2).

- Normal pH is 7.35–7.45. A pH <7.35 indicates *acidosis* and a pH >7.45 indicates *alkalosis*. For interpretation of abnormalities, see p684.
- Normal P_aO_2 is 10.5–13.5kPa. Hypoxia is caused by one or more of the following reasons: ventilation/perfusion (V/Q) mismatch, hypoventilation, abnormal diffusion, right to left cardiac shunts. Of these, V/Q mismatch is the commonest cause. Severe hypoxia is defined as a P_aO_2 <8kPa (see p180). **80-100 mm Hg**
- Normal P_aCO_2 is 4.5–6.0kPa. P_aCO_2 is directly related to alveolar ventilation. A P_aCO_2 <4.5kPa indicates *hyperventilation* and a P_aCO_2 >6.0kPa indicates *hypoventilation*. **35-45mm Hg**

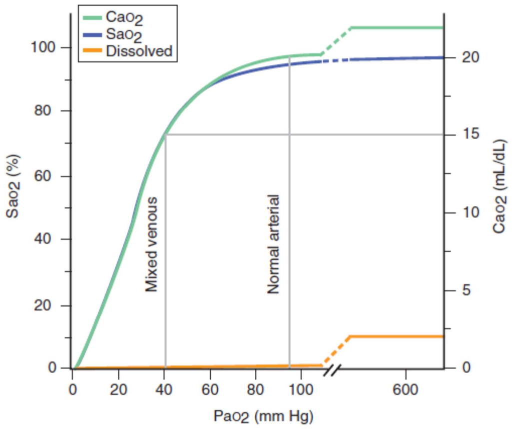
< 60 mm Hg **< 45 mm Hg**

Type 1 respiratory failure is defined as P_aO_2 <8kPa and P_aCO_2 <6.0kPa.

Type 2 respiratory failure is defined as P_aO_2 <8kPa and P_aCO_2 >6.0kPa.

< 60 mm Hg **> 45 mm Hg**

Oxyhemoglobin association-dissociation curve



The axis for oxygen saturation in the arterial blood (SaO_2) is on the left, and the axis for arterial content of oxygen (CaO_2) is on the right. CaO_2 is the sum of the oxygen dissolved in plasma plus the oxygen bound to hemoglobin.

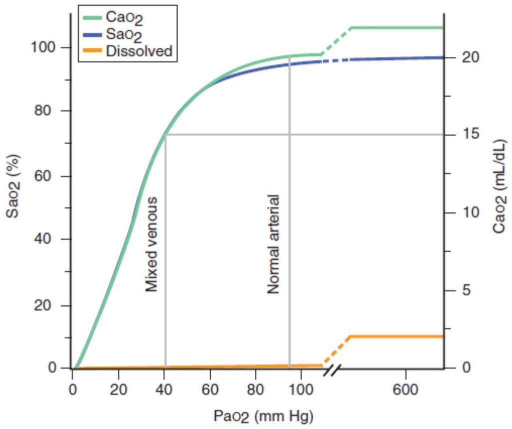
With a normal hemoglobin, most of the oxygen is carried in combination with hemoglobin, with only a relatively small amount of oxygen dissolved in plasma.

When the value of the arterial partial pressure of oxygen (PaO_2) is on the "flat" portion of the curve ($PaO_2 \geq 60$ mm Hg) raising the PaO_2 further has relatively little effect on total oxygen content.

Increases in temperature, PCO_2, hydrogen ion concentration cause a rightward shift in the oxyhemoglobin association-dissociation curve.

At low oxygen tensions, the hemoglobin tetramer is fully deoxygenated. Oxygen binding begins slowly as O_2 tension rises. However, as soon as some oxygen has been bound by the tetramer, an abrupt increase occurs in the slope of the curve. Thus, hemoglobin molecules that have bound some oxygen develop a higher oxygen affinity, greatly accelerating their ability to combine with more oxygen. Thus, substantial amounts of oxygen loading *and unloading can occur over* a narrow range of oxygen tensions. This S-shaped oxygen equilibrium curve is physiologically more useful than the high-affinity hyperbolic curve of individual monomers.

