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Influenza, briefly known as flu, is an acute respiratory infectious disease caused by influenza virus. It spreads via droplets, with strong infectivity. Its incident rate ranks first in legal infectious diseases, with occurrences of outbreaks or pandemics. Its clinical symptoms are characterized by acute onset of high fever, fatigue, systemic muscular soreness and pain, as well as mild respiratory tract symptoms. Influenza more commonly occurs in autumns and winters. Although it has a short disease course and is self-limited, it may be complicated by pneumonia and other serious complications in populations including the elderly, infants and young children, patients with cardiac or pulmonary diseases, patients with other chronic diseases, and patients with compromised immunity. In some serious cases, death may even occur.

## 21.1 Etiology

In the year 1971, the WHO officially claimed the nomination system of influenza virus. Based on the antigenic difference of the virus nucleocapsid protein (NP), influenza viruses are classified into types A, B, and C (Table 21.1). Influenza virus is an RNA virus, which is most stable in an environment with a pH value of 6.5–7.9 and has weak resistance to heat. It loses its pathogenicity at a temperature of 56 °C for several minutes and is inactivated at a temperature of 100 °C for 1 min. Influenza virus is more stable in an environment of low temperature. It can survive for more than 1 month at 4 °C and for more than 5 months at –70 °C. Influenza virus is sensitive to dryness, ultraviolet radiation, ethanol, iodine, and other common disinfectants. Rapid mutation and evolution are its main features, which is the result of antigenic structural changes in hemagglutinin and neuraminidase,

particularly hemagglutinin. Each variation of hemagglutinin and neuraminidase continually combines to form new mutant strains, and a new strain may defeat the established immunity against the former strain. Only when the population immunity is compromised to a certain level can the new strain likely invade the susceptible populations to cause an outbreak. This is the main reason for recurrent pandemics of influenza. Significant variation commonly occurs in influenza A virus, but rarely in influenza B virus and none in influenza C virus.

Influenza caused by H1N1 subtype, H2N2 subtype, H3N2 subtype of influenza A virus, and influenza B virus and influenza C virus is known as classical influenza. Apart from these viruses, influenza caused by other influenza viruses is known as a newly emerging influenza.

## 21.2 Epidemiology

### 21.2.1 General Introduction of Its Prevalence

As early as in the years of 412 BC, Hippocrates described a flu-like disease. But the first detailed description of influenza pandemic was in 1580. A total of 31 influenza pandemics have been recorded in documents, indicating periodic occurrence of influenza pandemics. Since the twentieth century, four global influenza pandemics have been recorded, respectively, in 1918, 1957, 1968, and 1977, all of which were caused by strains of influenza A virus.

### 21.2.2 Source of Infection

Patients with influenza and asymptomatic infected patients are the main sources of infection, whose infectivity lasts from the end of incubation period to the acute stage after onset. In the first 2–3 days after the onset, their infectivity is the strongest. When adults and elder children are sustaining seasonal influenza with no complications, virus

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**Table 21.1** Comparison of influenza viruses A, B, and C

	Influenza virus A	Influenza virus B	Influenza virus C
Genome	8 gene segments	8 gene segments	7 gene segments
Structure	10 virus proteins, with M2 being characteristic	10 virus proteins, with NB being characteristic	9 virus proteins, with HEF being characteristic
Host	Humans, pigs, horses	Only humans	Humans and pigs
Virus variability	Antigenic drift and shift	Antigenic drift with multiple mutants prevailing	Antigenic drift with multiple mutants
Clinical features	Pandemic, with high mortality rate	Not pandemic	Mostly sporadic with slight symptoms

excretion persists for 3–6 days in the respiratory secretions. Hospitalized adult patients can disseminate the viruses with pathogenicity for 1 week or longer after the onset. Studies have demonstrated that in infants and young children with influenza or human patients with influenza caused by avian H5N1 subtype of influenza A virus, long-term virus excretion is common, usually persisting for 1–3 weeks. In addition, patients with immunodeficiency such as patients with AIDS may also show a prolonged period of virus excretion.

### 21.2.3 Route of Transmission

Influenza mainly spreads via droplets in the air. The influenza virus exists in the respiratory secretions of symptomatic and asymptomatic patients. By talking, coughing, and sneezing, droplets or aerosols carrying the virus are disseminated into the air. The inhalation of the droplets or aerosols by a susceptible person can cause the infection. The virus can also spread via direct or indirect contact to mucosa of the mouth, nasal cavity, and eyes. Therefore, influenza has a strong infectivity, with rapid spreading and extensive prevalence. Its spreading speed is related to the population density.

### 21.2.4 Susceptible Population

Populations are generally susceptible and the susceptibility is not related to gender and occupation. Once cured, certain immunity can be acquired. The antibody can be firstly detected in 1 week after the infection, which peaks at weeks 2–3 after the infection and begins to decrease in 1–2 months. The antibody can be detected in the blood and secretions of nasal mucosa. No cross-immunity exists among influenza A, B, and C and among subtypes of influenza A. Influenza has a repeated onset and the acquired immunity after the infection only persists for a short period of time. Although antibody exists in the blood, the person can be reinfected by the same virus. The influenza virus is always subject to variance, and

the highest incidence rate is found in the populations of young adults and adolescents.

After infection of influenza virus, the following populations are likely to develop into serious cases. Therefore, focused attention should be paid on such patients. Influenza virus-related tests and examinations should be performed as early as possible to effectively treat such patients. These populations include (1) women during pregnancy; (2) influenza patients with accompanying diseases or conditions as follows: chronic respiratory disease, cardiovascular disease (with hypertension excluded), hepatic or renal disease, blood disorder, neurological disease, neuromuscular disease, metabolic and endocrine diseases, immune suppression (including HIV infection and use of immunosuppressant), being attended in health-care institutions, and long-term medication of aspirin under the age of 19 years; (3) obese population with a BMI above 30; (4) children under the age of 5 years (those under the age of 2 years are more likely to suffer from complications); and (5) the elderly above the age of 65 years.

### 21.2.5 Epidemic Features

Influenza occurs all year round. In the northern area of China, its incidence commonly peaks in winters and springs, while in the southern area of China, its incidence commonly peaks in summers and winters. Influenza A commonly occurs to cause outbreaks or even pandemics, with occurrence of a small-scale epidemic every 2–3 years. Based on the four pandemics of influenza, influenza A is likely to occur in pandemic every 10–15 years. Influenza B commonly occurs in outbreaks or small-scale epidemics and influenza C occurs sporadically. Influenza has a sudden onset and spreads rapidly. Its spreading peaks within 2–3 weeks and spontaneously terminates after 3–4 weeks. Its incidence rate is high but mortality rate is low. Its spreading is usually along the transportation lines, generally from urban to rural and from densely populated working places to scarcely populated resident communities.

