8.1 Introduction

Influenza, abbreviated as flu, is an acute respiratory infectious disease caused by influenza virus, which is mainly spread along with droplets with strong infectivity. The influenza virus may cause epidemics or pandemics of influenza and its incidence ranks the first among legally listed infectious diseases. The prevalence of influenza peaks in autumns and winters, with short illness course and self limitation. However, influenza can be complicated by pneumonia or other serious complications that may cause death in populations of infants, young children, the elderly, those with underlying heart and lung disease and those with compromised immunity.

8.1.1 Etiology

In the year of 1971, WHO officially issued the nomenclature system of influenza virus, and the influenza virus is divided into 3 types based on the antigenic properties of the virus nuclear protein since then, type A, type B and type C. Influenza virus is an RNA virus, which is the most stable in an environment with a pH value of 6.5–7.9 and is intolerant to high temperature. It loses its pathogenicity after heated to a temperature of 56 °C for several minutes, and can be inactivated at a temperature of 100 °C for 1 min. In an environment with a low temperature, the virus is more stable, being capable of surviving for more than 1 months at a temperature of 4 °C, and more than 5 months at a temperature of −70 °C. The influenza virus is sensitive to dryness, ultraviolet radiation, and commonly used disinfectants such as ethanol and iodophor.

8.1.2 Epidemiology

8.1.2.1 Source of Infection

The patients with influenza and persons with asymptomatic infection are the main sources of its infection. The infectivity persists from the terminal incubation period to the terminal acute period after onset, and the infectivity is the strongest in the initial 2–3 days after onset.

8.1.2.2 Route of Transmission

Influenza virus exists in the respiratory secretions of the patients or persons with asymptomatic infection and spreads via airborne transmission. By talking, coughing or sneezing, the virus spreads into air along with droplets or aerosols, and causes infection after their being inhaled into susceptible individuals. The virus can also spread via direct or indirect contacts to the mucosa in the oral cavity, nasal cavity, and eyes.

8.1.2.3 Susceptible Population

Populations are generally susceptible to influenza, which is not related to the gender and occupation. After infection, individuals acquire certain immunity. Among influenza virus A, B and C as well as different subtypes of influenza A virus, no cross immunity exists. And influenza virus can be repeatedly infected. After infection, the acquired immunity only persists for a short period of time. Despite of antibodies in the blood, the person can be infected by the same virus again.

8.1.3 Clinical Manifestation

The incubation period of influenza lasts for about 13 days, and several hours in some cases. Its onset is sudden and acute and the patients mainly experience systemic toxic symptoms but inapparant respiratory symptoms. According to the clini-
8.1.3.1 Simplex Type
The simplex type is the most common, and is often characterized by sudden onset of aversion to cold and high fever with a body temperature of up to 39–40 °C. Fever is the most important initial sign, often accompanied by headache, systemic muscle and joint soreness and pain, fatigue, poor appetite, and other toxic symptoms. Some patients may experience such symptoms as photophobia and tears. Other symptoms, such as nasal obstruction, runny nose, sore throat, voice hoarseness and other respiratory symptoms also show at the onset.

8.1.3.2 Pneumonia Type (Primary Influenza Virus Pneumonia)
Pneumonia type may be secondary to the simplex type or occurs as primary influenza virus pneumonia, which is caused by spread of influenza virus from upper respiratory tract to lower respiratory tract. The pneumonia type commonly occurs in the elderly, children, patients with underlying heart and/or lung disease, pregnancies, and individuals with compromised immunity. The main manifestations include persistent high fever, difficulty breathing, cyanosis, severe cough, expectoration of foamy mucous sputum or purulent sputum, expectoration of sputum with blood.

8.1.3.3 Toxic Type
The toxic type of influenza is extremely rare in clinical practice, which is caused by invasion of influenza virus into the central nervous system and cardiovascular system, with manifestations of toxic symptoms. Clinically, the patients experience symptoms of encephalitis or meningitis, with high fever, coma, delirium, convulsions, and even meningeal irritation sign and diffuse intravascular coagulation that indicate serious condition.