Estimating PaO_2 from a given SO_2



SO_2 (%)	PaO_2 (mmHg)
80	44
81	45
82	46
83	47
84	49
85	50
86	52
87	53
88	55
89	57
90	60
91	62
92	65
93	69
94	73
95	79
96	86
97	96
98	112
99	145

Administering oxygen[49]

Oxygen is usually given via a facemask or nasal cannulae. It is good practice to prescribe it—this avoids inadvertent administration of too much or too little. Titrate the amount guided by the S_aO_2 (aim for ~ 94-98% (or 88-92% if, or at risk of, hypercapnia)); and the clinical condition of the patient. Humidification is only required for longer-term delivery of O_2 at high flow rates and tracheostomies, but may ↑ expectoration in bronchiectasis. ► Be careful in those with COPD (p822).

Promoting oxygenation Other ways to ↑ oxygenation to reach the target S_aO_2 (this should be given as a number on the drug chart):

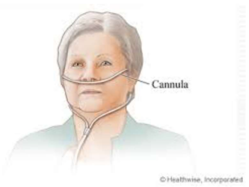
- Treat anaemia (transfuse if essential)
- Improve cardiac output (treat heart failure)
- Chest physio to improve ventilation/perfusion mismatch.

Nasal cannulae: preferred by patients, but O_2 delivery is relatively imprecise and may cause nasal soreness. The flow rate (1-4L/min) roughly defines the concentration of O_2 (24-40%). May be used to maintain S_aO_2 when nebulizers need to be run using air eg COPD.

Simple face mask: delivers a variable amount of O_2 depending on the rate of inflow. Far less precise than venturi masks—so don't use if hypercapnia or type 2 respiratory failure. Risk of CO_2 accumulation (within the mask and so in inspired gas) if flow rate <5L/min.

Non-rebreathing mask: these have a reservoir bag and deliver high concentrations of O_2 (60-90%), determined by the inflow (10-15L/min) and the presence of flap valves on the side. They are commonly used in emergencies, but are imprecise and should be avoided in those requiring controlled O_2 therapy.

Ogni L/min di O2 aggiunge il 3-4 % alla concentrazione frazionale di ossigeno (FiO2), che nell'aria ambiente è circa il 21%; quindi, in genere, un flusso di 1 L/min garantisce una FiO2 al 24%, 2 L/min al 28%, eccetera

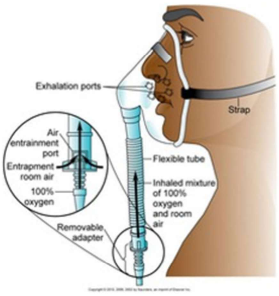


Method	O_2 flow (l/min)	Estimated FiO2 (%)
Nasel cannula	1	24
	2	28
	3	32
	4	36
	5	40
	6	44
Face mask	5	40
	6-7	50
	7-8	60
Face mask with reservoir	6	60
	7	70
	8	80
	9	90
	10	95

Venturi mask: provides a precise percentage of O_2 (FiO_2) at high flow rates.
Colour codes:

24%	BLUE
28%	WHITE
35%	YELLOW
40%	RED
60%	GREEN

Start at 24–28% in COPD.



Venturi valve colour	Inspired oxygen concentration (%)	Oxygen flow (l/min)
Blue	24	2–4
White	28	4–6
Yellow	35	8–10
Red	40	10–12
Green	60	12–15

PaO_2/FiO_2 Ratio

ratio of arterial oxygen partial pressure to fractional inspired oxygen

Examples:

PaO_2 80 mmHg with Ventimask 40% → PaO_2/FiO_2 200 mmHg
PaO_2 80 mmHg while breathing room air (FiO2 21%) → PaO_2/FiO_2 380 mmHg

PaO_2/FiO_2 = 400 PaO_2 = percent FiO_2 x 4
PaO_2/FiO_2 = 300 PaO_2 = percent FiO_2 x 3
PaO_2/FiO_2 = 200 PaO_2 = percent FiO_2 x 2
PaO_2/FiO_2 = 100 PaO_2 = percent FiO_2 x 1

DIAGNOSTIC CRITERIA FOR ARDS

Severity: Oxygenation	Onset	Chest Radiograph	Absence of Left Atrial Hypertension
Mild: 200 mmHg $< Pao_2/Fio_2 \leq 300$ mmHg *Moderate:* 100 mmHg $< Pao_2/Fio_2 \leq 200$ mmHg *Severe:* $Pao_2/Fio_2 \leq 100$ mmHg	Acute	Bilateral alveolar or interstitial infiltrates	PCWP ≤18 mmHg *or* no clinical evidence of increased left atrial pressure

Abbreviations: ARDS, acute respiratory distress syndrome; Fio_2, inspired O_2 percentage; Pao_2, arterial partial pressure of O_2; PCWP, pulmonary capillary wedge pressure.