2.1 Overview of SARS

2.1.1 Definition of SARS

Severe acute respiratory syndrome (SARS) is an acute respiratory tract infectious disease induced by SARS-CoV and mainly transmitted through the short-distance air droplets and close contact. Its main clinical characteristics is abrupt onset of the disease and the initial symptom is fever accompanied with systematic symptoms of headache, soreness and fatigue, and respiratory tract symptoms such as cough, chest dullness, and dyspnea. A few cases may progress to acute respiratory distress syndrome (ARDS). Due to its self-limiting feature, the prognosis is predominantly good but may be poor in severe cases, with mortality about 9.3%. Some patients may develop such complications such as lung fibrosis and necrosis of the head of femur. On April 8, 2003, SARS was defined as a legal infectious disease by the Ministry of Health of China.

2.1.2 Discovery and Epidemic of SARS

2.1.2.1 The Discovery of the Disease

1. The first SARS case was reported around the world on January 2, 2003; a hospital in Heyuan city of Guangdong province hospitalized two patients with severe pulmonary infection of unknown cause, which was the first traceable report of “SARS” around the global.

2. On February 28, 2003, SARS was first diagnosed by the WHO expert Carlo Urbani in Hanoi of Vietnam, who also named this new unexplained disease “Severe Acute Respiratory Syndrome” (SARS).

2.1.2.2 Control of SARS Epidemics

Following the emergence of SARS, WHO and governments around the world attached great importance and took consecutively effective control and prevention measures, which reined in the infection rapidly controlled in a short time. On April 28, 2003, WHO eliminated Vietnam from the name list of the SARS-infected area, which made Vietnam the first to get rid of SARS outbreaks. Since then, numerous countries were also ticked off the list. On July 5, 2003, WHO announced to remove Taiwan of China from SARS-affected area list, which is also the last. At present, there is no SARS-affected area around the world, signaling the victory of global battle against SARS. By the end of September 26, 2003, there were in total 8,098 people infected and 774 deceased, with the mortality at 9.5%.

2.2 Etiology

On April 16, 2003, a new coronavirus never seen was announced as the cause of SARS by WHO. It is the joint efforts of global scientists and biological scientific and technological advances that enabled establishment of international SARS research network, separation and identification of SARS coronavirus, and confirmation of SARS pathogenesis.
2.2.1 Discovery of SARS Pathogen and Determination of Pathogenesis

2.2.1.1 Screening and Exclusion of Known Pathogens
Some Canadian laboratories excluded influenza virus A and B; para-influenza virus type 1, 2, and 3; adenovirus; and respiratory syncytial virus by scanning electron microscopy and direct fluorescent antibody test. They also conducted immunohistochemistry on the corpse tissues of dead patients about viruses including influenza virus A and B, respiratory syncytial virus, adenovirus, circovirus, Hantaan virus, measles virus, intestinal tract virus, and pneumonia mycoplasma and chlamydia, which showed negative. Scholars from German, France, America, Hong Kong, and Taiwan applied specific PCR tests targeted at corresponding pathogens to examine pneumonia mycoplasma, pneumonia chlamydia, human cytomegalovirus, circovirus, herpes virus, human coronavirus OC43 and 229E and Arenaviruses, Bunyavirus, Hantaan virus, Crimean-Congo hemorrhagic fever virus, which also indicated negative.

2.2.1.2 Separation and Identification of SARS Coronavirus
On March 21, 2003, Hong Kong University firstly separated and cultured coronavirus from the nasopharyngeal specimen of SARS patients by Vero cells, and then several laboratories of Canada and America disease center and SARS international coordination group also cultured coronavirus. On April 16, 2003, based on the aforementioned research findings, WHO declared a new coronavirus as the pathogen of SARS and named it as SARS coronavirus (SARS-CoV).

2.2.2 Physicochemical Characteristics of SARS Coronavirus

2.2.2.1 Morphologic Structure
SARS-CoV is a single-stranded and positive RNA virus belonging to the genus Coronavirus of Coronaviridae family of Nidovirales order. It bears great morphological resemblance with known human coronaviruses. Under the electric microscopes, SARS coronavirus presents with pleomorphic spherical particles with envelopes in Vero E6 cell in vitro and with a diameter of about 80–140 mm. It has distinct coronavirus morphological characteristics that rodlike surface projections about 20–40 nm long protrude outside viral envelope to form a corona. For separation and culture of viruses in Vero E6 cells, viral particles are mostly found in vacuoles inside cells under electric microscope, mainly hollow particle, and viruses outside cells observed with spikes.

2.2.2.2 Physicochemical Characteristics
The Coronavirus is mainly composed of nucleic acid, protein, carbonate, and lipid. SARS-CoV are relatively stable in human specimens and environment but relatively sensitive to chemical and physical factors. The viruses could be killed by exposure to ultraviolet rays for 60 min. As the envelope of SARS-CoV contains lipoids, they are sensitive to lipid solvents and could be inactivated by ether, chloroform, tween, 70 % ethyl alcohol, methanol, pancreatic enzymes, and ultraviolet rays. Ether could sterilize the virus completely under 4°C after 24 h, 75 % ethyl alcohol could deactivate virus after 5 min, and disinfectants containing chlorine may kill the virus after.

2.3 Epidemiology

2.3.1 Overview of Epidemics
SARS is the first newly emerging infectious disease in the twenty-first century. Since the first case was detected in Guangdong on January 2, 2003, SARS spread to 29 countries at five states at an unprecedented speed with several months. According to the report of WHO, SARS epidemics was found in total 29 countries at five states (including Hong Kong and Taiwan of China) from January 2, 2003, to September 26, 2003. Since January 2, 2003, which infected 8,098 patients and caused 774 casualties. Besides, there were 5,327 patients in China mainland (including 1,002 medical workers) with 349 deaths; 1,755 patients in Hong Kong with 299 deaths; 346 patients in Taiwan with 37 deaths; 251 patients in Canada with 43 deaths; 238 patients in Singapore with 33 deaths; 63 patients in Vietnam with 5 deaths and 29 patients in America but without casualty. Meanwhile, SARS cases were reported in 24 provinces, municipalities under direct governance of central government and autonomous regions in China mainland, with 2,521 infection cases and 183 deaths in Beijing and 512 infection cases and 57 deaths in Guangdong.

2.3.2 Source of Infection
The main source of infection is SARS patients, and other infectious sources such as animals need to be further consolidated.

2.3.2.1 Symptomatic Patients
It is regarded that only symptomatic patients can effectively spread SARS-CoV.

2.3.2.2 Asymptomatic Patients
At present there still lacks clinical proof that asymptomatic SARS patients could spread SARS coronavirus.