## 21.3 Pathogenesis and Pathological Changes

### 21.3.1 Pathogenesis

Influenza virus causes damages to cells and cell atrophy via virus replication, with consequent occurrence of influenza. The loss of important cellular protein may lead to death of cells. The epithelial cells of the infected mucosa wrinkle and fold, with karyopyknosis, cilia loss, and shedding of mucosal columnar epithelium after infection.

In addition to the directly induced cellular death, influenza A and B viruses can induce apoptosis of infected cells. The mechanism underlying the apoptosis of infected cells induced by influenza viruses remains elusive, which is possibly related to Fas abnormality during virus replication.

### 21.3.2 Pathological Changes

After the initial infection, lesions may involve the trachea, bronchi, and lower respiratory tract. In the cases of simplex acute influenza, extensive inflammatory changes, mucosal lesions, and edema occur in the larynx, trachea, and bronchi. Biopsy demonstrates vacuolar degeneration of bronchial mucosa columnar epithelial cells, loss of cells, and even extensive shedding which involves basilar cells, shedding of ciliated cells, and metaplasia of epithelial cells. Antigen of influenza virus can be detected in surface layer of epithelial cells. There are congestion and edema of lamina propria mucosa cells with accompanying infiltrations of lymphocytes and monocytes that persist for more than 2–3 days. Subsequently, the undifferentiated basilar cells regenerate. With the conditions improved, the layer of epithelial cells can recover through rapid regeneration and metaplasia.

In fatal influenza-related viral pneumonia, the gross pathological changes include bleeding, severe tracheobronchitis, and pneumonia. The lesions are characterized by extensive bronchial and bronchiolar cell necrosis, with accompanying shedding of ciliated epithelial cells, fibrin exudation, inflammatory cell infiltration, hyaline membrane formation, congestion of alveolar and bronchial epithelial cells, interstitial edema, and mononuclear cell infiltration. The later changes also include diffuse alveolar damage, lymphocytic alveolitis, metaplastic regeneration of epithelial cells, or even extensive fibrosis of lung tissues. By autopsy, extensive necrotic tracheobronchitis can be found, with accompanying ulceration and tracheal mucosal shedding and necrosis. Above 1/3 of the cases have diffuse brain tissue hyperemia and edema, myocardial cell swelling, interstitial hemorrhage, lymphocytic infiltration, necrosis, and other inflammations.

## 21.4 Symptoms and Signs

The incubation period commonly lasts for 13 days and sometimes only for several hours. Its onset is sudden and acute, with mainly systemic toxic symptoms. The respiratory tract symptoms are slight or not obvious. According to the clinical manifestations, influenza can be divided into the following types:

### 21.4.1 Simplex Influenza

It is the most commonly found influenza, with sudden onset and symptoms of aversion to cold and high fever. The body temperature can be up to 39–40 °C. Fever is the most important initial symptom, commonly with accompanying headache, systemic muscular and joint soreness and pain, fatigue, poor appetite, and other toxic symptoms, whose severity is related to the degree of fever. Commonly, fever in patients with influenza is persistently high, typically for 3 days. Some patients may experience photophobia and lacrimation. And other symptoms including nasal obstruction, runny nose, sore throat, coarse voice, and other respiratory tract symptoms can be found at the onset. After the body temperature returns to normal, the systemic symptoms are improved, but with increasingly obvious respiratory symptoms. Coughing and physical strength commonly require 1–2 weeks to return back to normal. By physical examination in the acute stage, the patients have an acute complexion, with flushing on the face, mild conjunctival congestion, as well as damp and warm skin. In some patients with pharyngeal congestion, oral mucosal herpes may occur.

### 21.4.2 Pneumonic Influenza (Primary Influenza-Related Viral Pneumonia)

Pneumonic influenza can be either primary or secondary to simplex influenza. The occurrence of pneumonic influenza is the result of influenza virus infection spreading from the upper respiratory tract downward to the lower respiratory tract, which is more common in the elderly, children, patients with primary cardiopulmonary disease (especially rheumatic heart disease and left atrioventricular valvular stenosis), women in pregnancy, and populations with immunodeficiency. But in up to half of the cases, no underlying disease is reported. The manifestations of typical pneumonic influenza include high fever that persists for a long period of time, rapid occurrence of dyspnea, cyanosis, severe cough, foamy thick sputum or purulent sputum, and bloody sputum. By physical examination, breathing sounds of both lungs are low, with moist rales. Generally, the course of the disease

lasts for 3–4 weeks. Antibacterial therapies have no therapeutic efficacy. Death may occur due to heart failure or respiratory and circulatory failure and pneumonic influenza has a high mortality rate.

### 21.4.3 Toxic Influenza

Toxic influenza is extremely rare, which is caused by invasion of influenza virus into the central nervous system and cardiovascular system, with manifestations of toxic symptoms. Clinically, the symptoms are characterized by encephalitis or meningitis, including high fever, coma, delirium, and convulsion. Some serious symptoms may be found such as cerebral meningeal irritation and disseminated intravascular coagulation. Toxic influenza has a high mortality rate.

### 21.4.4 Gastrointestinal Influenza

Gastrointestinal influenza is common in children, with typical symptoms of nausea, vomiting, diarrhea, and abdominal pain. Generally, it can be cured within 2–3 days.

### 21.4.5 Manifestations in Special Populations

Influenza prevailing in different populations is characterized by different clinical manifestations. The main manifestations of influenza in special populations are described as the following:

#### 21.4.5.1 Children

During the flu-prevailing seasons, more than 40 % of preschoolers and 30 % of school-aged children sustain influenza. Influenza in common healthy children is mild, with symptoms of fever, cough, runny nose, nasal obstruction, sore throat, and headache. In some rare cases, muscular pain, vomiting, and diarrhea occur. Influenza in infants and young children commonly has atypical clinical symptoms, with possible occurrence of high fever and convulsion. Neonatal influenza is rare but its occurrence is commonly complicated by pneumonia. In addition, neonatal influenza commonly has septicemic manifestations including drowsiness, feeding refusal, and apnea. In young children, influenza-induced laryngitis, tracheitis, bronchitis, bronchiolitis, pneumonia, and gastrointestinal symptoms are more common than in adults.

