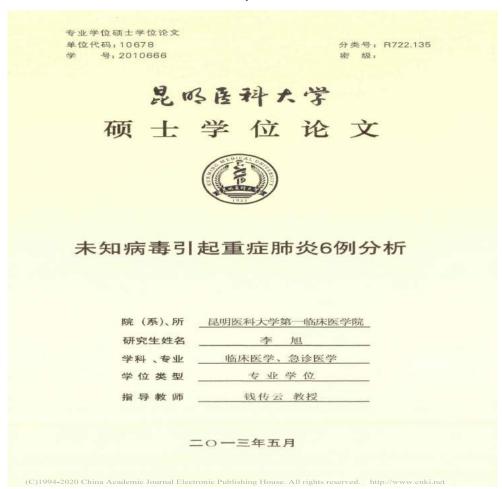
## Master's Thesis

### "The Analysis of Six Patients With Severe Pneumonia Caused By Unknown Viruses"

School/ College: No. 1 School of Clinical Medicine, Kun Ming Medical University Student's Name: Li Xu
Study field: Clinical Medicine and Emergency Medicine
May, 2013



Translation note: This translation was commissioned by *Independent Science News* (<a href="https://www.independentsciencenews.org/">https://www.independentsciencenews.org/</a>). Where the author (Li Xu) provided it, we have preserved the original English text (e.g. The Title and the Abstract). Page numbers match the original pdf file. Thesis accessed June 10th 2020.

# 見吸を科大学 硕士学位论文

#### 未知病毒引起重症肺炎 6 例分析

甲谓人姓名	<u> </u>
学科、专业	临床医学、急诊医学
申请学位类型_	专业学位
指导教师_	钱传云 教授

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#### **Kun Ming Medical University**

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#### 英文缩略词表

英文缩略语	英文全称	中文全称
Т .	temperature	体温
PR	pulse rate	脉率
RR	respiration rate	呼吸频率
ВР	blood pressure	血压
HR	heart rate	心率
CT	computed tomography	计算机断层扫描
CRP	C reactive protein	C 反应蛋白
PCT	procalcitonin	降钙素原
SAA	serum amyloid A protein	血清淀粉样蛋白 A
DD	D-dimer	D-二聚体
FDP	fibrin degradation product	纤维蛋白降解产物
PaCO <sub>2</sub>	partial pressure of carbon dioxide	二氧化碳分压
PaO <sub>2</sub>	partial pressure of oxygen	血氧分压
PH	hydrogen ion concentration	氢离子浓度指数
PF	oxygenation (PaO <sub>2</sub> /FIO <sub>2</sub> ) index	氧合指数
RLS	reaction leuel scale	机体反应水平分级
BNP	brain natriuretie peptide	B型尿钠肽
PCR	polymerase chain reaction	聚合酶链式反应
HIV	human immunodeficiency virus	人类免疫缺陷病毒
INR	international normalized ratio	国际标准化比值
ECG	electrocardiogram	心电图
DNA	deoxyribonucleic acid	脱氧核糖核酸

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RNA	ribonucleic acid	核糖核酸
ICTV	international committeeon taxonomy of viruses	国际病毒分类委员会
ARDS	acute respiratory distress syndrome	急性呼吸窘迫综合征
SARS	severe acute respiratory syndrome	严重急性呼吸综合征
SARS-CoV	SARS coronavirus	SARS 冠状病毒
SARS-like-CoV	SARS like coronavirus	SARS 样冠状病毒
ICU	intensive care unit	重症加强护理病房

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#### 未知病毒引起重症肺炎 6 例分析

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#### 摘要

2012年4月、5月,我院先后收住6例未知病毒引起相关重症肺炎患者。此6位患者均为同一矿洞工人,工作环境中接触大量蝙蝠及蝙蝠粪便。最终结局3位患者死亡,3位患者存活。据中国科学院昆明动物研究所鉴定,此6位患者工作矿洞内蝙蝠正为中华菊头蝠,然而我国科学家在寻找SARS病原的过程中,在中华菊头蝠体内提取出了SARS样冠状病毒(SARS-like-CoV)。本文针对6例患者所感染未知病毒相关重症肺炎的诊治过程及可能引起的病因、病原学进行推断与分析。

关键词:重症肺炎、蝙蝠、SARS 样冠状病毒

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# The analysis of 6 patients with severe pneumonia caused by unknown viruses

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#### Abstract

There were 6 patients with severe pneumonia caused by unknown viruses—sent to Dep. Emergency, the first affiliated hospital of Kunming medical university in April, May, 2012. They were all workers at the same mine where had a lot of bats and bats' feces. After the treatment, 3 patients died and 3 patients survived.

According to the appraisal of the Kunming institute of zoology, Chinese academy of sciences, the type of the bat in mine where 6 patients worked is Rhinolophus sinicus, from which was extracted SARS-like-CoV when Scientists in China were in the process of looking for SARS pathogen. The article aims at making an inference and analysis on the diagnosis and treatment process and the may causes, etiology of 6 patients with severe pneumonia related to infection by the unknown viruses.

Keywords: severe pneumonia, bats, SARS-like-CoV

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#### Case 1

Patient Zhou, male, age 63, was admitted to the hospital on April 26, 2012. He had signs of fever, coughing, difficulty in breathing, chest pain, and hiccups for more than ten days. 24 days prior to the hospitalization, he was working in the mining well for half of a month. He worked 7 hours a day. After exposing to the mining well where there were many bats and bats' feces, he started to show signs of coughing and fever and had a 38 Celsius body temperature. He immediately went to the local hospital. His fever went on and off in the next five consecutive days. The actual treatment remained unknown. The highest body temperature was 40 Celsius and the lower is 37 Celsius. He also experienced headache, dizziness, ear congestion and dry cough. There was no pattern of his illness in daytime or night time, along with chest pain. Difficulty in breathing was getting worse. Occasionally, having hiccups. No sign of nausea, vomiting, or diarrhea. To pursue more treatment, the patient was admitted to my department. Since the onset of the disease, the patient had felt lethargic. He has insomnia and loss of appetite, but regular bowel movement and urination. Self-reported that he did not have a history of high blood pressure, diabetes and heart disease or other chronic diseases, nor did he have hepatitis, typhoid or any other contagious disease. He did not have surgical operation, trauma, and blood transfusion in the past. He was not allergic to any medication or food. His vaccination record remained unknown. Physical checkup: body temperature is 37.8 Celsius, pulse rate: 74 times/minute, respiratory rate: 20 times/ minute, blood pressure: 110/63 mmhg. The patient stays alert and could answer all the questions. No sign of malnutrition or obesity. He was sent to the room by stretcher. Skin and mucous membranes remained normal, and so were the pupils. They were 3mm in diameter. The pupils remained sensitive to light. The chest and respiratory movements were symmetrical. The breathing sounds were rough. Dry crackles were heard on both bases of the lung. His heart rate is 74 beats/minute, regular heart rate and no heart murmur from any of the heart valves. Softness of the abdomen, no pain when pressured, no rebound tenderness, or guarding. Normal bowel sound: 5 times/minute. No inflammation at the lower part of the legs. Regular body reflex. No pathological reflexes. The blood report from 04/25/2012: WBC12.10X10<sup>9</sup>/L, N%89.3, Hemoglobin: 178g/L; Comprehensive Metabolic Panel was CRP 20.3 mg/L, blood ammonia: 43 umol/L; Normal result on the coagulation report. As the CT scan showed, there was extensive and patchy consolidated exudate bilaterally, elevated bronchovascular shadows and lung markings, some nodules in different sizes, parts were calcified. Mediastinal lymph node enlargement, partially calcified.