2.3.2.3 Super-Spreader
Few cases are highly contagious and able to directly infect over 10 patients, who are called super-spreader. The five super-spreaders in Singapore have been found infecting 103 people. Such powerful infectiousness is attributable to the high viral load inside patients who could discharge abundant viruses via respiratory tract in a short time.
2.3.2.4 Animal Source of Infection
Specialists from the department of microbiology of Hong Kong University and Guangdong Provincial Disease Control and Prevention Center tested abundant SARS coronaviruses from the samples collected from civet cats sold in Guangzhou and Shenzhen, suggesting that the human SARS coronavirus might originate from civet cats.

2.3.3 Route of Spread
SARS virus is spread mainly through the respiratory tract and also spread by aerosol and droplet.

2.3.3.1 Droplet Spread
High level of SARS coronavirus could be detected in the throat swabs and sputum specimens of the patients in acute phase. Viruses discharged by patients via cough would exist in the air within certain radius, thus forming short-distance respiratory tract droplet spread. It is a main route of SARS dissemination.

2.3.3.2 Contact Spread
Indirect or direct contact spread could also spread SARS coronavirus. It could be spread through contact with the respiratory tract secretion or through the mouth and nose via contaminated hands and toys.

2.3.3.3 Aerosol Spread
As viruses proliferate abundantly in the respiratory tract, exfoliated cells containing infectious viruses could be expelled outside the body through patients’ respiration, cough, and sneeze and suspend in the air, thus forming the aerosol of SARS virus. Cough and sneeze could greatly contribute to production of SARS virus aerosol.

2.3.4 Population Susceptibility
SARS is a new type of infectious diseases, and people effectively exposed to SARS pathogens are vulnerable.

2.3.4.1 Immunity After Illness
Present data reveal that SARS is an acute self-limiting infectious disease, and neutralizing antibodies to SARS could be detected 3 weeks after onset. However, the change patterns of neutralizing antibody titer have not been fully elucidated.

2.3.5 Epidemiological Characteristics
2.3.5.1 Characteristics of Time Distribution
The epidemics of SARS mainly take place in the winter and spring.

2.3.5.2 Characteristics of Area Distribution
SARS outbreaks are mainly concentrated at coastal tourism cities with prosperus economy, dense population, and convenient transport, particularly air transport. From the perspective of international geography, SARS primarily occurs in Southeastern countries or regions, including China mainland, Hong Kong, Taiwan, Singapore, and Vietnam.

2.3.5.3 Characteristics of Population Distribution
Analysis of the statistics of various countries shows that SARS onset is mainly recorded in young populations aged 20–50 years old, occupying around 80 % of the total.

2.4 Pathogenesis and Pathological Changes
2.4.1 Pathogenesis
SARS coronavirus (SARS-CoV), a mutant of Coronaviridae, is pathogenic to hosts in the following two aspects: firstly, viral infections could directly damage the structure and functions of infected cells and trigger cell apoptosis; secondly, immune reactions and release of various cytokines induced by viral infections could not only eliminate infectious pathogens but also may deal severe damages on histiocytes due to excessive immune reactions.

The member of Coronaviridae is a single-chain positive RNA virus, which taxonomically belongs to Nidovirales with Arteriviridae. The homological analysis of SARS-CoV structural protein amino-acid sequences shows that the main structural protein S (spike protein), M (membrane protein), N (nucleocapsid protein), and E (envelope protein) bear very low homology with other known coronaviruses, between 20 and 30 %. Besides, bioinformation analysis infers that SARS-CoV may also encode 5–9 nonstructural proteins of unknown functions. All these SARS-CoV specific proteins may play key roles in determining the viral virulence.

S-protein, existent on the viral surface in form of trimer, is the main component in constructing the coronal structure and major structural protein for the integration of virus and host cell receptors and fusion of viral envelope and cell membrane to enable invasion of viruses. After infection with sensitive cells, SARS-Cov could replicate enormously and release virions, which may disturb cell metabolism and directly result in injury of body tissues and cells.

In the early phase of the disease and in the continual progression phase, the active immune cells such as CD4+ and CD8+ T lymphocytes, NK cells, and DC cells are decreased prominently, to an extent positively correlated with severity of conditions and speed of progression. Besides, all dead patients are detected with irreversible significant decline. However, along with remission of conditions and entry into recovery phase, the number of aforementioned immune cells could be recovered to some extent, whose change presents distinct par-
allel correlation with disease evolution. Dynamic observations suggest that serum pre-inflammatory cytokine IL-6, IL-8, IL-16, and INF-α level of SARS patients could reach the peak at about second week of disease course, which relatively corresponds to the acute aggravation phase. All these consolidate the immune damage of SARS-CoV infections.

### 2.4.2 Pathological Changes

Autopsies of the over 20 patients who died after infected with SARS revealed that SARS is a disease detrimental to organs of the whole body, particularly lung tissue and immunity system. Primary pathologic changes can be classified into severe lung lesions, immune organ impairment, toxic changes of other organs, and secondary infections. The causes of death were as follows: (1) diffusive lung alveolar damages lead to progressive respiratory failure; (2) impairment of liver, kidney, heart, and several other organs may induce multiple organ failures and exacerbate conditions; (3) due to injury of immune organs particularly lymph nodes and spleen, the lymphocytes are decreased and immunity compromised, therefore resulting in secondary mycotic infections.

#### 2.4.2.1 Lungs

**Naked-Eye Observation**

Lung tissues become swollen and heavier. According to domestic report, the left lung may reach 500–1480 g (average 811.4 g) and right lung 700–1125 g (average 869.3 g), with the total lung up to 1170–2605 g (average 1460.7 g). The lung tissues appear in dark red. Texture is hard, indicative of consolidation. The surface is relatively smooth and free of pleural adhesions. Lung tissues are observed with blood vessel dilation and congestion, spotted and patchy necrosis, and hemorrhagic infarct foci and focal compensatory emphysema. Sections of various lung lobes are visualized with outflows of light red or/and a few foamy blood-stained fluids. The trachea and bronchi are found with exudations of slight mucoid or blood-stained secretions. Pulmonary hilar lymph nodes are revealed with slight enlargement and pleural cavity without or with a few effusions.