#### 21.4.5.2 The Elderly

The elderly influenza refers to infection of influenza by elderly population aged above 65 years. Because this population commonly has primary respiratory or cardiovascular

disease, the conditions of the elderly influenza are commonly serious, with rapid development. The possibility of pneumonia in the elderly patients with influenza is higher than that in the adult patients with influenza. In this population, influenza may involve other systems to cause influenza-related viral myocarditis and influenza-related viral encephalitis.

#### 21.4.5.3 Women in Pregnancy

In addition to fever and cough, women infected by influenza virus in middle and late stages of pregnancy are susceptible to pneumonia. The conditions rapidly progress into dyspnea, hypoxemia, and even acute respiratory distress syndrome (ARDS). Subsequently, miscarriage, premature birth, intrauterine fetal distress, and death may occur. Infection of influenza in middle and late stages of pregnancy can induce aggravation of the basic disease. In some serious cases, death may occur in 2 days after the onset; antiviral therapy should be administered. Otherwise, delayed treatment obviously increases the mortality rate.

#### 21.4.5.4 Population with Immunodeficiency

Immunodeficient individuals, such as recipients of organ transplantation, patients with HIV/AIDS, and long-term users of immunosuppressants, are at a significantly higher risk of severe influenza once infected. They are predisposed to influenza-related viral pneumonia and may experience rapid onset of fever, cough, dyspnea, and cyanosis, with a high mortality rate.

## 21.5 Influenza-Related Complications

### 21.5.1 Bacterial Pneumonia

The incidence rate of bacterial pneumonia in patients with influenza has been reported to be 5–15 %. Its common pathogens include *Streptococcus pneumoniae* and *Staphylococcus aureus*, especially methicillin-resistant *Staphylococcus aureus* (MRSA). The susceptible populations include the elderly and individuals with chronic pulmonary disease or heart disease.

### 21.5.2 Pneumonia Caused by Other Pathogenic Organisms

Other pathogenic organisms inducing pneumonia in patients with influenza include chlamydia, mycoplasma, *Legionella pneumophila*, and fungi (*Aspergillus*). When influenza complicated by pneumonia is ineffectively treated by routine anti-infective therapies, it is likely to be caused by these pathogens.

### 21.5.3 Reye Syndrome

It is a disease of the liver and central nervous system complicating influenza A and B. And Reye syndrome also occurs in patients with herpes zoster virus infection. Reye syndrome is commonly found in children under the age of 14 years, especially those using aspirin or other analgesic and antipyretic agents containing salicylic acid. Reye syndrome is rarely found in adult patients with influenza.

### 21.5.4 Other Complications

Other complications include myositis that commonly occurs in children and rarely occurring myoglobinuria and renal failure, myocardial lesions, encephalitis, and meningitis. Myositis is characterized by pain and tenderness of the gastrocnemius and soleus muscle, possible convulsion of lower limbs, and even inability in walking in serious cases. Myositis more commonly complicates influenza B, with a temporary increase in serum creatine phosphokinase level that generally returns to normal in 3–4 days.

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## 21.6 Diagnostic Examinations

### 21.6.1 Laboratory Tests

#### 21.6.1.1 Routine Blood Test

By routine blood test in the acute stage, peripheral WBC count decreases, lymphocyte count relatively increases, and there is possible absence of eosinophils. In cases with influenza complicated by bacterial infection, WBC count increases with increased percentage of neutrophils.

#### 21.6.1.2 Viral Antigen Detection

Mucosal epithelial cells from the nasopharynx of the patients are collected for smear. It can detect necrosis of columnar ciliated epithelial cell necrosis and eosinophilic inclusion bodies in the cytoplasm. Immunofluorescence or enzyme-labeled staining can be applied to detect the viral antigen in the exfoliative cells, with high sensitivity. Monoclonal antibody can be applied to distinguish influenza A, B, and C.

#### 21.6.1.3 Serological Test for Antibody Detection

Double sera are collected at the acute stage and at weeks 3–4 after onset are collected for hemagglutination inhibition test, enzyme-linked immunosorbent assay, and complement fixation test to detect antibody of influenza virus. An increase in titer by above four times has diagnostic significance, with a positive rate of 60–80 %.

#### 21.6.1.4 PCR Detection of Influenza Virus Genes

By using PCR technique, influenza virus genes can be detected directly from respiratory specimens of the patients, which is more sensitive and rapid than virus culture.

#### 21.6.1.5 Isolation and Culture of Influenza Virus

Isolation of virus is the golden standard for the diagnosis of influenza.

### 21.6.2 Diagnostic Imaging

#### 21.6.2.1 X-Ray

X-ray is the most commonly applied examination for the diagnosis of pneumonic influenza or secondary bacterial pneumonia.

#### 21.6.2.2 CT Scanning

CT scanning is a commonly applied facilitative examination to demonstrate intrapulmonary lesions that fail to be demonstrated by X-ray.

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## 21.7 Imaging Demonstrations

Imaging demonstrations show the severity of the disease, and high-risk populations are the focus of imaging examinations. In addition, imaging demonstrations of intrapulmonary basic disease should be paid focused attention for differentiation.

### 21.7.1 Primary Influenza-Related Viral Pneumonia

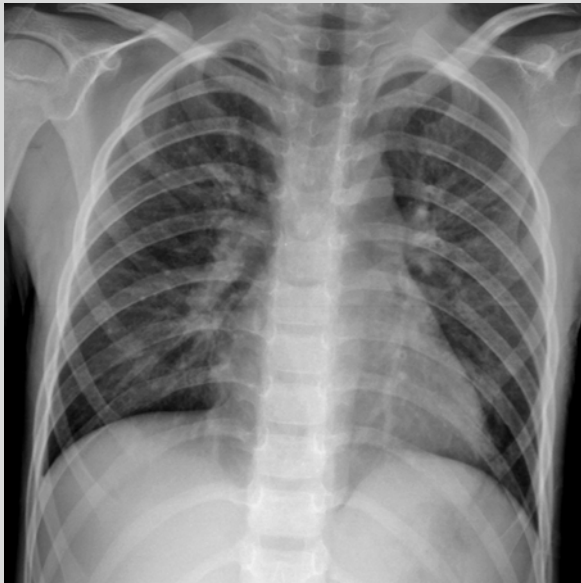
#### 21.7.1.1 Chest X-Ray

Chest X-ray demonstrations mainly include interstitial pneumonia and bronchial pneumonia, with early demonstrations of enhanced lung markings with blurry boundaries that are more obvious in both lower lungs and increased density in ground-glass opacities. Due to not obvious clinical symptoms, the diagnosis cannot be hardly defined. With progress of the conditions, the X-ray demonstrations are reticular shadow and reticulonodular shadow in the long fields with nodules being smaller than 5 mm, which can be concurrent with enhanced blurry lung markings. The lesions are commonly distributed in lower fields of both lungs and around the hilum (Figs. 21.1 and 21.2). The pathological changes include exudative inflammation at the alveolar wall and lobular septum. In the late stage, due to inflammatory obstruction of bronchioles, cystic changes occur in different sizes, with demonstrations of a honey-

comb-like lung, shrinkage of lung volume, elevated diaphragm, and shifted interlobar fissures. By lung biopsy, about 30 % of the cases can be confirmed with pulmonary interstitial fibrosis but no abnormalities by chest X-ray. X-ray is not sufficiently sensitive to alveolitis and the demonstrations are nonspecific.