Initial Diagnosis: 1. Fever, coughing, dyspnea, hiccup 2. Hyponatremia; 3. Malfunctioning in liver and bladder

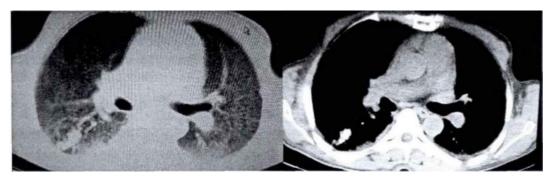
#### Method

The examination after hospitalization:

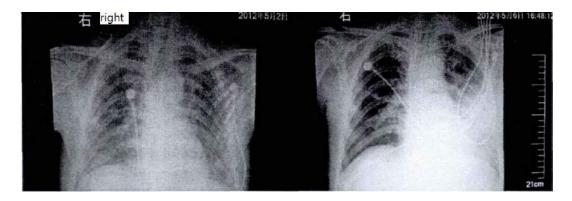
2012/4/25 Computed tomography report: extensive and patchy consolidated exudate over bilateral lung, increased Broncho vascular shadows and lung markings, some nodules in different sizes, parts were calcified. Mediastinal lymph node enlargement, partial were calcified.

2012/4/30 CT report: 1. No noticeable changes in the lung, little pleural effusion in both lungs...

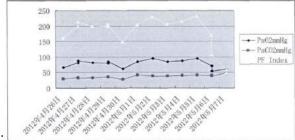
Pleural thickening posteriorly, and the rest was the same as the previous report. 2. As the scan showed, there was little ascites (see below).



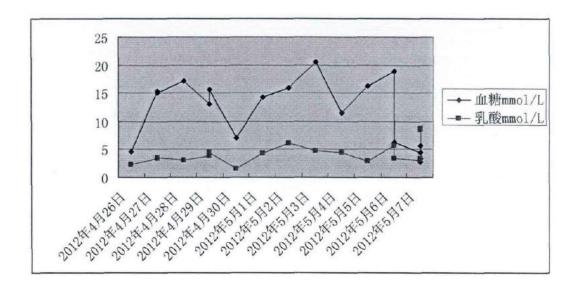
2012/5/2 bedside chest film: 1. Bilateral Lung markings worsening and getting blurry, and there were shadows of the clot. Nodular shadow was noted in 2<sup>nd</sup> intercostal space of right middle lobe, and a small opacity was over left hilar region. Requested a follow up examination after the clinical anti-inflammation treatment. 2. The outline of the heart is not too big 3. The diaphragm remains normal (see the left picture below).



2012/5/6 bedside chest film: 1. Bilateral Lung marking augmentation and getting blurry, and there were shadows of the clots. Increased laminar density in the middle and lower field of the left lung, the hilum of both lungs are blurred. Requested a follow up examination after the clinical anti-inflammation treatment. 2. Aorta is circuitous and the outline of the heart is normal. 3. Fluid in the left side of the pleural cavity and need to be evacuated. Please cooperate with the clinic (see the right picture on top). 2012/4/26 - 2012/5/7: Analysis on the arterial blood gas (see



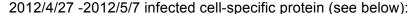
below):

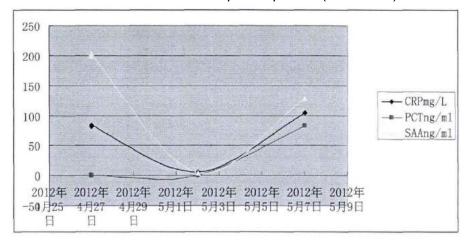


2012/4/27 tumor protein chip shows ferritin is 484.86 (Normal male < 322 microgram/ L ), Human chorionic gonadotropin is 0.65 (normal< 3.0 microgram/ L), prostate Specific Antigen is 0.02 (normal< 0.1 microgram/L) carbohydrate antigen 125: 42.22 (normal < 35.0KU/L).

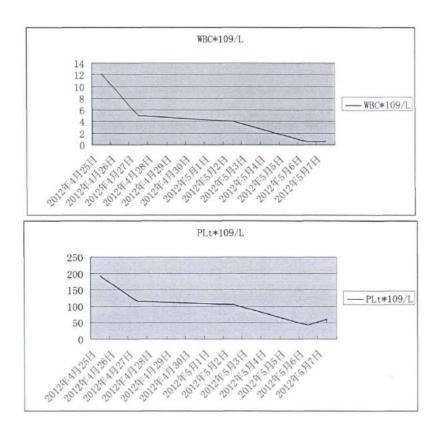
On 2012/4/27, the Widal test and WFR test both came back negative. Results for Herpes simplex virus, EB virus and CMV are all negative. Urine culture is negative and so is Ghb. The stool test is also normal. Autoantibody and anti-nuclear antibodies are both negative. 2012/4/24 report: compliment C3C4 has decreased; Glucose in Urine 4+, Ketone is negative. Thyroid test positive.

2012/4/27 - 2012/5/7: D-dimer reports 7.2 ug/ml (Apr, 27), D-dimer 3.6 ug/ml (May, 2), D-dimer 7.0 ug/ml (May, 6), D-dimer 5.0 ug/ml (May, 7).