**Observation Under the Light Microscope**

Microscopy reveals bilateral diffusive severe injuries of alveoli, characterized by acute exudative, hemorrhagic, and fibrinous inflammation. However, the injury may be inhomogeneous and diverse at different lung lobes and different parts of the same lobe. The characteristic change in early phase is pulmonary edema, with homogeneous pink serous or fibrinous effusions filling alveolar cavities as well as erythrocytes leakages in some cavities. The effusions from some alveolar cavities may condense to form thin-layer membranelike substance which adheres to alveolar walls, namely, formation of hyaline membrane (Fig. 2.1). Alveolar epithelia present with such diffusive injuries as degeneration and necrosis, with exfoliated or/and apoptotic type II alveolar epithelial cells observable in alveolar cavities, which are similar to changes of desquamative pneumonia (Fig. 2.2). Among them, some appear like apoptotic bodies. Partial regional type II alveolar epithelial cells and macrophages proliferate actively, with obvious increase of cell volume and distinct nucleolus. In some case, cells are detected fusing with each other to form syncytial monocytes and multinucleated giant cells (Fig. 2.3). The alveolar epithelia of some cases are examined with structures similar to viral inclusion bodies, mostly spherical and with eosinophilic staining, around which a transparent halo is visible (Fig. 2.4). Pulmonary interstitium and alveolar spaces are detected with

**Fig. 2.1** Alveolar cavities were full of homogenous acidophilic effusions which condensed to form hyaline membranes (indicated by arrow) and attach to alveolar walls HE ×200

**Fig. 2.2** Alveolar wall epithelial cells were disclosed with degeneration and necrosis, alveolar cavity with exfoliated type II alveolar epithelial cells (indicated by the arrow), and alveolar space with infiltration of a few lymphocytes and monocytes. HE ×200
high dilation and congestion of capillaries, swelling and exfoliation of epithelial cells, as well as widening of the latter, which present slight lymphocyte and monocyte infiltration, small vessel proliferation, and enlargement characteristic of vasculitis changes. Some regions are observed with pulmonary vascular embolism or fibrinous microthrombi in alveolar capillaries, while some alveolar capillary cavities manifest dilation but free of blood components. In addition, some patients are detected with lung tissue focal hemorrhage, compensatory emphysema, and small airway necrotizing inflammation and alveolar collapse or shrinkage. Patients with a disease course of over three weeks manifest fibroblast proliferation in alveolar septa, and individual cases demonstrate organization of fibrinous exudates from alveoli and fibroblast proliferation, which gives rise to glomeruloid structures, named “glomeruloid organizing pneumonia” (Fig. 2.5). The bronchial epithelial cells are revealed with exfoliation, scarce and exfoliated cilia, as well as structures similar to viral inclusions and squamous cell metaplasia at the inside. The bronchioli are detected with submucosal edema, inflammatory cell infiltration, and serous granular hyperplasia with hyperactive secretion.

2.4.2.2 Immune Organs

Chest and Abdominal Lymph Nodes

Pulmonary hilar lymph nodes demonstrate light swelling and present different degrees of congestion, hemorrhagic necrosis, and decrease of innate lymphocytes under the microscope. Blood sinus in the lymph nodes presents with grave congestion and dilatation, lymphoid nodule atrophy or disappearance, prominently the cortex, and lymphatic tissue focal necrosis, accompanied by apoptosis of some lymphocytes (Fig. 2.6).

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**Fig. 2.3** Alveolar cavities were seen with multinucleated giant cells (indicated by the arrow). HE ×400

**Fig. 2.4** Alveolar epithelial cells were detected with structures similar to viral inclusion bodies (indicated by the arrow), with spherical shape and acidophilic staining as well as transparent halo at the periphery. HE ×400

**Fig. 2.5** Imaging visualized organization of fibrinous exudates from alveoli and proliferation of fibroblast to form similar glomerular structures (indicated by the arrow) HE ×200

**Fig. 2.6** Pulmonary hilar lymph nodes were seen with congestive necrosis and decrease of the innate lymphocytes and lymphoid nodules with atrophy and disappearance. HE ×400
Spleen
The spleen mostly shrinks with soft texture, and has patchy and focal hemorrhage at the surface and sections. Splenic white pulp is detected obviously atrophic or absent, with central arterial wall thickened, endothelial cells swollen and partially shed, peripheral lymphatic sheath lymphocyte depleted greatly, and germinal center disappeared. Splenic corpuscle is observed with plasma protein sedimentation in central arterial walls, white pulp and marginal sinus lymph tissues with large patchy necrosis, and partial remaining lymphocytes with apoptosis. The splenic sinus inside red pulp is revealed with obvious congestion and focal hemorrhagic necrosis as well as proliferation of histiocytes (Fig. 2.7).

Bone Marrow
The number of hematopoietic cells in bone marrow declines, and granulocyte system and megakaryocytic system are relatively inhibited. Polychromatic erythroblasts present with small focal proliferation.

2.4.2.3 Other Main Organs
Tissues of the brain, liver, kidney, and heart demonstrate varying degrees of congestion, edema, degeneration, and necrosis as well as infiltration of a few lymphocytes.

2.4.2.4 Secondary Infection
Secondary bacterial pneumonia and fungal infection may occur (Fig. 2.8).

2.5 Clinical Manifestations
The initial symptom of SARS is frequently fever, accompanied by headache and general muscular and joint souring soreness, and often without nasal discharge, sore throat, and other upper respiratory tract catarrhal symptoms. Pulmonary signs are not obvious and signs and distinct systematic symptoms are inconsistent, which is typical to SARS. The clinical manifestations of SARS may vary, which can be divided into light type, common type, severe type, and atypical type, with the common type most commonly seen. Based on the clinical development, it could be divided into early phase, progression phase, and recovery phase.

2.5.1 Incubation Phase
Generally, the incubation phase lasts 2–14 days, with an average of 4–7 days and a median of 6 days, predominantly 2–10 days.

2.5.2 Symptoms
2.5.2.1 Fever
The initial symptom primarily is fever, mostly high fever, accounting for 94.4–100 %. Patient body temperature may reach 38–40 °C and 42 °C at the highest. The fever type varies, including remittent fever, irregular fever and continuous fever. The duration of fever is mostly 5–9 days.

2.5.2.2 Pain
It presents as headache, joint or/and systematic soreness, and chest pain. It is reported that the incidence of headache in SARS patients is 17–90 %.

2.5.2.3 Symptoms of T Respiratory System
Most SARS patients have cough, which is dry with scanty sputum. Generally SARS does not incur upper respiratory tract catarrhal symptoms. Severe cases may suffer from accelerated respiration, shortness of breath, or even acute respiratory distress syndrome, characterized by progressive dyspnea or even distress with respiratory frequency up to >20 times.
2.5.2.4 Palpitation and Chest Distress
Patients complain of heart beat or palpitation accompanied often by precordial discomfort. The incidence is 35–90 %.

2.5.2.5 Digestive System Symptoms
The incidence of diarrhea is reported mostly at 7–44 %, with single case up to 70 %.

2.5.3 Signs
One characteristic of SARS is severe symptoms and light signs. The signs are mostly not obvious or even absent.

2.5.3.1 Dyspnea
Dyspnea presents irregular respiratory frequency, depth, and rhythm. The incidence of dyspnea of SARS patients is 21–57 %. Severe patients may manifest nose fanning, orthopnea, and cyanosis, involvement of accessory respiratory muscles in respiration, as well as “three depression signs” upon inhalation.