### Case Study 1

A boy aged 7 years complained of fever for 4 days with a body temperature of 39.1 °C. Laboratory tests show a WBC of  $4.1 \times 10^9/L$ , LY% of 62.1 %, and GR% of 26.6 %.



**Fig. 21.1** Influenza-related viral pneumonia. Chest X-ray demonstrates thickened pulmonary markings in both lungs and spots of shadows along the pulmonary markings in the medial middle zone of middle and lower fields of both lungs

### Case Study 2

A boy aged 10 years complained of fever for 3 days with a body temperature of 39 °C. Laboratory tests show a WBC of  $4.68 \times 10^9/L$ , LY% of 22.2 %, and GR% of 67.1 %.



**Fig. 21.2** Influenza-related viral pneumonia. Chest X-ray demonstrates thickened pulmonary markings in both lungs, spots, and small flakes of shadows along the pulmonary markings in the medial middle zone of both lung fields

### 21.7.1.2 CT Scanning

Compared to traditional chest X-ray, CT scanning can more favorably demonstrate the conditions. It facilitates more accurate assessment about the severity, range, and location of the lesions. By adjusting the window width and window level, subtle dynamic changes and distribution of lesions can be demonstrated, providing more information than chest X-ray. CT scanning demonstrations include large flake of consolidation opacity in the lung lobe or segment with accompanying air bronchogram, small nodular shadows, ground-glass opacity, tree-in-bud sign, and mosaic perfusion as well as thickened interlobular septum, pleural inferior line, thickened adjacent pleura, and pleural effusion.

## 21.7.2 Influenza Complicated by Bacterial Pneumonia

### 21.7.2.1 Chest X-Ray

Bacterial pneumonia is characterized by alveolar pneumonia (lobar pneumonia) and bronchopneumonia (lobular pneumonia). The manifestations of alveolar pneumonia include alveolar consolidation, which can be found in the cases of pneumococcus infection, pneumobacillus infection, and legionella infection. The lesions involve singular or multiple lung lobes. Chest X-ray demonstrates lobar or partial lobe occupied consolidation opacity with high even density with internal bronchial shadow containing air. The lesions at different locations have different radiological demonstrations. The intrapulmonary lesions are mostly absorbed within 2 weeks. In addition to the abovementioned pathogenic bacterial infections, bronchial pneumonia can also be caused by *Haemophilus influenzae*, *Staphylococcus aureus*, and Gram-negative bacillus. Bronchial pneumonia commonly occurs in infants and young children, the elderly, and extremely weak patients. Chest X-ray demonstrates enhanced and thickened pulmonary markings, blurry nodular shadows in diameters of 6–8 mm, or blurry flakes of shadows in diameters of 10–25 mm. And relatively larger patches of uneven shadows with poorly defined boundaries are the result of overlapped multiple lobular alveolitic shadows (Fig. 21.3). Bronchial blockage by mucus can be demonstrated as lobular atelectasis

or focal emphysema in the lesion area. Bronchial blockage can result in a small triangular atelectasis. The lesions are mostly located in the medial zone of both lower lungs, with more posterior lobar lesions than anterior lobar lesions. They are distributed along the bronchial branches, with unobstructed bronchi in the pulmonary segment and lobe. Congestion, edema, and inflammatory exudates of the terminal bronchial mucosa can cause obstructive emphysema, with manifestations of increased transparency of both lung fields, expanded thorax, widened intercostal space, and flat low diaphragm.

### Case Study 3

A female patient aged 45 years complained of cough for 7 days and fever for 3 days, with a body temperature of 38.4 °C. Laboratory tests show a WBC of  $11.25 \times 10^9/L$ ,  $PCO_2$  of 35.5 mmHg, and  $PO_2$  of 76 mmHg.



**Fig. 21.3** Influenza complicated by pneumonia. Chest X-ray demonstrates thickened pulmonary markings, multiple masses, and flakes of shadows along pulmonary markings in the medial middle zone of middle and lower lung fields of both lungs, with poorly defined boundaries