2012/4/25 - 2012/5/7 white blood cell and blood platelet (see below):



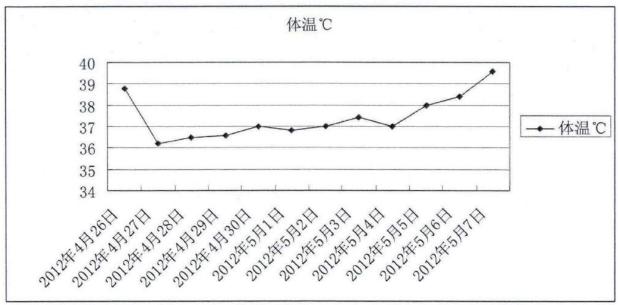
#### T, B, NK lymphocyte percentage and count (see below )



2012/4/27 sputum culture and blood culture were both negative (three times). 2012/5/7 blood culture implies positive for Acinetobacter baumannii and negative for candidiasis 2012/5/7 sputum culture Acinetobacter baumannii, pan resistant 2012/5/6 ultrasound reports severe ascites

2012/5/7 Ascites. Result of tumor cell testing is negative. Gram positive in cultivation ascites regular test is negative. The Rivalta test is also negative.

#### Body temperature chart (see below):



#### Prescription after admission:

2012/4/26 – 2012/5/2 (J) Methylprednisolone 80mg, ivgtt, Q 12h.

21012/5/2 – 2012/5/7 (J) Methylprednisolone 40mg, ivgtt, Q 12h.

2012/5/7 – death (J) Methylprednisolone 80mg, ivgtt, Q 12h.

2012/4/26 – 2012/5/2 Meropenem 0.5gx2 shots, ivgtt, Q8h.

2012/5/7 – death Meropenem 0.5gx2 shots, ivgtt, Q8h.

2012/5/7 – death Vancomycin 0.5gx2 shots, ivgtt, Q12h.

2012/4/26 – death L - Voriconazole 0.1gx 2 shots (double the dosage on the first day), ivgtt, Q12h.

2012/4/26 - death Acyclovir 0.25g\*2, ivgtt, Q8h.

#### **Discussion**

The patient worked from the mining site since 2012/4/2 for up to 14 days.

Patient admitted to the hospital: 2012/4/26. Patient discharged: 2012/5/7. Total days: 12 days.

Discharged Diagnosis: 1. Severe lung infection 2. Sepsis 3. Septic shock and infection in abdominal cavity 4. Asystole and stop breathing

Discharge reason: death

According to CT and Chest radiograph, the illness was progressively developed.

As the analysis on the arterial blood gas shows, during hospitalization, the patience had Type I respiratory failure. Oxygenation index was poor. According to the "ARDS Berlin Criteria" in 2012, for sure it was ARDS. Consequentially, one of the causes of death could be respiratory failure.

According to several researches from either abroad or domestically, glucose variability is associated with rate of prognosis or death. During the hospitalization, the patient was given intensive insulin treatment by our department. We tried to keep the blood sugar between 6-10 mmol/L. However, the patient's glucose varies, poor prognosis.

The result for tumor protein chip came back positive, which means the patient had tumor related disease. As a result, the systems of the whole body was impacted.

After the patient was admitted to the hospital, WBC and PLt were constantly decreasing. Indicated by other virus infection related researches, WBC, PLt, T, B, NK Lymphocyte percentage and count of the patients are also decreasing. It shows that the immune system of the patient was impaired, had poor resistant to the disease and could easily be infected by hospital-acquired infection.

The day the patient died, the blood and mucus culture showed Acinetobacter baumannii, severe ascites. There was Gram-positive bacteria in ascites culture. On the same day, the PCT report was 83.30ng/ml. As a result, one of the causes of death is septic shock. (severe lung infection and abdominal cavity infection).

After admitted, the patient's D-dimer was 7.2 ug/ml (Apr, 27), 3.6 ug/ml (May, 2), 7.0 ug/ml (May, 6) and 5.0 ug/ml (May, 7). The patient was bed ridden after admitted to the hospital and also had tumor. The oxygen level in the blood was significant low two days prior to his death. There was a possibility of pulmonary thromboembolism. However, the patient was severely ill, it was not recommended to have an intensified chest CT checkup. Therefore, acute pulmonary infection could be one of the causes of death. The family of the patient refused the autopsy procedure.

After the suspension of Meropenem on May 2, 2012, the patient was no longer treated with any antibiotics. His temperature went back up right after. Therefore, antibiotics play an important role in the treatment.

Cause of death analysis: the patient was the oldest out of the six patients and had some tumor related disease. His immune system was weak so had a poor body resistant to the disease. The disease was acute and fierce.

#### Case Two

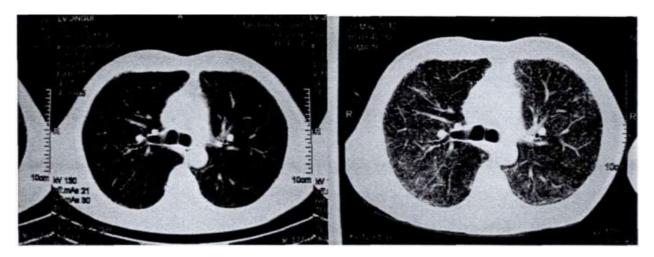
Patient Lu. Male. 42 years old, was admitted to the hospital on April 25, 2012. He had fever and been coughing for half of a month and for the past three days had difficulties in breathing. He worked in the mining hole before and was exposed to large amount of feces of bats. Half of month ago, he started to have fever. His body temperature was 38.5 Celsius at first. Occasionally, when he coughed, there was rusty colored mucus with blood clots. Felt bloated in the stomach, loss of appetite and hiccup. He initially went to the small clinic for transfusion but it was not helpful. Then, he was transferred to Yu Xi People's Hospital for treatment. During hospitalization, his body temperature was 40 Celsius and the fever did not follow any pattern. No sign of chills before the fever. Still coughed with rusty-colored mucus and blood clots. Difficulty in breathing for three days, especially after moving around. Chest tightness but no chest pain. No problem lying down. No sign of paroxysmal dyspnea at night. No abdominal pain. No visible hematuria. No history of high blood pressure, diabetes, coronary heart disease or stroke. He was born in Zhao Tong, Yun Nan and had been to Mo Jiang. He worked in the mining field prior to the illness and was exposed to large amount of bats' feces. Five of his colleagues had similar illness. He denied hepatitis, typhoid, tuberculosis or any other infectious disease. No history of blood transmission or allergy reaction. The vaccination report remained unknown. On examination: 36.6 Celsius, Pulse 110 times/ minute, Respiration rate 32 times/ minute, blood pressure 98/55mmHq, in poor condition. He was sent into the ward on a stretcher. Reaction level scale was rated 1. No deformation on the head and features. The pupils were big and round with 3 mm diameter. He was sensitive to the lights. Soft neck, no rigidity. Airway was in the center. The chest looked symmetric from the outside. Rough breath sounds bilaterally, and moist crackles were heard on both bases of the lung. The breathing sounds rough. Moist rales from the bottom of the lungs. Heart was in normal size. Heart rate 110 times/ minute, regular rhythm, no murmur, rubs or gallops. Abdomen soft, non-tender. Normal bowel sounds: 3 times/minute. Did not notice any rashes or eschar. No inflammation on the legs. Muscle strength and tension remained normal. Additional checkup: According to the CT from Yu Xi People's hospital on April 25, 2012: severe pneumonia over bilateral lung. The bottom of the left lung had limited pulmonary emphysema and bullae in the right lung; HBsAg (+), HbeAb (+), HbcAb (+). Our blood gas analysis shows pH 7.431, PaO<sub>2</sub>66.2mmHg, Oxygenation Index 162, lactic acid 1.7 mmol/L. Potassium in the blood 4.04mmol/L. Sodium in the blood 134.7 mmol/L.