2.5.3.2 Tachycardia
According to report, 11 % of typical patients and 14 % of severe patients have sinus tachycardia, and 2.3 % of SARS patients suffer from paroxysmal supraventricular tachycardia.

2.5.3.3 Pulmonary Signs
The pulmonary signs of SARS patients are frequently unobvious or absent in the early phase. Light moist rales may be audible (17–62 %). Patients may also demonstrate pulmonary consolidation sign and attenuated breath sounds. There may also be a few pleural effusions.

2.5.4 Classification
In light of conditions, it could be classified in clinics into light type, common (typical) type, severe type, and special (atypical) type.

2.5.5 Complications

2.5.5.1 Pulmonary Fibrosis
The follow-up visit of 267 SARS patients via X-ray and HRCT by Choi et al. found that about 3–4 % patients developed fibrotic changes of lung interstitium and shrinkage of lung volume.

2.5.5.2 Ischemic Necrosis of the Femoral Head
Application of glucocorticoids could to some extent alleviate lung injury of patients with severe infectious atypical pneumonia. However, long-term and abundant use of glucocorticoids may generate numerous side effects, and it is an undisputable fact that hormones may induce femoral head ischemic necrosis. Literature reports suggest that the incidence of femoral head ischemic necrosis is 5–25 %.

2.6 Laboratory Examinations

2.6.1 Blood Routine Examination
The white blood cell count remains within normal range in majority patients and may decrease in some patients (24.2 %). 95 % of severe patients without secondary infections are revealed with decreased total white blood cell, and normal neutrocyte and monocyte differential white blood cell count. However, 80 % initially diagnosed patients manifest a decrease of absolute lymphocyte count, suggestive of a tendency of gradual decline, and morphocytology change, with abnormal lymphocytes observable. 13.2–41 % patients are examined with thrombocytopenia. Many evidences prove that SARS-CoV could directly invade the immune system and act mainly on lymphocytic system, especially the T lymphocytes, which could lower peripheral blood lymphocytes. The peripheral blood white cell count is normal or decreased in most SARS patients, but CD3+, CD4+, and CD8+ T lymphocyte counts are distinctly lower compared with those of healthy population. The more severe the condition, the more drastically declined the T lymphocyte count.

2.6.2 Blood Gas Analysis
Blood gas analysis reveals hypoxemia of different degrees and commonly no carbon dioxide retention. Generally under 3–5 L/min oxygen uptake, patients with severe hypoxemia are measured of arterial partial pressure from oxygen (PaO₂) <70 mmHg or blood oxygen saturation (SpO₂) <93 %, or develop acute lung injury (ALI) or acute respiratory distress syndrome (ARDS).

2.6.3 Measurement of Peripheral Blood T Lymphocyte Subgroup
One of the main immunopathogenesis changes in SARS patients is insufficiency of T-lymphocyte-mediated specific cellular immunity, characterized by distinct damages of T lymphocytes and its subgroups, particularly CD3+, CD4+, and CD8+. There exists distinct correlation between the extent of T lymphocyte damages and severity of the disease.
2.6.4 Test of SARS-Specific Antibodies

The method recommended by WHO for test of serum SARS-CoV antibodies is enzyme-linked immunosorbent assay (ELISA). Upon test of the SARS-CoV-specific antibodies in the infected patients, including IgG, IgM, or total antibody, seroconversion or increase by 4 times and above of any serum antibody in progress phase and recovery phase could serve as evidence for definite diagnosis.

2.6.5 PCR Test of SARS Virus

Polymerase chain reaction (PCR), a type of molecular biological test, could identify SARS virus genes from various specimens (blood, feces, respiratory tract secretions, tissue sections, etc.), that is, SARS virus RNA.

2.6.5.1 Positive Results

Presence of any of the following three circumstances could be SARS virus positive:

1. Clinical specimens from at least two different sites are tested positive (nasopharyngeal secretions and feces).
2. The same clinical specimens collected by at least 2 days apart are tested positive (two or more specimens of nasopharyngeal excretions).
3. The same clinical specimen is tested positive by two different methods or in different laboratories.
4. Repeated PCR examination indicated positive.

2.7 Clinical Diagnosis

2.7.1 SARS Diagnosis and Treatment Regimens

2.7.1.1 Basis of Diagnosis

Epidemiologic History

1. The patient has a history of intimate contact with patients or is one of the infected population or consolidated having infected others by definite evidences.
2. The patient had been to or lived in the areas with SARS patients and secondary infection epidemics.

Symptoms and Signs

The onset is acute and initial symptom is fever, with body temperature ≥38 °C, and occasionally accompanied by concurrent chillness. Patients may also suffer from headache, joint and muscular soreness, fatigue, and diarrhea, and generally there is no upper respiratory tract catarrhal symptom. Patients may have cough, mostly dry with scanty sputum, and chest dullness. Severe patients demonstrate accelerated respiration, shortness of breath, or obvious respiratory distress. Pulmonary signs are not obvious, and light moist rales may be audible or pulmonary consolidation observable.

Laboratory Examination

There is generally no increase of peripheral white blood cell count or decrease. Besides, the lymphocyte count is found generally declined.

Chest X-Ray Examination

Lungs present different degrees of patchy and plaque-shaped infiltration shadows or reticulate changes, which may progress rapidly into large patchy shadows. These commonly occur at multiple lobes or both sides, and absorption and dissipation of shadows are relatively slow. Pulmonary shadows and symptoms and signs may be inconsistent. If the test indicates negative, reexaminations shall be conducted after 1–2 days.

Effects of the Antibiotics Treatment

There are no remarkable responses to antibiotics.

2.7.1.2 Criteria for Clinical Diagnosis

Criteria for Diagnosis of Suspected Cases

Patients in compliance with any of the following three circumstances are diagnosed as suspected cases.

1. The patient has a history of intimate contact with patients, or is one of the infected population, or is confirmed having infecting other people by concrete evidences, who also manifest aforementioned clinical symptoms but not high white blood cell count by test of peripheral blood.
2. The patient has been to or lived in areas reported with infectious SARS patients and patients suffering from secondary infections 2 weeks before the disease onset, who also have abovementioned clinical symptoms and consistent pulmonary shadows on chest X-ray films with the abovementioned characteristics.
3. Despite the lack of epidemic data, the patient has abovementioned clinical manifestations and not high peripheral white blood cell count, as well as pulmonary shadows on chest X-ray that accord with abovementioned characteristics.

In other words, the patient conform to the aforementioned 1 (1) + 2 + 3 or 1 (2) +2 + 4 or 2 + 3 + 4.
Criteria for Diagnosis of Clinically Diagnosed Cases

In case of any of the three following circumstances, the patient could be clinically diagnosed with SARS.

1. The patient has a history of intimate contact with patients, or is one of the infected population, or is confirmed having infecting other people by concrete evidences, who also manifest aforementioned clinical symptoms and pulmonary shadows on chest X-ray image.