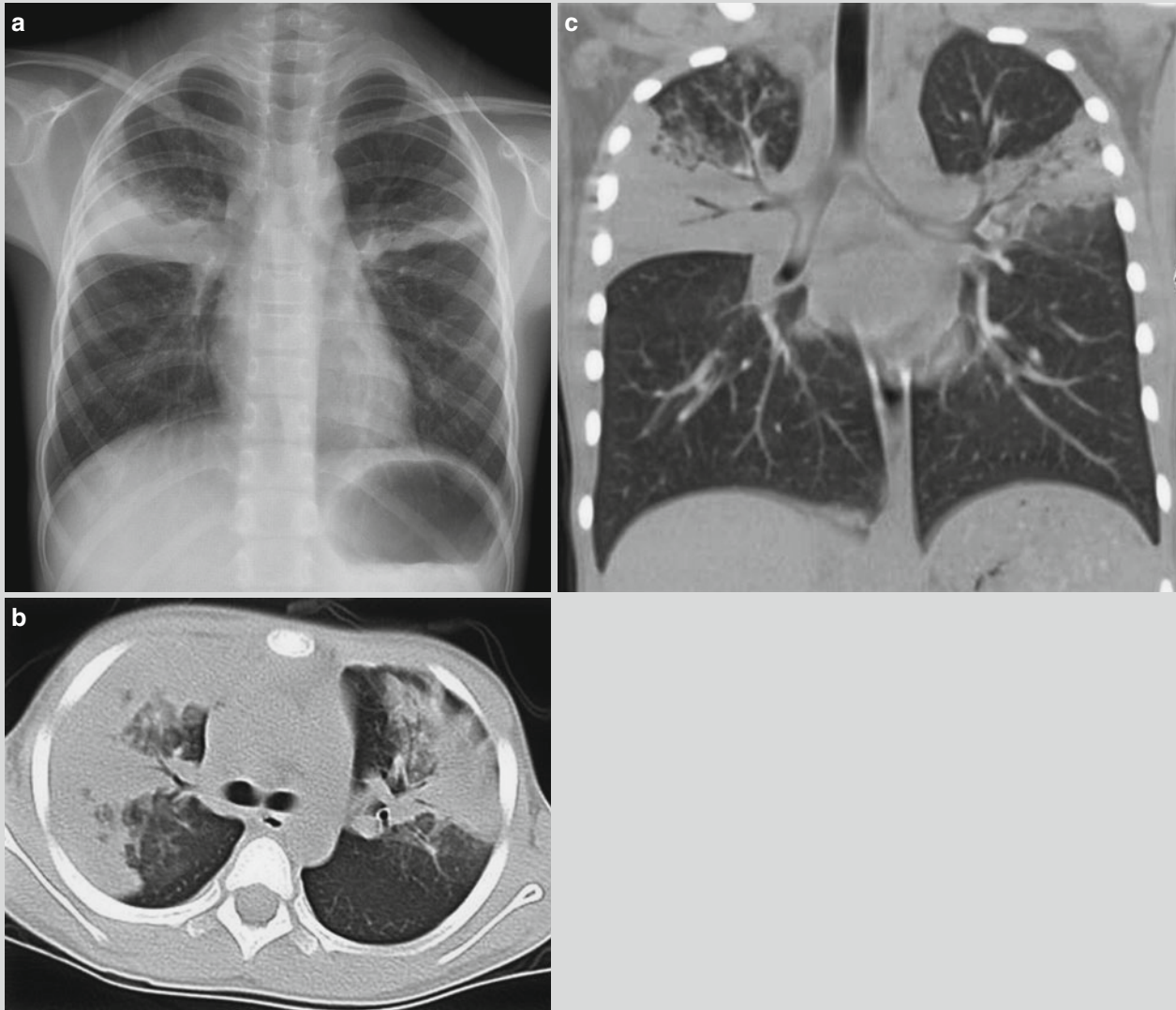
### 21.7.2.2 CT Scanning

Chest CT scanning is commonly applied for early diagnosis, lesion assessment, and differential diagnosis. The demonstrations are characterized by consolidation opacities with morphologically consistent distribution with lung

lobes, air bronchogram, and nodular shadow and patches of shadows with different sizes and blurry boundaries along with bronchial bundles as well as possible occurrence of lobular atelectasis or focal emphysema (Figs. 21.4 and 21.5).

#### Case Study 4

A boy aged 15 years complained of fever for 3 days, with a body temperature of 39.2 °C. Laboratory tests show a WBC of  $11.1 \times 10^9/L$  and GR% of 86 %.



**Fig. 21.4** Influenza complicated by pneumonia. (a) Chest X-ray demonstrates thickened pulmonary markings and wedge-shaped consolidation shadow extending outward from the hilum in both upper lung fields. (b–c) CT scanning demonstrates wedge-shaped

consolidation shadow in both upper lung lobes, with internal air bronchogram that is more obvious in the right lung, as well as small patches of blurry shadows in the right upper lung lobe



### 21.7.3 Imaging Demonstrations of Special Populations with Influenza Complicated by Pneumonia

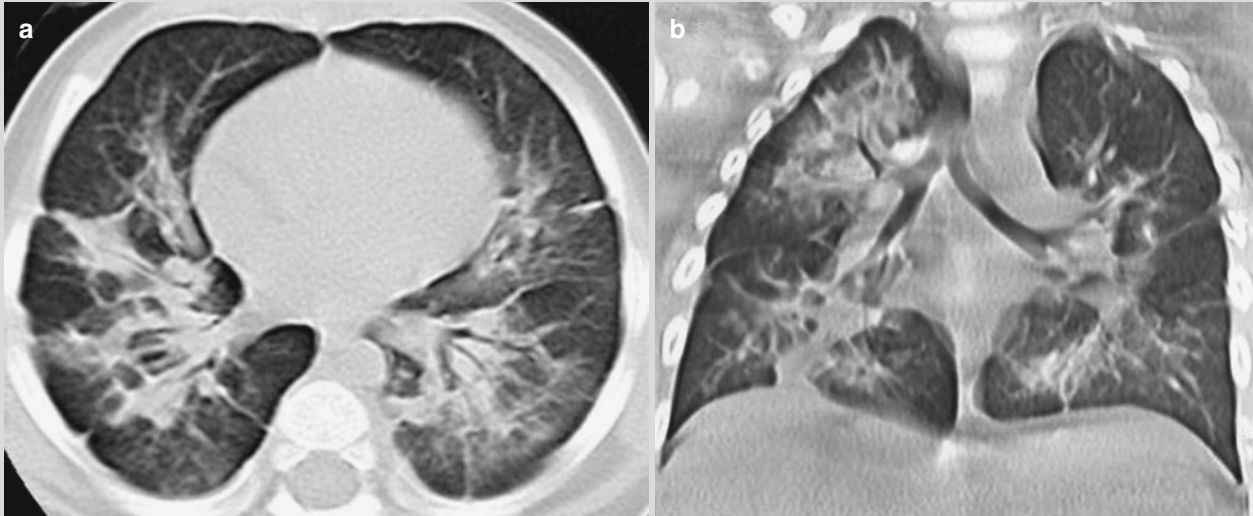
#### 21.7.3.1 Children

Infants and young children as well as preschoolers are high-risk populations of influenza. Generally, healthy children

infected by influenza virus may have slight symptoms. Neonatal influenza is rarely found, but is commonly complicated by pneumonia (Figs. 21.5 and 21.6).

#### Case Study 5

A boy aged 1 year complained of fever for 3 days and drowsiness.



**Fig. 21.5** Influenza complicated by pneumonia. (a, b) CT scanning demonstrates thickened bronchial vascular bundles in both lungs and flakes of blurry shadows along the pulmonary markings in both lung fields

#### Case Study 6

A boy aged 12 years complained of cough for 14 days and fever for 3 days, with a body temperature of 39.8 °C. Laboratory tests show a WBC of  $3.8 \times 10^9/L$ , pH of 7.513,  $PCO_2$  of 34.9 mmHg, and  $PO_2$  of 77.9 mmHg.