8.1.3.4 Gastrointestinal Type
The gastrointestinal type of influenza is common in children, and is mainly characterized by nausea, vomiting, diarrhea, and abdominal pain.

8.1.4 Radiological Demonstration
8.1.4.1 Primary Influenza Virus Pneumonia
Chest X-ray demonstrates mainly interstitial pneumonia and bronchial pneumonia, initially with poorly defined thickening of the lung markings, predominantly both lower lung field significantly; increased density of the lung markings resembling to GGO. During the progressive stage, the lung fields are demonstrated with grid like opacity and network like nodular opacity, with the nodules smaller than 5 mm. Such signs may be concurrently shown with thickened and blurry lung markings, with a distribution in both lower lung fields and around the hilum. In the late stage, cystic changes are shown in different sizes due to bronchiolar inflammatory occlusion in honeycomb like lungs, in addition to shrinkage of lungs, elevated diaphragm and shift of interlobar fissure. CT scan demonstrates small nodular opacity, GGO, tree-bud sign and mosaic like perfusion as well as interlobular septal thickening, subpleural line, adjacent pleural thickening, and pleural effusion.

8.1.4.2 Complication of Bacterial Pneumonia
Chest X-ray shows alveolar pneumonia (lobar pneumonia) or bronchial pneumonia (lobular pneumonia). Alveolar pneumonia is mainly demonstrated as lobar consolidation opacity with high homogeneous density or consolidation opacity with high homogeneous density occupying part of lung lobe, possibly with air bronchogram. Due to the different location of the lung lesions, the radiological demonstrations are accordingly different, with one or multiple lung lobes involved. Bronchial pneumonia is demonstrated as thickened lung markings, with poorly defined nodular opacity in diameters of 6–8 mm or poorly defined flake of opacity. Large poorly defined patch of opacity with uneven density is the result of overlapping lesions of lobular alveolitis. Bronchial obstruction by mucus is demonstrated as lobular atelectasis or focal emphysema in the diseased area. Bronchiolar occlusion may cause a small triangular shaped lesion of atelectasis. The lesions are commonly located in the medial parts of both lower lung fields, with more lesions in the posterior lung lobe than in the anterior lung lobe. And the lesions distribute along bronchi, with smooth air flow in the segmental and lobar bronchi. Terminal bronchiolar mucosa may be subject to congestion, edema and inflammatory exudation to cause obstructive emphysema, which is demonstrated as increased transparency of both lungs, thoracic extension, widened intercostal space, lowered and flat diaphragmatic muscle. CT scan demonstrates consolidation with uniform shape, lobar distribution and inner air bronchogram as well as poorly defined nodular and patches of opacity in different sizes that distributes along bronchial bundles. In addition, lobular pulmonary atelectasis and focal emphysema are also shown by CT scan.
8.2 Typical Cases

Case 1

[Brief Case History]
A 7-years-old boy complained of fever and cough for 2 days, with the highest body temperature of 37.7 °C. Laboratory tests revealed WBC count 4.21 × 10^9/L, and nucleic acid of influenza virus positive.

[Radiological demonstration] Fig. 8.1

[Diagnosis] Influenza virus pneumonia

[Discussion]
This is a case of influenza virus pneumonia, demonstrated by chest X-ray as interstitial inflammation in both lungs. Chest X-ray demonstrates primary influenza virus pneumonia mainly as interstitial pneumonia and bronchial pneumonia, early with poorly defined but enhanced lung markings, predominantly in bilateral lower lung fields. In addition, the lung markings show an increased density, resembling to GGO. During the progressive stage, the lung fields are demonstrated with reticular opacity and reticular nodular opacity, with nodules smaller than 5 mm. Such opacities may be concurrently demonstrated with poorly defined but enhanced lung markings. The lesions are commonly located in both lower lung fields and around the hilum. Chest CT scan demonstrates small nodular opacity in lungs, GGO, tree-buds sign and mosaic like perfusion, interlobular septal thickening, subpleural line, adjacent pleural thickening and pleural effusion. By radiology, the condition of this case was mild, present difficulty for the diagnosis, which depended on rich experience of the radiological clinician.