Initial diagnosis after admission: 1. Severe pneumonia 2. Type I respiratory failure 3. Sepsis 4. Hepatitis B

Method (Some of the information was missing)

After admission, the complete examination:

Chest CT on 2012/4/30: 1. Increased lung markings, blurry and noticed multiple nodular shadows. Bilateral lung patchy exudate. 2. Mediastinal lymph node enlargement, regular heart shadow. Did not notice any abnormal in the artery. (see the left picture below)



2015/5/29 CT reports: Compared to the scan on 2015/5/23 about the treatment on bilateral lungs, marked interstitial opacities and exudation in both lungs. No significant increase of fibrosis. Scant pericardial effusion as before, same as the old scan (right picture above).

2012/5/7 CT reports: 1. increased of lung marking and more opacities same as before. Spotted multiple shadows of nodules spread across. The exudation seemed to recover a bit. 2. Inflammation of the mediastinal lymph node is the same as before. So are the heart and artery.

2012/5/14 CT reports: 1. increased lung marking and more opacities same as before. Spotted multiple shadows of nodules spread across. The exudation seemed to be the same. 2. The mediastinal lymph node is the same as before. So are the heart and artery.

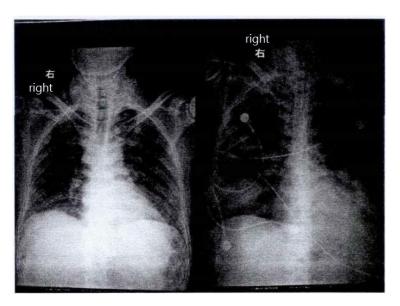
2012/5/18 CT reports: increased of lung marking and more opacities. Spotted multiple shadows of nodules in more density. The outline is blurry. Basically remain the same as before. Emphysema existed in lower left lobe. The structure of the hilar remain define and clear. The airway is clear. The mediastinal lymph node is the same as before. No sign of pleural effusions.

2012/5/23 CT reports: 1. marked interstitial opacities and exudation in both lungs. No significant increase of fibrosis 2. No cardiomegaly but the mediastinal lymph node was inflamed.

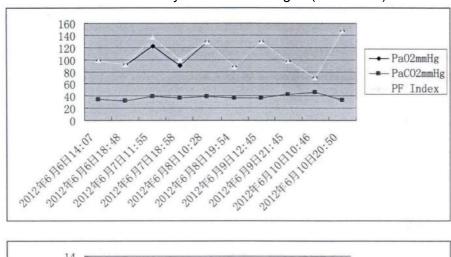
2012/6/2 bedside CT reports: 1. Noticed spread of flaky shadow and chestnut-shaped nodules in both lungs and it seemed progressed compared to before. The structure of the hilar appeared unclear. Need further confirmation. Please work with clinical for further diagnosis. 2. The outline of the heart is normal. 3. The diaphragm looked normal.

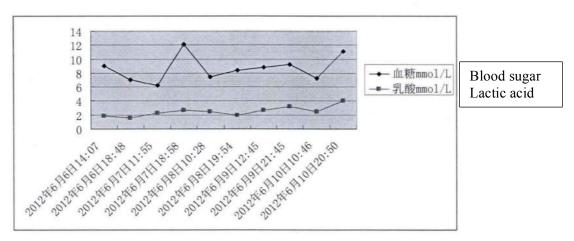
2012/6/5 bedside CT reports: 1. Noticed spread of flaky shadow and chestnut-shaped nodules in both lungs and it seemed progressed compared to before. 2. The outline of the heart looked poor. 3. The diaphragm looked normal. 4. Deep vein thrombosis at the right side of the first rib.

2012/5/16 – 2012/6/10 Chest film comparison (see below)



2012/6/6 – 2012/6/10 Analysis of the blood gas (see below)





Infection related protein (missing some data, did not make a table analysis):

2012/4/26 infection related protein report: C-Reactive protein 117.0 mg/L, SAA 398.00 ng/L.

2012/5/2 infection related protein report: C-Reaction protein 2.2 mg/L, PCT 0.04ng/ml, SAA 4.80ng/L.

2012/5/7 infection related protein report: C-Reaction protein 12.0 mg/L, PCT 0.04ng/ml, SAA 127.00 ng/L.

2012/5/18 infection related protein report: C-Reaction protein 66.3 mg/L, PCT 0.04ng/ml, SAA 230.00 ng/L.

2012/5/29 infection related protein report: C-Reaction protein 0.8 mg/L, PCT 0.04ng/ml, SAA 5.79 ng/L.

2012/5/30 infection related protein report: C-Reaction protein 23.7 mg/L, PCT 0.27ng/ml, SAA 190.00 ng/L.

2012/4/25 – 2012/5/2 No significant abnormality in the coagulation test (PT, APTT, TT, FIB).

2012/4/25 – 2012/5/6 Comprehensive Metabolic panel reports: hypoalbuminemia, others were normal

2012/5/2 blood test reports: FDP 6.5ug/ml, Antithrombin III 108.4%, D-dimer 4.4 ug/ml.

2012/5/18 blood test reports: FDP 5.3 ug/ml, Antithrombin III 146.5%, D-dimer 3.9 ug/ml.

2012/4/25 - 2012/5/2 no abnormally in the routine blood test.

2012/5/2 routine urine test is negative.

2012/4/25 troponin reports negative

2012/4/26 BNP 33.44 pg/ml.