**Fig. 21.6** Influenza complicated by pneumonia. Chest X-ray demonstrates thickened pulmonary markings in both lungs, decreased transparency of the right lung field, and flakes of blurry shadows along the pulmonary markings in the right lung, with fusion of some shadows in consolidation opacity

### 21.7.3.2 The Elderly

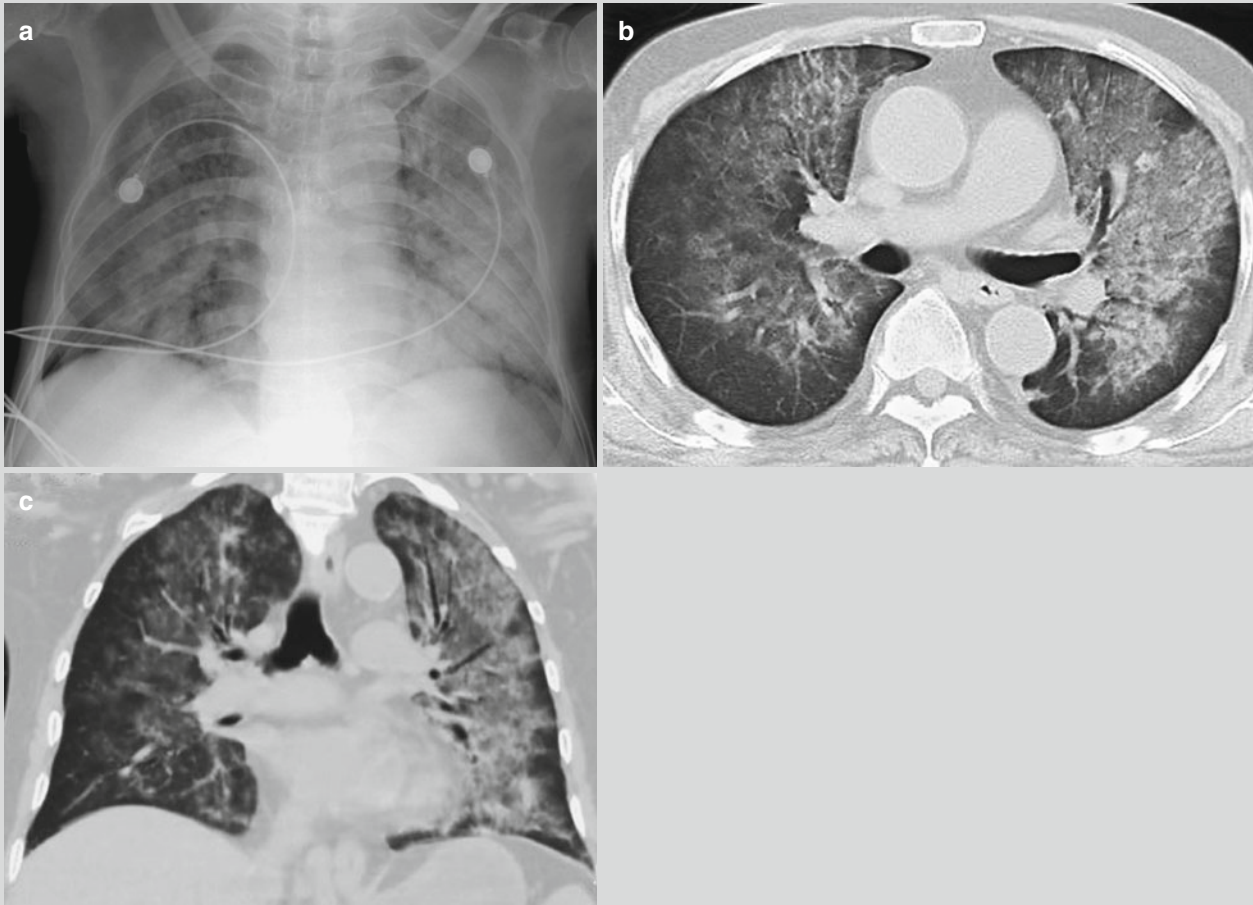
Due to relatively weak immunity of the elderly and common occurrence of basic disease in this population, the conditions are commonly serious after infection of influenza virus, with

rapid progress and a high incidence rate of pneumonia. Influenza complicated by pneumonia in the elderly is likely to develop into severe pneumonia, with possible occurrence of death (Fig. 21.7).

#### Case Study 7

A male patient aged 70 years complained of fever for 5 days, with cough, fatigue, and a body temperature of

38 °C. Laboratory tests show a WBC of  $3.5 \times 10^9/L$  and  $SaO_2$  of 89 %.



**Fig. 21.7** Influenza complicated by pneumonia. (a) Chest X-ray demonstrates decreased transparency of both lung fields, poorly defined pulmonary markings, and diffusive flakes of blurry shadows

in both lung fields. (b, c) CT scanning demonstrates ground-glass opacities along bronchial vascular bundles in both lungs

### 21.7.3.3 Women in Pregnancy

Women in the middle and late stage of pregnancy with infection of influenza virus are susceptible to pneumonia with possible occurrence of acute respiratory distress syndrome (ARDS) and even death (Fig. 21.8).

#### Case Study 8

A female patient aged 22 years had been pregnant for 39 weeks and complained of cough for 7 days and fever for 4 days, with a body temperature of 39.5 °C. Laboratory tests show a WBC of  $14.3 \times 10^9/L$  and SaO<sub>2</sub> of 85 %.



**Fig. 21.8** Influenza complicated by pneumonia. Chest X-ray demonstrates decreased transparency of both lung fields, absent pulmonary markings, and large flakes of blurry shadows in both lungs that are more obvious in the right lung and have internal air bronchogram

### 21.7.3.4 Individuals with Immunodeficiency or Compromised Immunity

Individuals with immunodeficiency are more likely to sustain serious influenza after their infection of influenza virus. In addition, multiple complications tend to occur (Fig. 21.9).

## 21.8 Diagnostic Basis

During the prevailing period of influenza, its diagnosis presents no challenge, which can be made based on clinical symptoms and stratified diagnosis. However, early sporadic cases should be diagnosed comprehensively based on the epidemiological history, clinical manifestations, and

laboratory findings. The diagnostic basis includes history of contact to influenza, typical symptoms and physical signs, and pathogen detection. Successful detection of influenza virus or virus antigen or serious antibody from nasal or pharyngeal secretions can define the diagnosis.

### 21.8.1 Suspected Cases of Influenza

During the prevailing period of influenza, the occurrence of (1) fever with cough and/or sore throat and other acute respiratory symptoms; (2) fever with acute aggravation of underlying chronic lung disease; (3) fever in infants and young children, with no other symptoms and signs; (4) newly onset respiratory symptoms or aggravation of underlying respiratory symptoms in the elderly above the age of 65 years, with or without fever; and (5) fever or low body temperature in seriously ill patients should be suspected as the cases of influenza. In any other periods, the occurrence of fever with cough and/or sore throat and other acute respiratory symptoms should be suspected as the cases of influenza after an epidemiological history related to influenza is reported. The epidemiological history may be a visit to the area or community with outbreak of influenza within 7 days before the onset, living together or having close contacts to suspected cases of influenza, and traveling back from the country or area with prevailing influenza.