In this case, influenza virus pneumonia manifested as interstitial pneumonia should be differentiated from other viral pneumonia, such as hand-foot-mouth virus pneumonia and measles virus pneumonia. The initial lesions of hand-foot-mouth virus pneumonia are mainly interstitial changes with an extensive distribution and possible involvement of each lung lobe. The lesions commonly distribute bilaterally, with enhanced and deranged lung markings in both lungs as well as common grid like and cords like opacity. Along with the progression of the lesions, chest X-ray demonstrates changes of the lesions, with peripheral spread of the lobular lesions along bronchi and inflammatory consolidation of alveoli and adjacent lung tissue. The lesion may also invade alveolar duct, alveolar sac and alveoli in the lung lobule to cause lobular inflammatory exudation, demonstrated as small patches of increased density opacity confined within lung lobe or segment. There are more exudation opacities in the upper lung lobes than in the lower lung lobes and more in the right lung lobes than in the left lung lobes. Chest X-ray demonstrates measles virus pneumonia as flakes or diffuse ground glass opacity and/or thickened bronchovascular bundles. CT scan demonstrates poorly defined centrilobular nodules, ground glass opacities, interlobular septal thickening as well as lobular or segmental consolidations. Adenovirus pneumonia is demonstrated as thickened and blurry lung markings as well as small nodular opacities along lung markings in the middle and medial parts of bilateral middle and lower lung fields, possibly with fused lesions.

The radiological demonstrations of influenza virus pneumonia resemble to those of other viral pneumonia, and the radiological diagnosis of the primary disease is, therefore, challenging. The diagnosis can be defined based on laboratory tests.
The disease should be mainly differentiated from measles virus pneumonia, pulmonary alveolar pneumonia and allergic pneumonia. Chest X-ray demonstrates measles virus pneumonia as flakes or diffusely distributed GGO and/or thickened bronchovascular bundles. By CT scan, measles virus pneumonia is demonstrated as poorly defined centrilobular nodules, ground glass opacity, interlobular septal thickening as well as lobular or segmental consolidation opacities. Bacterial pneumonia is mainly demonstrated as alveolar pneumonia or bronchial pneumonia. Alveolar pneumonia is mainly demonstrated as alveolar consolidation opacity with high uniform density or consolidation opacity occupying part of lung lobe, with air bronchogram inside. Bronchial pneumonia is demonstrated as thickened lung markings, with poorly defined nodular opacity or poorly defined flakes of opacity. Allergic pneumonitis is a non-asthmatic allergic lung disease caused by a group of different allergens. Chest X-ray may show no abnormalities or diffuse interstitial fibrosis, commonly with bilateral patches or nodular infiltration, thickening of the bronchial lung markings or small acinar like changes. The demonstrations by CT scan are diversifying and overlapping, including small nodules in lungs, tree-buds sign with sporadic and centrilobular distribution, ground glass opacity with lobar distribution, diffuse ground glass opacities accompanied by thick interstitial change as well as interlobular septal thickening, subpleural line, adjacent pleural thickening, and pleural effusion. The radiological findings are in consistency with the histopathological demonstrations.

Case 2

[Brief Case History]
A 6-years-old boy complained of fever and cough with skin rashes for 6 days, with the highest body temperature of 38.9 °C. Laboratory tests revealed WBC count 2.26×10⁹/L, PCO₂ 42.6 mmHg, and PO₂ 86.5 mmHg; the nucleic acid of influenza virus positive.

[Radiological demonstration] Fig. 8.2

[Diagnosis] Influenza virus pneumonia.