2012/4/26 red blood cell ESR 25 mm

2012/4/26 IgM 2.98 (Normalcy: 0.4 – 2.3 g/L), Complimentary C 0.78 (Normalcy: 0.9 – 1.8 g/L)

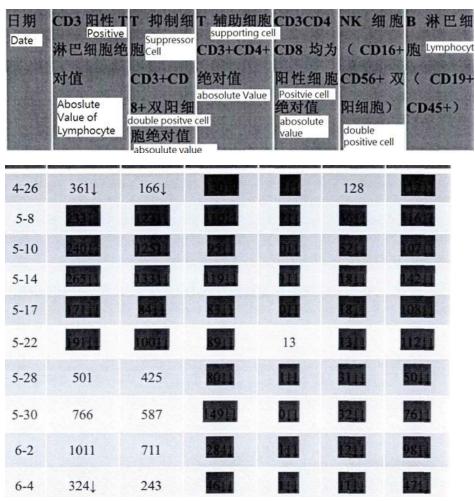
2012/4/26 Result for Widal test and WFR are both negative.

2012/4/26 Hepatitis study report: HBsAg quantity 157.5 ng/ml, HBeAb quantity 2.12 U/ml, HbcAb quantity 2.55 U/ml. HBsAg positive.

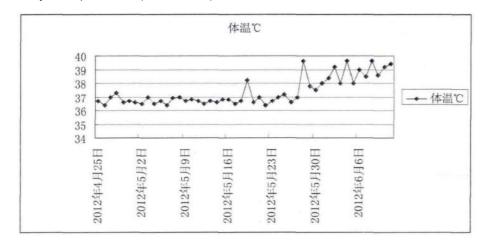
2012/4/26 PCR test: EBV positive 5200 (normalcy: 5000 measurement/ml).

# 2012/4/26 PCR test showed TB negative 2012/5/1 PCR rest showed HSV1 negative

#### T, B, NK cell percentage and count (see below):



#### Body Temperature (see below):



English translation of the MSc: "The Analysis of Six Patients With Severe Pneumonia Caused By Unknown Viruses" By Li Xu of Kunming Medical University, 2013. Translation completed: Jun 23rd 2020 (https://www.independentsciencenews.org/)

Prescription after being admitted to the hospital (some information is missing):

2012/4/25 – 2012/4/26 (J) Methlyprednisolone injection 40mg, jvgtt, Q12h.

2012/5/2 – 2012/5/4 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h.

2012/4/25 – 2012/5/4 Ganciclovir injection 125mg x 2 shots, ivgtt, Q12h.

2012/4/26 - 2012/5/2 Meropenem 0.5g x 2 shots, ivgtt, Q8h.

2012/5/1 – 2012/5/2 L- Voriconazole 0.1g x 2 shots, ivgtt, Q12h.

#### Remote Meeting Minute 1

Meeting time: 2012/6/4

Meeting location: Number 1 hospital

Experts Attendee: Dr. Xie Can Mao , Chief Physician, Respiratory department of The First

Affliated Hospital, Sun Yat-Sen University

After hearing the report of the medical history of the patient and other examination report, Dr. Xie diagnose: 1. Severe Pneumonia (possibly Fungus infection? Virus infection?); 2. Type I respiration failure 3. Sepsis 4. Hepatitis B.

The patient can complete the G test, and fiberoptic bronchoscopy examination. If the circumstances allow, we should also consider conducting biopsy of lung. However, the patient is on noninvasive ventilator, the biopsy is not appropriate. Treatment wise, Dr. Xie agrees with what we have done so far. He suggested that we should also prescribe 2 tablets of compound Sulfamethoxazole (oral), 3 times/ day. Fluconazole for the fungus and Thymosin for boosting up immune system.

#### Remote Meeting Minute 2

Meeting time: 2012/6/7

Meeting location: Number 1 hospital

Experts Attendee: Shi Jing, department of Occupation Toxicology, Shang Hai Pulmonary

Hospital

After hearing the report of the medical history of the patient and other examination report, Dr. Shi suggests: 1. Have a consultation with the Toxicology department 2. Further treatment from the respiratory department 3. Do not take Pneumoconiosis into consideration. Dr. Shi also agrees with our treatment so far.

#### Discussion

The patient started working in the mining site on 2012/4/2 and last for 14 days.

The first day of hospitalization is 2012/4/25 and the day left is 2012/6/12, total of

48 days.

Discharge Diagnosis: 1. Asystole and stop breathing 2. Severe Pneumonia 3. Type I respiration failure 4. Sepsis 5. Hepatitis B

Discharge reason: death

According to CT and Chest radiograph, the illness was progressively developed.

As the analysis on the arterial blood gas shows, during hospitalization, the patient had Type I respiratory failure. Oxygenation index was poor. According to the "ARDS Berlin Criteria" in 2012, for sure it was ARDS. Consequentially, one of the causes of death could be respiratory failure.

During hospitalization, the T, B, NK Lymphocyte percentage and count of the patients were decreasing. It shows that the immune system of the patient was impaired, had poor resistant to the disease and could easily be infected by hospital-acquired infection.

After admitted to the hospital, suggested by the Hepatology, it could also be Hepatitis B.

(Some information of the patient is missing so we failed to do a thorough analysis)

#### Case Three

Patient, Mr. Guo, male, 45 years old, was admitted to the hospital. He had signs of coughing, productive cough, shortness of breath, and fever for two weeks. The patient went into a 150 meter deep cave 24 days ago. He continuously inhaled some unknown gas for 10 days. About two weeks ago, started having signs of coughing, tightness in chest, shortness of breath, fever, yellow and greenish mucus (about 2-3 times a day, about 5 ml each time). When he rests, he feels tightness in chest, shortness of breath and fever around 39 – 40 Celsius. Before the fever, there are no chills. Along with headache and soreness in limbs. After taking some antipyretics (not sure what kind), the body temp went back to normal. 10 days ago, the mucus turned white and with some blood string (light red, 2-3 times a day). Went to the local clinic for treatment and was prescribed antibiotics (not sure what kind). The coughing with blood stopped three days after but other symptoms remained the same. 2 days ago came to the emergency and was admitted by us. CT reports: lung marking increase, blurry, septal thickening. Multiple nodules and floccular exudate. Multiple inflamed lymph nodes in mediastinum. Was given Cefmenoxime 0.5g x 6. ivatt. Qd and methylprednisolone 40mg, ivatt. Qd for inflammation for two days. The patient was getting better and the body temperature was between 38 – 39 Celsius. For further treatment, the patient was admitted to our department for respiratory impairment. During the whole process, the patient did not have any chest pain, faint, coughing pink bubbly mucus or sign of paroxysmal dyspnea at night. The patient eat and sleep well. Normal bowel movement and urination. He lost 10 kilograms. Had a bowel obstruction surgery in 1985 (no further detail). No history of allergy to any medication. Physical examination: Body temperature 36.2 Celsius, pulse 96 times/minute, Respiration rate 20 times/minute, BP 120/85 mmHg, stay sharp, soft neck, no resistant, the lips and tip of the fingers appear cyanotic, the outline of the chest looks normal, no enlargement in between the ribs, no tenderness on the chest when pressured; oxygenation is 83% without inhaling, resonant to percussion over bilateral lung, rough breathing sounds, slightly moist crackles in lower right lung. Did not hear any dry crackle from either lung. No lump on the heart area, no apical impulse, normal cardiac boundary, heart rate 96 times/ minute, no murmurs or gallop. Abdomen soft, non-tender. No inflammation on the legs. Additional checkup: 2012/4/25 CT report: lung markings increased, blurry, septal thickening. Multiple nodules and floccular exudate. Multiple inflamed lymph nodes in mediastinum. 2012/4/25 our regular blood test report: WBC13.01 x 10<sup>9</sup>/L, Percentage of Neutrophil is 70.3 %, ANC is 9.15 x 109/L, RBC 5.87 x 1012/L, Hemoglobin 175 g/L, PLT 352 x 109/L, CRP 60mg/L.