2. The patient has been to or lived in areas reported with infectious SARS patients and patients suffering from secondary infections 2 weeks before the disease onset, who also have abovementioned clinical symptoms, not high peripheral blood white cell count and pulmonary shadows on chest X-ray films.

3. The patient has been to or lived in areas reported with infectious SARS patients and patients suffering from secondary infections 2 weeks before the disease onset, who also have abovementioned clinical symptoms, pulmonary shadows on chest X-ray films, and no obvious response to anti-infectious treatment.

In other words, the patient conform to aforementioned 1 (1) + 2 + 4 or 1 (2) + 2 + 3 + 4 or 1 (2) + 2 + 4 + 5.

2.7.2 Clinical Classification and Staging

2.7.2.1 Criteria for Classification of Clinically Diagnosed Cases

Light Type
The conditions are mild without pulmonary fibrosis and other sequelae. The prognosis is good.

Common Type
Patients have typical clinical manifestations of the early phase, progression phase, and recovery phase. The onset is acute, and the first symptom is fever, with body temperature generally >38 °C. Besides, the patients have no obvious respiratory distress or hypoxemia. Some patients are auscultated with slight moist rales or observed with pulmonary consolidation. The prognosis is good without sequelae.

Severe Type
Severe type accounts for about 30%. It is same with the common type in clinical process but presents severe conditions and rapid progression. Some cases may progress to acute pulmonary injury or ARDS, rapidly incurring respiratory failure or even death. The diagnosis could be reached in case of any of the following three circumstances:

1. Dyspnea adult respiratory frequency is ≥30 times /min, accompanied by one of the following conditions:
   - The chest imaging shows that the total surface of multilobar lesions or foci occupies more than 1/3 of the two lungs on orthotopic imaging.
   - Conditions progress, with the focal area increased by over 50% within 48 h or accounting for over 1/4 of the two lungs on orthotopic imaging.
2. Obvious hypoxemia is detected, with the oxygenation index lower than 300 mmHg.
3. Shock or multi-organic dysfunction syndrome occurs.

Miscellaneous
There are still some atypical cases of this disease.

2.7.2.2 Criteria for Staging of Clinically Diagnosed Cases

Early Phase
This generally refers to the first 1–7 days. The onset is acute and initial symptom is fever. Half of the patients are accompanied by the nonspecific systemic symptoms such as chillness, headache, and joint and muscular soreness.

Progression Phase
This phase spans the day 8–14 of the disease course. Infectious toxic symptoms such as fever, fatigue, muscular soreness continue to exist or even aggravate. Patient’s body temperature rises, possibly to 39 °C or higher in a short time, and the high fever is persistent. Lung lesions demonstrate progressive exacerbation. A few patients (10–15%) may develop ARDS, which is life threatening.

Recovery Phase
It mostly takes place at day 15–21 of disease course. Most patients have good prognosis after recovery for about 2 weeks. Some severe patients could gradually recover within 2–3 months after discharge.

2.8 Imaging Techniques and Protection

2.8.1 Chest Imaging Techniques of SARS

2.8.1.1 Conventional Chest X-Ray Examinations
These mainly encompass standing chest X-ray and bedside chest X-ray, which are economic and effective examination methods and first optional examination for preliminary diagnosis and reexamination. Mobile X-ray bedside imaging should be applied for patients under observation and inpatients. As lung disease of SARS patients progress rapidly,
chest X-ray reexamination within a short period could help observe changes of conditions, commonly once every 1–2 days at the early phase and progression phase. Regular chest X-ray also need to be conducted during recovery phase so as to ascertain absorption and dissipation of lesions, residual foci, and pulmonary interstitial fibrosis.

### 2.8.1.2 Chest CT Scan

For SARS patients, CT scan generally is not a preferred method and, if necessary, could be conducted under strict disinfected quarantine. If the foci could not be absorbed for a long term in SARS recovery phase or patients still have symptoms but normal chest presentations, CT scan need to be carried out for further observation as it can better visualize the subtle pulmonary interstitial changes, such as lung interlobular septum thickening, intralobular septum thickening, subpleural linear shadow, and small ground-glass-density lesion and regional and segmental bronchiectasis, and therefore is helpful for clinical diagnosis of pulmonary interstitial fibrosis. Thin-layer CT scan or HRCT scan can better visualize intrapulmonary low-density small lesions, thus contributory to early diagnosis of pulmonary interstitial fibrosis. CT examination could also aid identification of other concurrent lung lesions.

### 2.8.2 Protection and Quarantine of Department of Radiology

Medical staff in the room of imaging examination and department of radiology shall prevent infections in strict compliance with SARS disinfection and prevention requirements and meanwhile conscientiously implement X-ray protection.

#### 2.8.2.1 Protection Requirements of Photographs at Bedside or Fever Clinic

1. Ward shall be equipped with bedside X-ray machine; Imaging for all SARS inpatients shall be conducted in wards and patients shall wear masks.
2. The personal protection for imaging technician should be subject to the level-two protection requirements and, when necessary (imaging for critically ill patients), to level-three protection requirements.
3. X-ray film magazine should be put into the isolation bag before imaging (one isolation bag for each person).
4. The imaging technicians should sterilize their hands before return to the radiological department and then remove protective clothing, gloves, and protective glasses at the designated place. They should wash hands thoroughly, gargle, take a shower, and change clean working clothes before work.

#### 2.8.2.2 Disinfection and Protection of Department of Radiology

1. The department must strengthen interior ventilation and air disinfection. Ultraviolet irradiation may be assumed at night, 2–3 times per day, 30 minutes per time, and per-acetic acid spray conducted 2 times per day.
2. Rigorous isolation measures: all subjects must wear masks. The operation staff must wear protective masks, gloves, and gowns, with masks changed every 4 h and gowns replaced in time, and should use disposal bed sheet and shoe covers, and dispose of and replace them timely after the examination.
3. SARS examination zone should be separated from conventional patient examination zone and examination staff shall be fixed. If feasible, special chest X-ray examination room and X-ray machines may be set up in the isolation zone to avoid cross-infections.

#### 2.8.2.3 Protective Technical Requirements for CT Scan

1. The protective measures for subjects and operation staff are similar to those required about isolation protection in radiological department.
2. All the subjects must wear masks and, for examination in CT room, shall minimize the stay time as much as possible.
3. After the patient leaves, the environment and articles which may be polluted by patients shall be given terminal disinfection.
4. The department must enhance interior ventilation and air disinfection and, in addition to use of chemical disinfectant spray, may also initiate long-term ultraviolet irradiation at night for disinfection.
5. A pathway specific for SARS patients should be established.