[Discussion]
This case of influenza virus pneumonia is typically as virus pneumonia. Chest X-ray demonstrates primary influenza virus pneumonia as interstitial pneumonia and bronchial pneumonia, with initial radiological signs of enhanced but poorly defined lung markings, predominantly in bilateral lower lungs. The lung markings also show increased density resembling to ground glass opacity. During the progressive stage, the lung fields are demonstrated with reticular and reticular nodular opacities, with nodules smaller than 5 mm. Such opacities can be concurrently demonstrated with enhanced but poorly defined lung markings. The lesions commonly distribute in both lower lung fields and around the hilum. The demonstrations by CT scan are diversifying and overlapping, including small nodules in lungs, tree-buds sign with sporadic and centrilobular distribution, ground glass opacity with lobar distribution, diffuse ground glass opacities accompanied by thick interstitial change as well as interlobular septal thickening, subpleural line, adjacent pleural thickening, and pleural effusion. The radiological findings are in consistency with the histopathological demonstrations.

Unlike bacterial pneumonia, the radiological signs of viral pneumonia may be inconsistent with the clinical symptoms. Therefore, radiological diagnosis of primary virus pneumonia is challenging and the diagnosis can be defined based on the laboratory tests.
Fig. 8.2 Chest X-ray showed thickened lung markings, decreased transparency of the right lung field, sporadic flakes of poorly defined opacities in both lung fields (a). CT scan demonstrated ground glass opacities along bronchovascular bundles in both lungs and right pleural effusion (b–d).
Case 3

[Brief Case History]
A 7-years-old boy complained of fever and cough for 2 days, with aversion to cold and the highest temperature of 39.4 °C. Laboratory tests revealed WBC count 15.4 × 10⁹/L; the nucleic acid of influenza virus positive.

[Radiological demonstration] Fig. 8.3

[Diagnosis] Influenza complicated by bacterial pneumonia.

[Discussion]
This is a case of influenza complicated by bacterial pneumonia, with typical signs of lobar pneumonia. Lobar pneumonia is commonly caused by Streptococcus pneumoniae, with sudden and acute onset and a short course of illness. Chest X-ray demonstrates bacterial pneumonia as alveolar pneumonia (lobar pneumonia) or bronchial pneumonia (lobular pneumonia). Alveolar pneumonia is mainly demonstrated as lobar consolidation with high uniform density or consolidation with high uniform density occupying a part lung lobe, with air bronchogram inside. The lesions at different sites show different radiological signs, with lesions involving one lung lobe or multiple lung lobes. Bronchial pneumonia is demonstrated as thickened lung markings, with poorly defined nodular or flakes of opacity in a diameter of 6–8 mm. And the large poorly defined patches of opacity with uneven density is actually overlapping opacities of multiple lobular alveolitis. Occlusion of bronchi by mucus is demonstrated as lobular atelectasis or focal emphysema, while occlusion of bronchiole causes radiological sign of a small triangle shaped lung atelectasis. The lesions are commonly located in the medial parts of both lower lung fields, with more lesions in the posterior lung lobe than in the anterior lung lobe, which distribute along bronchial branches with smooth air flow in the segmental and lobar bronchi. Congestion, edema and inflammatory exudation of terminal bronchiolar mucosa may cause obstructive emphysema, which is demonstrated as increased transparency of both lung fields, extended thorax, widened intercostal space, and lowered flat diaphragm. CT scan demonstrates uniform shaped consolidations with lobar distribution, with air bronchogram inside, and poorly defined nodular and patches of opacity in different sizes along bronchial bundle as well as lobular atelectasis or focal emphysema.