### 21.8.2 The Basis for Definitive Diagnosis

The cases with clinical manifestations and that are positive in at least one of the following pathogen detections can be defined as influenza: (1) nucleic acid detection of influenza virus, (2) rapid antigen detection of influenza virus which should be combined with epidemiological history, (3) isolation and culture of influenza virus, and (4) specific IgG antibody of influenza virus in double sera from acute stage and convalescence stage showing an increase of above four times.

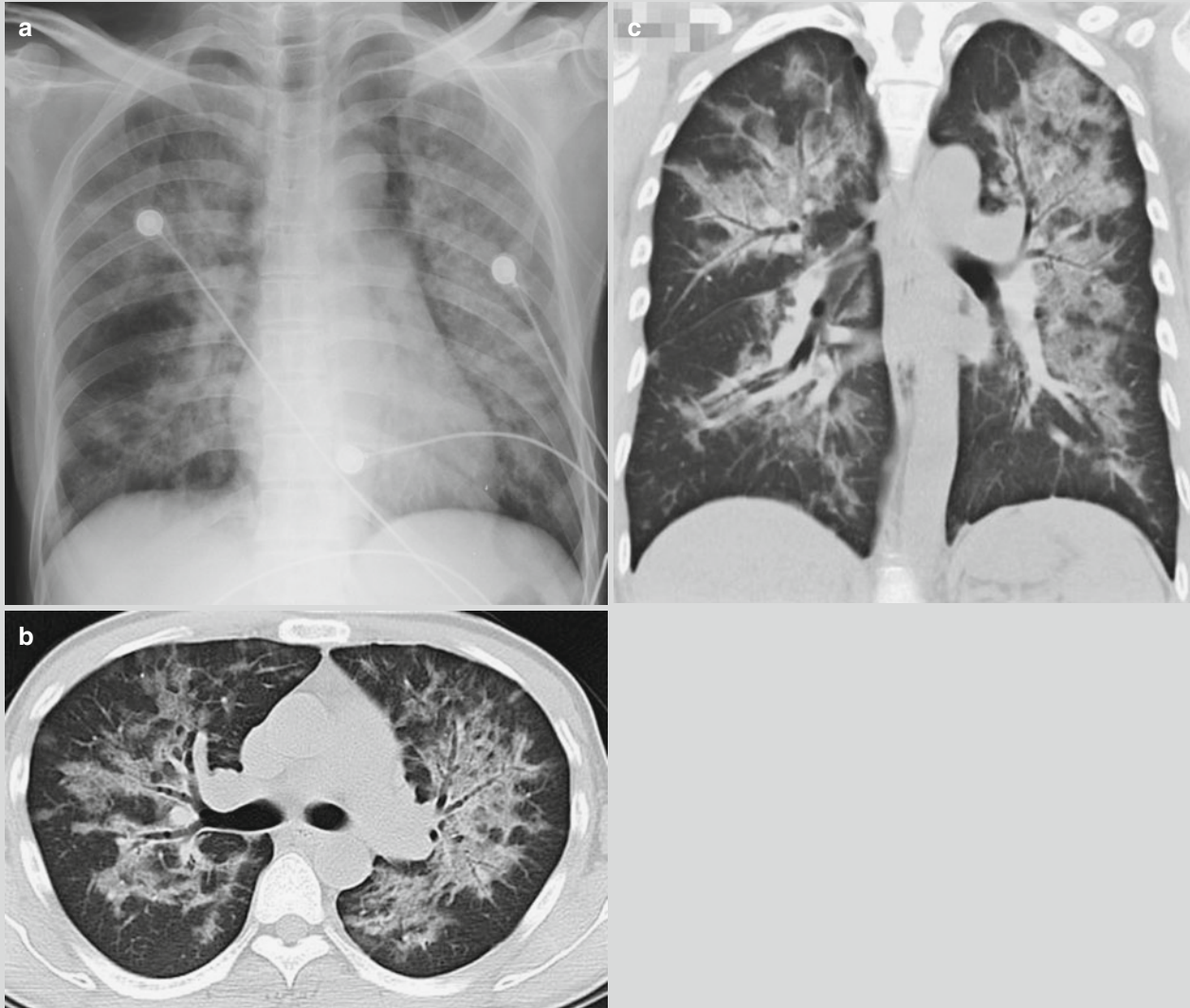
### 21.8.3 Imaging Demonstrations

Radiological findings demonstrate the severity of the conditions in a certain degree. In slight cases, chest radiology demonstrates no obvious abnormalities or only thickened pulmonary markings and blurry interstitial pneumonia. In serious cases complicated by pneumonia, intrapulmonary consolidation changes can be found in a large range. The lesions may be distributed consistently with morphology of pulmonary lobe or segment. In some cases, the complications of emphysema and acute respiratory distress syndrome occur, with multiple diffusive lesions in both lungs that rapidly changes. In rare cases, life can be threatened.

### Case Study 9

A male patient aged 35 years had a case history of positive HIV antibody and complained of fever for 4 days,

with chest pain, fatigue, and a body temperature of 38.7 °C. Laboratory tests show a WBC of  $10 \times 10^9/L$ , GR% of 85 %, and SaO<sub>2</sub> of 86 %.



**Fig. 21.9** Influenza complicated by pneumonia. (a) Chest X-ray demonstrates decreased transparency of both lung fields and extensively distributed flakes of blurry shadows in both lungs that are

more obvious in the left lung. (b, c) CT scanning demonstrates ground-glass opacities along bronchovascular bundles in both lungs

## 21.9 Differential Diagnosis

### 21.9.1 Common Cold

It is also known as acute rhinitis or upper respiratory catarrhal inflammation. Common cold is caused by rhinovirus, parainfluenza virus, respiratory syncytial virus, echovirus, and coronavirus. Adult patients with common cold are commonly infected by rhinovirus, while children are commonly infected by parainfluenza virus and respiratory syncytial virus (Table 21.2).

### 21.9.2 Other Viral Pneumonias

Other viral pneumonias include respiratory syncytial virus pneumonia, adenovirus pneumonia, and measles virus pneumonia, with imaging demonstrations of intrapulmonary ground-glass opacity.