### 2.9 Chest X-ray Diagnosis

#### 2.9.1 Pathological Basis of Chest Imaging Manifestations

The imaging manifestations of SARS are closely related to its pathological changes. Besides edema, inflammatory cell infiltration and other nonspecific inflammatory changes, the more prominent pulmonary pathological feature of SARS is abundant exfoliation of epithelial cells, inducing obvious thickening and damage of alveolar septum, as well as significant organization of effusions inside alveolar cavities. All the
three changes of inflammation in early phase (degeneration, exudation, hyperplasia) are observable. The mechanism of acute lung injury induced by SARS may be ascribed to SARS coronavirus direct attack of alveolar epithelia and alveolar capillary epithelia or (and) indirect damage via lymphocyte, macrophage and effector cells, and lymphokine, cytokine, and inflammatory mediator released by them. This suggests that besides viral direct infection, immune reactions are also involved in lung injury.

In severe lung injury, pulmonary interstitial and pulmonary parenchymal air cavity changes detected by autopsy pathology, especially pulmonary air cavity not completely filled by lesion or filled but coexistent with unfilled alveoli, are visualized as ground-glass-density shadows on X-ray and CT. Varying degrees of residual lung cavity present with different densities of ground-glass shadows on thin-layer CT or high-resolution CT (HRCT). Complete filling of the alveolar space leads to pulmonary consolidation shadows.

Once pulmonary edema and alveolar hyaline membrane are formed, patients clinically manifest decreased lung compliance, progressive dyspnea, and intractable hypoxemia. It is such rapid pathological changes of SARS that give rise to characteristic presentations by chest X-ray examination, including rapid progression of lesions, diverse morphological states, and wide range, often spanning several segments and lobes. Therefore, dynamic observation of chest image holds great significance for diagnosis of SARS.

2.9.2 Basic Imaging Manifestations of SARS

2.9.2.1 Ground-Glass-Density Shadows
Ground-glass-density shadows are pathologically the result of lesions mainly at pulmonary interstitium and alveoli, with pulmonary interstitial lesions frequently complicated by alveolitis. Ground-glass-density shadows incurred by alveolar consolidation are attributable to partial filling of alveoli or coexistence of filling and unfilled alveoli. Such shadows on X-ray and CT can be determined if the density of lesions is lower than that of blood vessels, and blood vessel presentations are observable inside. The density of lesions lower than that of pulmonary hila on X-ray could also help identify ground-glass-density shadows.

2.9.2.2 Pulmonary Consolidation Shadows
Pulmonary consolidation shadows are pathologically due to filling of alveoli by pathological tissues, which is frequently complicated with lung interstitial lesions. Pulmonary consolidation could be confirmed if the lesions are found with higher density than vascular shadows and without vascular shadows inside but with air bronchogram on X-ray and CT. It could also be determined if the lesions present higher density than pulmonary hila or similar density to mediastinum. The lesions are solitary or multiple in small patches, and some lesions are distributed along lung lobes and segments.

2.9.3 Chest X-Ray Manifestations of SARS

2.9.3.1 Early Phase of Onset
96% of SARS patients may develop subsequently solitary and multiple small patchy shadows within seven days of onset, with relatively low density, blurry borders, and irregular shapes, predominantly solitary. Occasionally, the pulmonary textures around lesions are revealed increased and thickened and mainly distributed at peripheral area, more commonly at bilateral inferior lungs. Since chest X-ray can poorly visualize relatively small lesions and at sometimes posteroanterior X-ray can hardly display lesions overlapping with heart shadows, orthotopic chest imaging should be conducted at the same time (Fig. 2.9).

2.9.3.2 Progression Phase
The conditions of most patients become worse within 14 days after onset. The small patchy shadows in the early phase may progress into large patchy, multiple, or diffusive lesions. The lesions may spread from unilateral lung to both lungs and from one lung field to several fields. Severe patients may demonstrate obvious changes 1–2 days after onset.

Lesions present mainly as ground-glass-density shadows or coexist with lung consolidation shadows. The center of some shadows with high density indicates consolidation, and relatively low-density peripheral area suggests ground-glass density shadows.
density which may be complicated with thickening and increase of pulmonary textures. Severe patients may develop “white lung.”

Some cases may have pneumothorax, pneumomediastinum, and subcutaneous emphysema after the use of ventilator.

A small part of lesions adjacent to the pleura may be complicated with local pleural thickening or revealed with mild tentiform adhesion. Pleural changes may reside after absorption of intrapulmonary lesions. Complication of slight pleural effusions may also be observable (Fig. 2.10).

2.9.3.3 Recovery Phase
The lesions of SARS patients begin to be absorbed in 15–30 days, which can be completely absorbed for majority patients. A few patients may show pulmonary fibrosis or pulmonary interstitial hyperplasia, with apparent pulmonary interstitial hyperplasia occurring 30–40 days after the onset. The intrapulmonary patchy shadows present with shrinkage and increase of density to gradually form high-density cord-like and honeycomb-shaped shadows in lungs. Severe pulmonary interstitial proliferation could dwindle the lung volume and make the mediastinum shift to the affected side. The imaging may reveal local irregular high-density plaque and cord-shaped shadows. Occurrence of intrapulmonary honeycomb-shaped shadows and tractional bronchiectasis is the characteristic of pulmonary interstitial fibrosis (Fig. 2.11).

2.9.4 Section Four Dynamic Changes of Chest X-Ray Manifestations
As rapid change is an important feature of SARS chest X-ray manifestations, dynamic X-ray studies and observations could provide evidences for SARS definite diagnosis. Therefore, observation of the disease dynamic change is critical to SARS chest X-ray, which is a major difference from X-ray examinations of other pneumonia. In the early phase and progression phase of SARS, lung foci may undergo remarkable changes within a short time (24 h at the shortest), such as expansion and dissemination, which are characterized by changes in shape, extent, and site of the foci. This suggests that clinical physicians shall conduct chest orthotopic imaging once every 24–48 h after the SARS patients are hospitalized so as to ascertain the disease changes.

Imaging dynamic changes are associated with multiple factors, such as age, original underlying disease, treatment method, and efficacy. The lesions are generally absorbed 14 days after onset but possibly on day 7 in some mild patients. The focal shadows may become smaller with the density gradually decreased. One characteristic dynamic change of SARS is migrating change of lesions in some patients, suggesting that the foci firstly occur at the unilateral inferior lung field and then spread to contralateral and/or superior and middle lung field. Patients with worse lesions may manifest wider imaging extent and new foci, and severe patients may develop “white lung.” ARDS is a key cause leading to death of patients (Fig. 2.12).
The male patient aged 34 years old was tested positive for specific segment RT-PCR of SARS virus RNA and was diagnosed with SARS. (a) 31 days after onset, both the middle and superior lung fields were detected with patchy and strip shadows as well as spotted shadows. (b) 38 days after onset, the foci at both superior lung fields presented with absorption and improvement, but a few linear shadows were observed. (a–e) The male patient aged 34 years old was confirmed with SARS. (a) 4 days after onset (February 12, 2003), right inferior lung and left middle lung field was detected with large patchy and strip shadows, which had inhomogeneous density and blurry borders. (b) 6 days after onset, the foci at both lung fields expanded obviously to inferior lung field, which presented light-density patchy and strip shadows with migrating changes. (c) 10 days after onset, partial foci at both lung fields were absorbed and improved and became lighter in density, with absorption of right inferior lung field foci more obvious. (d) On day 13 of onset, foci at right inferior lung field were absorbed and improved and both superior lung fields were observed with ill-defined patches and strips of increased density. (e) On day 26 of onset, the blurry patchy and strip shadows on both superior lung fields were visualized with lighter density and slight shrinkage.
2.10 Chest CT Diagnosis

2.10.1 CT Manifestations of SARS

Lung imaging examination is an important basis for SARS diagnosis, and continual imaging examination could visualize the dynamic change characteristics of the disease.

