Patient 1

A 28-year-old obese woman (body mass index [BMI], 57 kg/m2) presented to the emergency department (ED) with a history of 5 days of sore throat, lethargy and myalgias, and a clear chest x-ray, followed by 2 days of dyspnoea, productive cough, and pleuritic chest pain. She was febrile (40°C), and had tachypnoea (respiratory rate, 36 breaths/min) and hypoxia (oxygen saturation measured by pulse oximetry [Spo2], 87% on 15 L/min oxygen via face mask). Her admission chest x-ray showed widespread alveolar infiltrates. She had a normal white cell count (WCC) of 6.3 × 109/L, but an elevated serum C-reactive protein (CRP) level of 221 mg/L (reference ranges shown in <u>Box 1</u>). She was admitted to the intensive care unit (ICU) and, after a brief trial of non-invasive ventilation (NIV), was intubated and treated with mechanical ventilation (MV) with a fraction of inspired oxygen (Fio2) of 1.0 and positive endexpiratory pressure (PEEP) of 20 cm H2O for the first 24 hours to maintain an Spo2 > 89%. She was treated with inotropes for septic shock and with renal replacement therapy for acute renal failure. Therapy with oseltamivir in addition to empiric broad-spectrum antibiotics was commenced. Bacterial cultures of blood, urine and tracheal aspirate were negative. The result of a test for urine pneumococcal antigen was negative. The patient was successfully weaned from ventilatory support on Day 14.



Patient 2

A previously well 24-year-old man (BMI, 22 kg/m2) was admitted to a regional hospital with a 1-week history of dry cough, fever, headache, abdominal pain, and vomiting. Thirty-six hours later, he was transferred to a metropolitan hospital because of worsening dyspnoea and hypoxia (Spo2, 88% on 15 L/min oxygen via face mask). He had tachycardia (110 beats/min), tachypnoea (respiratory rate, 34 breaths/min) and was febrile $(39.9^{\circ}C)$. He had a normal WCC $(4.2 \times 109/L)$ but an elevated CRP level (256 mg/L). A chest x-ray showed unilateral lobar consolidation. He was transferred to the ICU and treated with oseltamivir, broadspectrum antibiotics, and NIV with an Fio2 of 1.0. After 96 hours, his hypoxia remained severe (partial pressure of arterial oxygen [Pao2] to Fio2 ratio, < 100), another chest x-ray showed bilateral alveolar infiltrates, and he was intubated and MV was commenced with an Fio2 of 1.0 and high-level PEEP (20 cm H2O) for several days. Bacterial cultures and urine pneumococcal antigen test results were negative. Oseltamivir therapy was continued for 7 days, and MV for 15 days.



Patient 4

A previously well 41-year-old man (BMI, 30 kg/m2) presented with a 7-day history of cough, coryza, malaise, back pains and rigors. On the day of presentation, he became febrile (39.6°C) and developed tachypnoea (respiratory rate, 45 breaths/min) and severe hypoxia (Spo2, 84% on 10 L/min oxygen via face mask). His chest x-ray showed widespread pulmonary infiltrates. He had a WCC of 4.4 × 109/L and a CRP level of 166 mg/L. He was intubated in the ED and MV was commenced, and he was given oseltamivir and broad-spectrum antibiotics. He remained severely hypoxic (requiring an Fio2 of > 0.8) for 10 days, and was treated with MV in the prone position and inhaled nitric oxide. His condition gradually improved, and he was extubated on Day 13.



Patient 4

A 26-year-old obese man (BMI, > 40 kg/m2) with a history of mild asthma presented after 2 days of nausea without vomiting, and no fever or cough. On the day of admission, he developed shortness of breath. He was found to be hypoxic (Spo2, 90% on an Fio2 of 1.0) with bilateral pulmonary infiltrates showing on a chest x-ray. His WCC was 5.6 × 109/L and CRP level was 137 mg/L. Therapy with broad-spectrum antibiotics and oseltamivir was commenced. He was intubated, and MV was commenced with an Fio2 of > 0.6 and high-level PEEP (15 cm H2O); the patient was successfully extubated after 10 days.



Patient 5

60-year-old man presented to hospital with an exacerbation of his severe chronic obstructive pulmonary disease (COPD). He also had severe peripheral and coronary vascular disease. On examination, he had tachypnoea (respiratory rate, 36 breaths/min) but no fever. He had no prodrome of coryza or myalgias, and a chest x-ray showed mild bibasal opacities. His WCC was elevated (11.4 × 109/L), but his CRP level was 12 mg/L. He was admitted to the respiratory ward and treated with oseltamivir, broad-spectrum antibiotics, and NIV. Two days later he was intubated, and MV was commenced for hypercapnic respiratory failure. Bacterial cultures were negative. His hypoxia was mild (requiring an Fio2 of < 0.5), but he required MV for 14 days.



Patient 6

An 18-year-old pregnant woman presented with a 4-day history of cough, fever, and persistent vomiting without diarrhoea. Oseltamivir therapy for possible H1N1 influenza infection was discussed with the patient, but not administered. After intravenous rehydration, she was discharged home, but she returned several hours later in premature labour. Her WCC was 8.2 × 109/L but her CRP level was high (90 mg/L). She was given steroids for fetal lung immaturity and transferred to a tertiary obstetric/neonatal hospital. Twenty-four hours after delivering a 26-week live infant, she developed hypoxic respiratory failure with tachypnoea (respiratory rate, 35 breaths/min) and bilateral pulmonary infiltrates. She required a high level of inspired oxygen therapy (Fio2, o.6) by face mask, and monitoring in the ICU. The mother, but not her baby, had a positive polymerase chain reaction (PCR) test result for H1N1 influenza 09, and both were treated with broad-spectrum antibiotics and oseltamivir.



Patient 6

An 18-year-old pregnant woman presented with a 4-day history of cough, fever, and persistent vomiting without diarrhoea. Oseltamivir therapy for possible H1N1 influenza infection was discussed with the patient, but not administered. After intravenous rehydration, she was discharged home, but she returned several hours later in premature labour. Her WCC was 8.2 × 109/L but her CRP level was high (90 mg/L). She was given steroids for fetal lung immaturity and transferred to a tertiary obstetric/neonatal hospital. Twenty-four hours after delivering a 26-week live infant, she developed hypoxic respiratory failure with tachypnoea (respiratory rate, 35 breaths/min) and bilateral pulmonary infiltrates. She required a high level of inspired oxygen therapy (Fio2, o.6) by face mask, and monitoring in the ICU. The mother, but not her baby, had a positive polymerase chain reaction (PCR) test result for H1N1 influenza 09, and both were treated with broad-spectrum antibiotics and oseltamivir.