Initial diagnosis after admission: 1. inhaling respiratory impairment (restrictive lung disease); 2. Severe Pneumonia

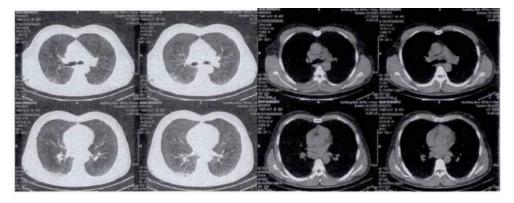
Method

After admission, more complete examination:

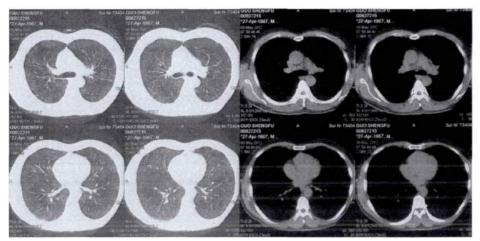
2012/4/25 CT reports: lung markings more numerous and prominent, septal thickening. Multiple nodules and floccular exudate; Multiple inflamed lymph nodes in mediastinum. The shadow of the heart remain normal; no effusion (see below).



2012/4/30 CT reports: Compared to before, the lung markings are more numerous and prominent. Septal thickening, multiple nodules and floccular exudate; multiple inflamed lymph nodes in mediastinum. Others unchanged (See below).

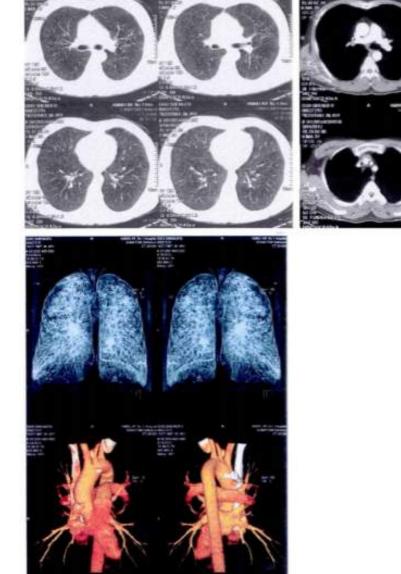


2012/5/6 CT: the exudation on the lower right lobe seems to be absorbed, others remained the same as before: multiple nodules and floccular exudate; multiple inflamed lymph nodes in the mediastinum (See below).



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2012/5/14 intensified 3D CT: the lung marking was clearer: the flaky exudation on the lower right lobe of the lung seemed to absorb, the shadow of the multiple nodules and floccular exudation have also improved. The lymph nodes in the mediastinum remained the same. Whether the artery in the lung and its major branches were intact remained unknown.



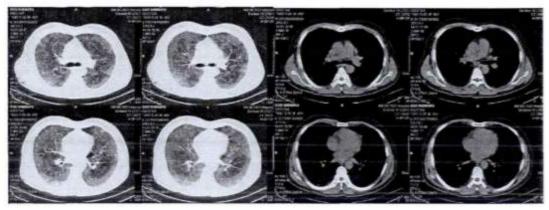
2012/5/26 CT: Clear increment of the lung marking, thickening, blurry. Overall thickening of the septum. Glassy and high density shadows in both lungs and partial pulmonary emphysema. Above are the substantial changes and may relate to infection or pneumoconiosis. Requested a check on the history of occupational disease (see below)



2012/6/3 Chest film reports: Compared to the films shot on 5/29, substantial changes in both lungs, and multiple scattered spotty shadows, partial lesion fusion. The shadow of both hila looks bigger and thicker. The illness progressed. Please work with the clinical for further diagnosis. (See below)

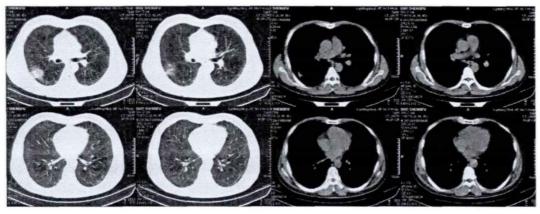


2012/6/7 CT reports: bilateral lung multiple patchy opacities and exudative consolidation, little fluid found in the left side, average amount of fluid in right side, possibly infection. Suggested double examination after treatment. Small mediastinal lymph nodes. Widening of the pulmonary artery. The shadow of the heart is enlarged. Calcification on the wall of the major artery. Found the shadow of the stent in the left coronary artery (see below).



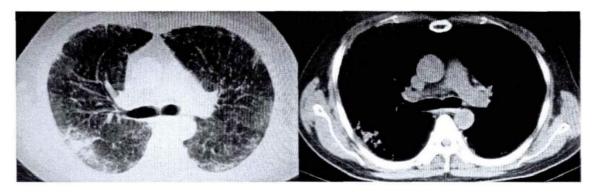
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2012/6/18 CT Reports: Interstitial fibrosis in both lungs, pulmonary emphysema remained the same. Shadow of lumpy consolidation found on the right back side of the lower lobe and the upper lobe toward the end. Suggest a double checkup after treatment (see below).



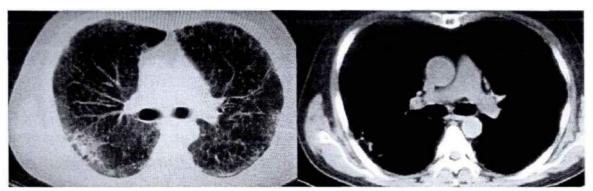
2012/7/1 CT reports: the pathological changes became more defined.

2012/7/8 CT reports: noticed diffused web-like shadow in both lungs. Multiple mediastinal lymph nodes were inflamed same as the CT report on 2012/7/1 (see below).