It should be mainly differentiated from viral pneumonia, Klebsiella pneumonia and mycoplasma pneumonia. Chest X-ray demonstrates viral pneumonia mainly as interstitial pneumonia and bronchial pneumonia. During its early stage, chest X-ray demonstrates enhanced but poorly defined lung markings, predominantly in the both lower lung fields, with increased density like GGO. During the progressive stage, the lung fields are demonstrated with reticular opacity and reticular nodules, which mainly distribute in both lower lung fields and around the hilum, with a diameter of less than 5 mm. During the advanced stage, bronchiolar inflammatory occlusion causes cystic changes in different sizes, with honeycomb like lung. The lung is demonstrated with shrinkage, elevated diaphragm and shift of interlobar fissure. CT scan demonstrates small nodules, ground glass opacity, tree-buds sign and mosaic like perfusion. Klebsiella pneumonia is an acute lung inflammation caused by Klebsiella pneumoniae, which commonly occurs in populations of those with chronic alcoholism or malnutrition and the elderly. Chest X-ray demonstrations can be classified into 3 types: increased lung markings type; lobular type or diffuse pneumonia type; and lobar consolidation type or lung abscess type. Compared to chest X-ray, CT scan can more favorably display the lesions. In its early stage, Klebsiella pneumonia is demonstrated with lobular sporadic distribution of patches or irregular dense opacities, which involve multiple lung segments and fuse rapidly to show lobar consolidation in the right upper lung lobe. Due to the thick exudated fluid from the lesion, the interlobar fissure is demonstrated to drop. The lesions are susceptible to necrosis, followed by formation of lung abscess, which is commonly multiple small cavities with a diameter of less than 2 cm. The healing processes of these cavities is long, commonly with residual extensive fibrosis. Mycoplasma pneumonia is an acute respiratory infection and pneumonia caused by Mycoplasma pneumoniae, with common occurrence in both children and adults. Most of the patients show cold agglutination test positive. In its early stage, chest X-ray demonstrates increased poorly defined lung markings and blurry cloud like or homogenous opacities, commonly in the middle and lower lung fields. Such opacities adjacent to the hilum are dense, and its density gradually lightens along with its distance from the hilum, with poorly defined boundary and involvement of partial lung lobe. Mycoplasma pneumonia with lobar lesion can not be differentiated from lobar pneumonia induced by other pathogenic bacteria. Chest CT scan mainly shows ground glass like opacity in lungs, nodular or small patches of consolidation with air cavity, thickened bronchovascular bundle, buds-in-tree sign, large consolidation as well as accompanying mediastinal lymphadenectasis and pleural effusion.
Case 4

[Brief Case History]
A 22-years-old woman, pregnant for 38 weeks, complained of fever and aversion to cold for 2 days with the highest body temperature of 39.1 °C. Laboratory test revealed WBC count 19.48 × 10⁹/L, PCO₂ 33.8 mmHg, PO₂ 43.6 mmHg, SaO₂ 80.9 %; the nucleic acid of influenza virus positive.

[Radiological demonstration] Fig. 8.4

[Diagnosis] Influenza complicated by ARDS.

[Discussion]
Different populations with influenza, show different clinical manifestations, and the special populations include children, the elderly, the pregnancy and those with compromised immunity. In the middle or late stage of pregnancy, women, after infected by influenza virus, experience the symptoms of fever and cough, with vulnerability to pneumonia. The condition rapidly progresses into dyspnea, hypoxemia and even ARDS, with outcomes of miscarriage, premature delivery, fetal distress and intrauterine fetal death. In addition, it may induce aggravation of the underlying diseases, with occurrence of death in severe cases. In this case, the patient was a young woman during her pregnancy, who was diagnosed with influenza complicated by ARDS and death occurred after active treatment due to multiple organs failure.

ARDS is the typical manifestation of advanced stage acute lung damage, which is basically diffuse capillary damage of lung with increased permeability due to intrapulmonary or extrapulmonary serious disease. Its pathological changes include pulmonary edema, hyaline membrane formation and pulmonary atelectasis, with clinical manifestations of acute respiratory failure syndrome characterized by progressive respiratory distress and intractable hypoxemia. The radiological abnormalities of ARDS are related to leakage of edema fluid containing a large amount of protein and its filling into the alveolar cavity after damage to the alveolar epithelium or diffuse damage to alveolar wall. And its staging by radiology is closely related to the pathological changes, including the exudative stage, the proliferative stage and the fibrosis stage, with intercorrelation and overlapping. Chest X-ray commonly demonstrates diffuse opacity in both lungs, and detectable lesions of the underlying disease, e.g. severe pneumonia induced by a variety of pathogens. CT scan demonstrates uneven distribution of the lesions: (1) with almost no abnormality in the gravity independent region (e.g. supine, anterior thoracic cavity); (2) with GGO in the anterior and middle thoracic cavity; and (3) with consolidation in the gravity dependent region.