2.10.1.1 Initial Phase

After SARS infection, chest abnormal changes frequently occur on day 1–7. In initial phase, focal shadows are frequently seen, which might be unilateral but dominantly bilateral. CT reveals small patchy ground-glass-density shadows, some of which are quasi-circular. Lesions present as solitary small patchy lung consolidation and multiple small patchy or relatively large patchy shadows. Large foci may appear as
ground-glass-density shadows and concurrent lung consolidation shadows, with relatively higher-density vascular shadows observable in the former. Besides, some foci are found with increased vascular shadows at the periphery. In addition, lesions are unveiled frequently at the bilateral lung inferior fields and lung margins (Fig. 2.13).

2.10.1.2 Progression Phase

Lesions in majority patients may progress and worsen within 14 days after onset. The small patchy shadows in early phase could expand into large patchy, multiple, or diffusive lesions within 3–7 days. Besides, lesions extend from unilateral lung to bilateral lungs, from one lung field to multiple lung fields. Most patients could develop the severest infiltration of lungs on day 8–14, namely, peak phase or “critical” phase. CT presentations are still predominated by ground-glass-density shadows, which may be complicated by pulmonary consolidation. Lesions are commonly multiple and in diffusive distribution at both lungs, and lesions of varying shapes may coexist, with quasi-circular foci relatively common. Some cases appear with ground-glass-density shadows all the time from onset to absorption of lesions.

When ground-glass-density shadows are complicated by pulmonary consolidation, the large patchy, small patchy, or quasi-circular ground-glass-density shadows could be observed with pulmonary consolidation shadows of relatively high density. Ground-glass density and pulmonary consolidation may also occur at different parts of the lung and could be visualized on the same layer or different layers of CT. For lesions typical of pulmonary consolidation, pulmonary consolidation appears as plaque-shaped high-density shadows or consolidation signs at lung lobes and segments. In addition, lesions are frequently recorded at lung lobe segment of the inferior lobe and outer band of lung field (Fig. 2.14).

2.10.1.3 Recovery Phase

Lesions usually begin to be absorbed 2–3 weeks after onset, with the shadow shrunk and density gradually reduced and absorbed. Although the clinical symptoms of some patients improve and disappear, light ground-glass-density shadows could still be seen in lungs on CT. It may prolong a relatively long time. During the absorption of intrapulmonary lesions, there is also concurrent pulmonary interstitial proliferation, which begins to be absorbed under dynamic observation. Some lesions may develop into pulmonary interstitial fibrosis, characterized by lobular septum, intralobular septum, interstitial thickening, and subpleural curvature imaging signs as well as regional irregular high-density plaque and cord-like presentations. Occurrence of intrapulmonary honeycomb manifestations and tractional bronchiectasis signifies pulmonary interstitial fibrosis (Fig. 2.15).

2.11 Imaging Diagnosis of Complications

SARS complication is an important factor affecting prognosis, which should be given enormous attentions. During SARS treatment, antiviral drugs are administered as well as glucocorticoids and broad-spectrum antibiotics. Some patients may still need airway positive pressure ventilation, tracheotomy, and tracheal intubation. Reasonable use of such measures is of great significance for improving the treatment rate and lowering mortality of SARS patients. However, to be noted, such treatment drugs and methods may incur adverse reactions and cause complications. SARS complications already detected encompass pulmonary secondary infection, mediastinal and subcutaneous emphysema, pneumothorax, bone aseptic necrosis, empyema, brain secondary infection, and pulmonary interstitial
fibrosis. Such complications or sequela changes are also mainly identified by imaging examinations. Familiarity about SARS imaging manifestations and knowledge about complication imaging presentations could elevate SARS diagnostic level, therefore increasing cure rate and decreasing mortality.

2.11.1 Imaging Diagnosis of Pulmonary Interstitial Fibrosis

2.11.1.1 Pathogenesis and Clinical Data

In the early phase, SARS manifests bronchiolar and peripheral interstitial pneumonia, which could further progress into
alveolar consolidation, with interstitial lesions present persistently and mostly reversible. In the recovery phase, only some cases develop into pulmonary interstitial proliferation and then cause fibrotic changes. Pulmonary interstitial proliferation and fibrosis degree and outcome are associated with the extent of pulmonary involvement in peak phase, occurrence of complications, and treatment. Generally, if lesions on chest image are light in peak phase, there will be fewer pulmonary changes left in recovery phase. Contrarily, patients with diffusive lung interstitial thickening in recovery

Fig. 2.15 (a–e) The male patient aged 44 years old was confirmed with SARS. On day 82 of onset (April 16, 2003), chest CT plain scan revealed cord-like shadows and ground-glass-density shadows at the left lung superior segment ligule and right lung inferior lobe antero-basal segment. Right lung middle and inferior lobe was detected with lobular septum thickening and subpleural curvature shadows.
phase are often those suffering from relatively severe pulmonary injury in peak phase and involvement of the great mass of lungs, particularly patients with recurrent conditions, protracted course, and concurrent infections. Researches demonstrate that 7–8% of SARS patients have pulmonary fibrosis of varying degrees and male patients display relatively more obvious pulmonary impairment than female patients. Primary manifestations are lung dysfunction, such as decrease of pulmonary diffusion capacity, lung capacity impairment, and change of total lung capacity particularly residual volume.

2.11.1.2 Imaging Manifestations
Generally obvious pulmonary interstitial proliferation occurs at about 30–50 days after onset, which presents firstly lobular septum and intralobular thickening and subpleural curvature shadows. Then there is the shrinkage of intrapulmonary patchy shadows with increase of density and gradual formation of high-density cord and honeycomb shadows inside lungs. Severe pulmonary interstitial proliferation could diminish lung volume and compel the mediastinum to affected side. Besides, pulmonary interstitial proliferation could occur extensively inside lungs, predominated by lobular septum, intralobular interstitial thickening, and subpleural curvature shadows, as well as irregular high-density plaque and cord-like shadows at some regions. Honeycomb-shaped shadows and tractional bronchiectasis are signs of pulmonary interstitial fibrosis. CT reveals cord, reticulate, and honeycomb-shaped shadows, and HRCT could better visualize the subtle abnormal changes of pulmonary interstitium, such as lobular septum thickening, intralobular interstitial thickening, subpleural curvature shadows, and honeycomb-shaped shadows. Whether the cord-like and reticulate changes visualized by CT are completely absorbed or induce persistent fibrosis still entails long-term follow-up observation (Fig. 2.16).