#### 21.9.2.1 Adenovirus Pneumonia

The X-ray demonstrated morphology of adenovirus pneumonia lesions is closely related to the severity and stage of the disease. The early demonstrations include thickened

**Table 21.2** Differentiation of influenza from common cold

	Common cold	Influenza
Pathogen	Rhinovirus, parainfluenza virus	Influenza virus
Influenza virus detection	Negative	Positive
Communicability	Weak	Strong
Seasonal occurrence	Not obvious	Obvious
Severity of fever	No or mild	High fever (39–40 °C) with chills
Duration of fever	1–2 days	3–5 days
Respiratory symptoms	Obvious	Not obvious in the early stage
Systemic symptoms	Slight or no	Obvious
Course of the disease	5–7 days	5–10 days
Complications	Rare	Pneumonia, myocarditis, meningitis, or encephalitis

and blurry pulmonary markings and small nodular shadows along the pulmonary markings in the medial middle zone of the middle and lower fields of both lungs. In 3–5 days after the onset, pulmonary consolidations occur, with flakes of lesions in different sizes or fusion of the lesions that are more commonly found in the lower field of both lungs and in the right upper lung. The density of the lesions increases along with the progress of the conditions, with increased quantity of lesions and extensive distribution and fusion of lesions. Emphysema is common. Pleural effusion occurs in rare cases.

### 21.9.2.2 Respiratory Syncytial Virus Pneumonia

Respiratory syncytial virus is the most common pathogen that causes infantile viral pneumonia. The typically change is diffusive interstitial infiltration. Most of the cases have small flakes of shadows that are commonly found in 2–3 lung lobes. About 1/3 of the patients experience emphysema or excessive gases in the lung of different severities. About 15 % of the cases have only X-ray demonstration of excessive gas in the lungs. About 1/4 of the cases have pulmonary consolidation or atelectasis, with the lesions confined inferior to the pulmonary segments and commonly found in the right upper lung lobe. Imaging demonstration of absorption of pulmonary consolidation obviously lags behind the actual improvement of the symptoms and signs.

### 21.9.2.3 Measles Virus Pneumonia

Measles virus pneumonia is more common in infants, young children, and individuals with compromised immunity and commonly occurs in the early period of the disease. Chest X-ray demonstrations are mainly flakes or diffusive ground-glass opacity and/or thickened bronchial vascular bundles. CT scanning demonstrates lobular central nodules with poorly defined boundaries, ground-glass opacity, thickened lobular septum, and consolidation shadows in lobules or segments.

## 21.9.3 Other Pathogen-Induced Pneumonias

### 21.9.3.1 Mycoplasma Pneumonia

Mycoplasma pneumonia is an acute respiratory tract infection with accompanying pneumonia caused by mycoplasma. It occurs in both children and adults, with positive cold agglutination test. Chest X-ray demonstrates early lesions of only increased pulmonary markings with poorly defined boundaries. The lesions then develop into blurry cloudy or homogeneous shadows that commonly distribute in the middle and lower lung fields. The shadows close to the hilum are denser with gradually lighter shadows towards the periphery and poorly defined boundaries. The lesions commonly have no involvement of the whole lobe. Mycoplasma pneumonia with lobar lesions cannot be differentiated from lobar pneumonias caused by other pathogens. CT scanning demonstrations are mainly pulmonary ground-glass opacity and nodular shadow or small patches of consolidation shadows of air cavities that is the characteristic CT scanning demonstration, thickened bronchial vascular bundles, tree-in-bud sign, large flakes of consolidation shadows and possibly accompanying mediastinal lymphadenectasis, and pleural effusion. The pulmonary lesions are usually absorbed in 2 weeks or even in 4–6 weeks.

### 21.9.3.2 Allergic Pneumonia

Allergic pneumonia is a group of non-asthmatic allergic lung disease caused by different allergens. Chest X-ray may demonstrate normality or diffusive interstitial fibrosis. The commonly demonstrated lesions include bilateral patches or nodular infiltration, thickened bronchial lung markings, or small acinus-like changes. Hilar lymphadenectasis and pleural effusion are rare. CT scanning demonstrates thickened bronchial vascular bundles, small patches of shadows along bronchial vascular bundles with poorly defined boundaries, and ground-glass opacity. CT scanning demonstrations are not regular. The severity of lesions by radiology may be inconsistent with the clinical symptoms.

### 21.9.3.3 *Klebsiella* Pneumonia

*Klebsiella* pneumonia is an acute pulmonary inflammation caused by *Klebsiella*. It is more common in individuals with chronic alcoholism, individuals with malnutrition, and the elderly. Chest X-ray demonstrations can be divided into three types: (1) increased lung markings, (2) lobular or diffuse pneumonia, and (3) lobar consolidation or pulmonary abscess. CT scanning can more favorably demonstrate the lesions than chest X-ray. The early consolidations in the cases of *Klebsiella* pneumonia have lobular distributions, with patches or irregular dense shadows that scatter and commonly involve multiple pulmonary segments. The lesions rapidly fuse to lobar consolidation that is more common in the right upper lobe. Due to thick and heavy exudate fluid in the lesions, the interlobar space drops. Necrosis of the lesions induces pulmonary abscesses, which are multiple small cavities with a diameter of less than 2 cm. The healing is slow, commonly with residual extensive fibrosis.

### 21.9.4 Acute Respiratory Distress Syndrome

Acute respiratory distress syndrome (ARDS) is an acute respiratory failure syndrome caused by extrapulmonary and intrapulmonary serious diseases. The lesions are basically diffusive damages to pulmonary capillaries with increased permeability. The pathological changes mainly include pulmonary emphysema, formation of hyaline membrane, and pulmonary atelectasis. And clinically it is characterized by progressive respiratory distress and intractable hypoxemia, which are typical manifestations of acute pulmonary lesions in the advanced stage.

The radiological demonstrations of ARDS are related to leakage of edema fluid containing a large quantity of proteins to fill in the alveolar cavity because of damaged alveolar epithelial cells or diffusively destructed alveolar walls. Chest X-ray commonly demonstrates diffusively distributed shadows in both lungs and characteristic radiological changes of basic diseases such as severe pneumonia caused by various pathogens. CT scanning demonstrates unevenly distributed lesions, including (1) normal or

nearly normal gravity-independent area (mainly the anterior chest in supine position), (2) ground-glass opacity at the anterior and middle regions, and (3) consolidation shadow in the gravity-dependent area. In the cases with no lesions in the pulmonary capillary membrane, the patches of shadows in both lungs are evenly distributed, with no gravity dependency and no gravity-dependent change after changing body posture, which facilitates the differentiation from pulmonary infectious diseases. The advanced manifestations of ARDS include twisted bronchi and traction of bronchi and shrinkage of pulmonary segment or lobe volume, with grid-like shadow, cord-like shadow, and honeycomb-like shadow. In serious cases, honeycomb-like lung occurs.

### Further Reading

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