2012/7/11 Chest film indicates: interstitial changes in both lungs, spotty and flaky shadow diffused in both lungs, both hilar enlarged and murky. Possible infection. Other pathological changes need further confirmation, please work with clinical.

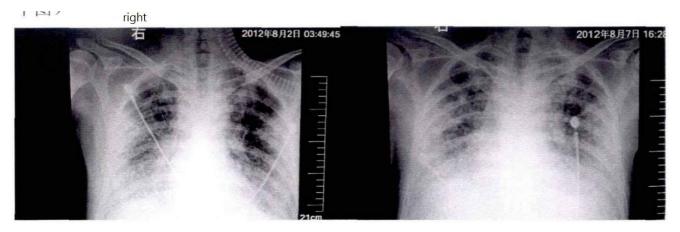
2012/7/14 Chest film indicates: highly density spotty and webbed shadow all over the lungs. Multiple mediastinal lymph nodes were inflamed same as the CT report on 2012/7/8 (see below).



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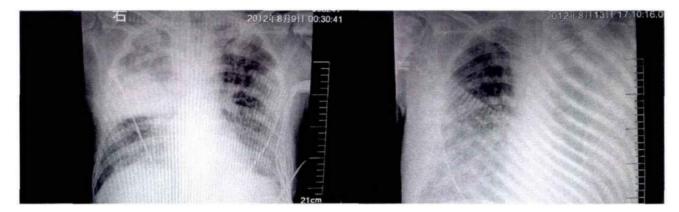
2012/7/26 CT reports: The symptom of Interstitial or fibrosis became more apparent, intensified heart, lung and mediastinum, others remain the same. Whether the lung artery and other major branches remain intact or not need to be confirmed.

2012/8/2 Chest film: interstitial changes in both lungs, flaky opacity at the bottom and on the ring of the upper lung. Compared to the 2012/7/24 film, the lesion has progressed. Please work with the clinical to do a thorough analysis (see the left picture below).



2012/8/7 Chest film: interstitial changes in both lungs, flaky opacity in the upper rings and lower lungs, lesion progressed. Please work with clinical (see the upper right picture).

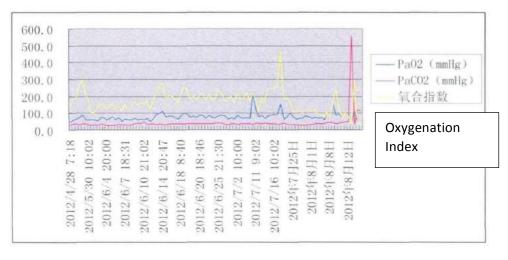
2012/8/9 Chest film: the lung markings increased and murky, spotted shadow of the nodules. Increase flaky density in the lobe of the right lung. The lesion progress. Both hila remain bushy. The structure did not look clear. Please work with clinical (see the left picture below).

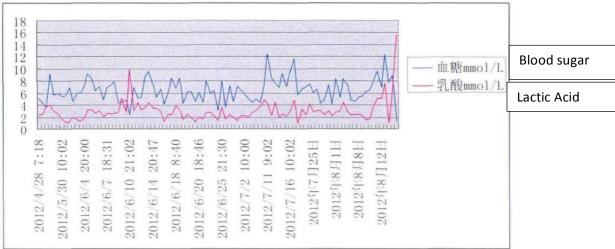


2012/8/13 Chest film: Compared to last time, the infected lesion in the upper right lung slightly absorb. The infected lesion in the lower right lobe progressed. Both hilar remain bushy, the structure is poorly defined. Please work with clinical. The infected lesion in the lobe of the left lung progressed. The left hilar, top of the diaphragm and costophrenic angle were unclear. The left chest was not visualized. Please work with clinical and make further examination if necessary (see the upper right picture).

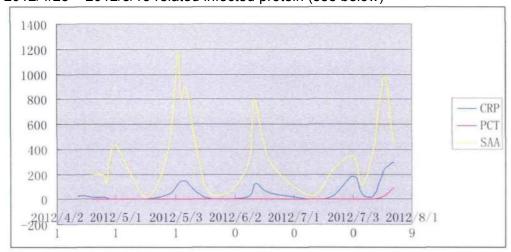
#### 2012/4/28 - 2012/8/13 Analysis of blood gas (see below):

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2012/4/25 – 2012/8/13 related infected protein (see below)



2012/5/15 Etiological examination: throat swab, complete blood test SARS-CoV, Hemorrhagic fever, Dengue fever, Japanese encephalitis, H5N1- negative

2012/4/27 PDD - negative

2012/4/28 Tumor protein chip: negative

2012/4/25 - 2012/8/13 Blood test: normal

2012/4/25 - 2012/7/23 Stool and urination test: normal

2012/4/25 - 2012/8/13 Coagulation test (PT, APTT, TT, FIB): normal

2012/4/25 - 2012/8/10 fiber blood test for three items: normal

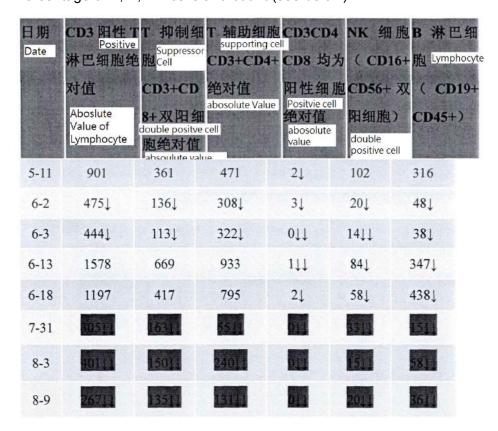
2012/4/28 – 2012/8/13 Comprehensive metabolic panel: normal

2012/8/13 B-type Natriuretic peptide: 323.91 pg/ml

2012/8/12 B-type Natriuretic peptide: 252.60 pg/ml

2012/8/7 B-type Natriuretic peptide: 8.52 pg/ml

Percentage of T, B, NK cells and count (see below):



2012/6/2 Deep vein catheterization

2012/7/10 Deep vein catheterization

2012/8/8 Deep vein catheterization

#### 2012/8/11 Picco 2 catheterization

2012/6/2 Noninvasive ventilator for aeration

2012/7/10 Noninvasive ventilator for aeration

2012/8/8 ventilator for breathing

2012/4/26 – 2012/5/29 mucus culture, sputum smear and blood culture: negative

2012/6/1 mucus culture smooth candida

2012/6/1 – 2012/7/1 mucus culture, sputum smear and blood culture: negative

2012/7/3 sputum smear shows Gram-positive bacteria and Gram-negative bacteria

2012/7/6 mucus culture Acinetobacter baumannii positive, only sensitive to levofloxacin and amikacin