Fig. 8.3  Chest X-ray demonstrated thickened lung markings in both lungs, decreased transparency of the right lower lung field, and poorly defined flakes of opacities in the right lower lung (a). CT scan demonstrated wedge shaped consolidation opacity in the right lower lung lobe, with its sharp end pointing to the hilum, air bronchogram inside and surrounding poorly defined small patches of opacities (b).
In the cases with no capillary damage in lung, the patches of opacities evenly distribute in both lungs, with no gravity dependent lesions and no gravity dependent changes of the lesions. Such a phenomenon facilitates its differential diagnosis from other lung infections. In the advanced stage of ARDS, radiology demonstrates twisted and stretching of the bronchi, shrinkage of lung segment or lobe, grid like opacity, cords like opacity, honeycomb like opacity, and even honeycomb like lung in severe cases.

It should be mainly differentiated from viral pneumonia, bacterial pneumonia and pulmonary edema. Chest X-ray demonstrates viral pneumonia mainly as interstitial pneumonia and bronchial pneumonia. In its early stage, chest X-ray demonstrates enhanced but poorly defined lung markings, predominantly both lower lung fields, with increased density like GGO. In its progressive stage, the lung fields are demonstrated with reticular opacity or reticular nodules and the nodules commonly distribute in the both lower lung fields and around the hilum, with a diameter of less than 5 mm. It its advanced stage, bronchiolar inflammatory occlusion causes cystic changes in different sizes to show honeycomb like lung, with shrinkage of lung, elevated diaphragm and shift of interlobar fissure. CT scan demonstrates small nodular opacity, ground glass opacity, tree-buds sign and mosaic like perfusion in lungs. Chest X-ray demonstrates bacterial pneumonia mainly as alveolar pneumonia or bronchial pneumonia. Alveolar pneumonia is demonstrated as lobar consolidation with high uniform density or consolidation with high uniform density occupying part of lung lobe, with air bronchogram inside and one or multiple lung lobes involved. Bronchial pneumonia is demonstrated as thickened lung markings, poorly defined nodular or flakes of opacity in a diameter of 6–8 mm. Bronchial occlusion by mucus can be demonstrated as lobular atelectasis or focal emphysema in the diseased area.

The lesions are commonly located in the medial part of both lower lung fields, with more in the posterior lung lobe than in the anterior lung lobe, that distribute along bronchial branches. And the segmental and lobar bronchi show smooth air flow. CT scan demonstrates consolidations with uniform shape and lobar distribution, with air bronchogram inside, and poorly defined nodular or patches of opacities of different sizes along bronchial bundles as well as lobular atelectasis and focal emphysema. Pulmonary edema and acute or chronic systolic or diastolic heart dysfunction due to various etiological factors can lead to increased pressure in the pulmonary vein and pulmonary capillaries as well as pulmonary congestion. The liquid firstly accumulates in the perivascular sheath in lungs and interlobular space to cause pulmonary interstitial edema, which then flow into the alveolar cavity to cause pulmonary parenchyma edema. Chest X-ray demonstrates interstitial edema as thickened, deranged and re-ranged lung markings, thickened but poorly defined vascular markings in both upper lung fields, enlarged and dense hilar opacities in both lungs, thickened and dilated but poorly defined vascular markings in the middle and medial parts of both lung fields. However, chest X-ray demonstrates interstitial edema with fine vascular markings in peripheral lung field and well defined peripheral lung field. Its further progression can be demonstrated with flakes of opacity in both lungs with butterfly wing like shape and concentric distribution. Chest X-ray demonstrates alveolar edema as initially poorly defined flakes of opacities in different sizes with sporadic distribution in both lungs. Along with its progression, chest X-ray demonstrates large flakes of high density opacity after fusion, which extends from the hilum to the peripheral lung with gradually light density, in typical butterfly wing like sign.
Fig. 8.4 Chest X-ray demonstrated decreased transparency of both lung fields and large consolidation opacity in both lungs, with air bronchogram inside (a). Reexamination after treatment for 2 days showed that absence of lung markings in both lungs, further decreased transparency of both lung fields, and diffuse high density in both lungs (b).

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