2.11.2 Aseptic Necrosis of Femoral Head
2.11.2.1 Pathogenesis and Clinical Data
Numerous SARS patients develop osteonecrosis after recovery, which mostly appears as femoral head necrosis and also possibly necrosis of the ankle joint, knee joint, and shoulder joint. Scans of bilateral hips and knees of 82 SARS patients in rehabilitation phase disclosed that 51 patients (62%) suffered from osseous abnormality, of which bone ischemia accounts for 17% and implication of three sites for 20%. Its pathogenesis still remains not completely ascertained, and it may be ascribed to improper use of hormones and injury of sclerotin from SARS viruses, bacterial embolism, lipid embolism, or multiple mixed factors. The primary pathological change of aseptic necrosis of femoral head is degenerative alteration due to femoral head blood circulation disturbance, mainly characterized by limping and pain. The lower limb of the affected side is relatively shorter and presents with light flexion and adduction, as well as with slightly limited abduction and intorsion.

2.11.2.2 Imaging Manifestations of Aseptic Necrosis of Femoral Head
Initial X-ray examinations suggest that the involved femoral head has normal appearance but inhomogeneous density, with spotted osteoporosis. Gradually ensue the increase of density as a result of osteonecrosis, which meanwhile is interspersed with some transparent shadows. Femoral head may become flat, fragmented, and irregular in contour from pressures. Typical femoral head necrosis appears in the shape of wedge, with the base toward articular surface and the top toward metaphysis. Since lesions are dominantly confined at the anterosuperior area of femoral head, lateral imaging of hip joints could clearly reproduce the extent of lesions. The necrotic area is encircled by a ring of transparent band. Hip articular cavity may become wider and irregular due to flattening of the femur. Sometimes, there may be complication of dislocation. The fragments of femoral head may be shed off into the joint, giving rise to joint mouse.

Normal femoral head is located at the acetabular center in the transverse CT image and may appear in the shape of sphere or hook on different layers, with delicate high-density bone cortex at the periphery. The high-density trabeculae inside femoral head are arranged in stelliform formation from the center continually to bone cortex, named as “stelliform sign.” CT manifestations of aseptic necrosis of femoral head can be divided into early and advanced phase. In the early phase, the stelliform sign formed by the trabeculae of femoral head is deformed or absent, presenting spotted and patchy shadows of increased density inside femoral head and fasciculate changes or mutual fusion at its periphery. In the advanced phase, femoral head become ruptured and out of shape, and absorption of sclerotin between bone fragments appears as irregular low-density area, with stelliform sign disappeared.

MRI manifestations of aseptic necrosis of femoral head include: necrotic areas of femoral head of early cases have no repair reactions or mechanic collapse and still maintain normal lipid signals of medullary bones. However, low-signal margins incurred by sclerosis reactions could be seen at the periphery of foci. The T1 high signals of normal femoral head on T1-weighted image are detected with black linear low signals (representing demarcation between normal and ischemic bone tissues). On T2-weighted image, a high-signal line is visible at the medial low-signal sclerotic reaction line, thus forming the typical double-line sign. The double-line sign could reflect congestion and inflammation of granula-
tion tissues and proves specific to aseptic necrosis of femoral head. Severe inflammation, congestion, fibrosis, and sclerosis could greatly deplete the amount of lipids of femoral head, which presents liquid-like signals on MRI, low signals on T1-weighted image, and high signals on T2-weighted images. Advanced cases are typical of fibrosis and sclerosis, and the affected area present with fibrotic MRI features, that is, low signals on T1- and T2-weighted and proton density-weighted imaging. Complication with effusions in hip joints appears as T1 low signals and T2 high signals.

Based on MRI presentations, aseptic necrosis of femoral head could be classified into four phases: phase I is characterized by homogenous or inhomogeneous low-signal areas adjacent to the joint above the femoral head on T1-weighted imaging; phase II is visualized with wedge-shaped low-signal bands; phase III presents with sequestrum crescent sign and cortex collapse; phase IV manifests joint degeneration and joint space narrowing besides presentations of phase III. In light of the aforementioned MR staging criteria, SARS cases complicated by aseptic necrosis of femoral head already reported are mostly in phase II.

Additionally, aseptic necrosis after use of hormones, besides most frequently involvement of the femoral head, could also implicate other joints, such as the knee joint, elbow joint, ankle joint, and acetabulum. Therefore, if necessary, MR examinations of other joints shall be conducted to ascertain the extent and degree of lesions. If SARS patients complain of pain at both hip joints and limited movement, CT scan or MRI examination of both hip joints is recommended to conclude definite diagnosis. X-ray plain scan is not sensitive to early bone ischemic necrosis, which therefore is not preferred (Fig. 2.17 and 2.18).

Fig. 2.16 (a–c) The female patient aged 54 years old was detected with SARS complicated by pulmonary interstitial fibrosis. On February 20, 2003, the patient had continuous fever, cough without sputum but accompanied with shortness of breath. The patient was hospitalized on March 4, 2003, and cured and discharged on May 15, 2003. On July 21, 2003, CT revealed scattered plaque shadows of increased density, subpleural curvature shadows, and other pulmonary interstitial fibrosis presentations at both lung fields.

2 SARS
Fig. 2.17  (a–f) The male patient aged 28 years old was examined with SARS and concurrent ischemic necrosis of right femoral head. Methylprednisolone 1880 mg was administered. (a) Early chest imaging demonstrated band or patchy blurry shadows in the left inferior lung field. (b–f), 33 months after onset, CT visualized irregular low-density damaged area at the right femoral head and neck.
The female patient aged 40 years old was confirmed with SARS complicated by left femoral head ischemic necrosis. Methylprednisolone 4180 mg was given. (a) On day 15 after onset, both middle and inferior lung fields were seen with large patchy irregular color shadows of increased density. (b) On day 32 after onset, X-ray plain scan indicated bilateral femoral heads free of obvious abnormalities in shape and density. (c) On day 40 after onset, axial CT scan suggested bilateral femoral heads without obvious abnormalities in shape and density. (d) On day 185 after onset, MRI T1WI revealed left femoral head with linear T1 low signals. (e) On day 185 after onset, MRI T2WI visualized left femoral head with wedged-shaped T2 high signals.
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