2012/7/12 - 2012/7/28 mucus culture, sputum smear and blood culture: negative

2012/7/29 mucus culture positive

2012/7/29 mucus culture acinetobacter baumannii positive, only sensitive to levofloxacin and Tobramycin

2012/7/31 mucus culture acinetobacter baumannii positive, only sensitive to levofloxacin and Tobramycin

2012/8/1 – 2012/8/3 mucus culture and blood culture: negative

2012/8/5 mucus culture acinetobacter baumannii positive, only sensitive to levofloxacin

2012/8/10 mucus culture stenotropho monas maltophilia, multiple reactions

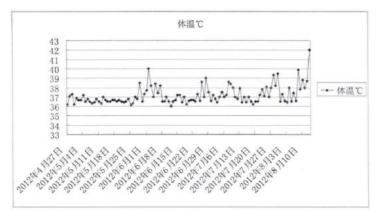
2012/8/11 mucus culture acinetobacter baumannii positive (twice).

2012/8/11 blood culture A.junni, multiple reactions to antibodies (twice).

2012/8/13 blood culture acinetobacter baumannii and candida negative

2012/8/13 mucus culture negative

Body temperature (see below):



31

Prescription during hospitalization:

2012/4/27 - 2012/4/28 Cefixime 0.5g x 2, ivgtt, Bid

2012/4/28 – 2012/5/4 Cefoperazon Sodium and Tazobactam sodium 2.25g, ivgtt, Q8h.

20125/4 – 2012/5/7 Z piperacillin sodium/tazobactam sodium 4.5g, ivgtt, Q8h.

2012/5/30 – 2012/6/3 Z piperacillin sodium/tazobactam sodium 4.5g, ivgtt, Q8h

2012/6/3 – 2012/6/19 Vancomycin 0.5g x 2, ivgtt, Q12h

2012/6/4 – 2012/6/28 Cefoperazon Sodium and Tazobactam sodium 1.5g x 2, ivgtt, Q12h.

2012/6/4 - 2012/6/28 Meropenem 0.5g x 2, ivgtt, Q8h.

2012/7/8 – 2012/7/17 levofloxacin 0.1g x 4, ivgtt, Qd.

2012/7/9 – 2012/7/19 Cefoperazon Sodium and Tazobactam sodium 2.25g, ivgtt, Q8h.

2012/7/26 – 2012/8/1 Cefoperazon Sodium and Tazobactam sodium 2.25g, ivgtt, Q8h.

2012/7/26 -2012/8/1 levofloxacin 0.5, po, Qd.

2012/7/28 – 2012/8/1 Fosfomycin 6g, ivgtt, Q8h.

2012/8/8 – 2012/8/10 Z piperacillin sodium/tazobactam sodium 4.5g, ivgtt, Q8h

2012/8/10 – death Fosfomycin 6g, ivgtt, Q8h.

2012/8/10 – death Tygecycline 50mg, ivgtt, Q12h.

2012/4/27 – 2012/5/2 (J) Methlyprednisolone injection 40mg, ivgtt, Qd

2012/5/2 – 2012/5/7 (J) Methlyprednisolone injection 30mg, ivgtt, Qd

2012/5/7 – 2012/5/21 (J) Methlyprednisolone injection 40mg, ivgtt, Q12d.

2012/5/21 – 2012/5/25 (J) Methlyprednisolone injection 30mg, ivgtt, Q12h

2012/5/25 – 2012/5/27 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h

2012/5/27 - 2012/6/6 Methlyprednisolone injection 40mg, po, Qd

2012/6/6 – 2012/6/7 Methlyprednisolone injection 40mg, po, Q12h

2012/6/7 – 2012/6/19 (J) Methlyprednisolone injection 40mg, iv, Q12h

2012/6/19 – 2012/6/23 (J) Methlyprednisolone injection 40mg, iv, Qd

2012/6/23 – 2012/6/26 (J) Methlyprednisolone injection 20mg, iv, Qd

2012/6/26 - 2012/6/3 Methlyprednisolone injection 80mg, po, Qd

2012/6/30 – 2012/7/4 Methlyprednisolone injection 40mg, po, Qd

2012/7/10 - 2012/7/17 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h

2012/7/17 – 20127/26 (J) Methlyprednisolone injection 40mg, ivgtt, Qd

2012/7/26 – 2012/7/30 prednisone 20mg, po, Qd

2012/7/30 – 2012/8/3 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h

2012/8/3 – 2012/8/7 (J) Methlyprednisolone injection 40mg, ivgtt, Qd

2012/8/11 – 2012/8/13 (J) Methlyprednisolone injection 80mg, ivgtt, Q8h

2012/8/13 – death (J) Methlyprednisolone injection 40mg, ivgtt, Q8h

2012/6/3 - 2012/7/9 Caspofungin 50mg, ivgtt, Qd

2012/6/5 - 2012/6/19 Fluconazole 40mg, ivgtt, Qd

2012/7/13 - 202/8/1 Micafungin 150 mg, ivgtt, Qd

2012/8/1 – death Fluconazole 0.2g, po, Q12h

2012/5/7 - 2012/5/28 Ganiciclovir 0.3g, ivgtt, Q12h

2012/8/11 – death Qseltamivir 75mg, po, Bid

2012/8/13 – death Ganiciclovir 0.3g, ivgtt, Q12h

2012/6/6 - 2012/6/14 a - Thymosin 1.6mg, ih, Qod

2012/8/8 - 2012/8/10 a - Thymosin 1.6mg, ih, Qod

#### Remote Meeting Minute

Time: 2012/6/4

Location: First Affiliated Hospital

Expert Attendee: Dr. Xie Can Mao , Chief Physician, Respiratory department of The First

Affliated Hospital, Sun Yat-Sen University

After learning the report of the patient and related information, Dr. Xie diagnose: Interstitial pneumonia, great possibility for fungi infection. Have the patient to complete the G examination, and fiber bronchoscope checkup. If the circumstances allow, we should also consider conducting biopsy of lung. However, the patient is on noninvasive ventilation, the biopsy is not appropriate. Treatment wise, Dr. Xie agrees with what we have done so far. He suggested that we should also prescribe 2 tablets of compound Sulfamethoxazole (oral), 3 times/ day. Fluconazole for the fungus and Thymosin for boosting up immune system.

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Reported back to Dr. Qian. After Dr. Qian Chuan Yun, Wang Yun Hui and Liu Rong's discussion, they decided to use Caspofungin and Fluconazole for fungi treatment. Also, prescribe some compound Sulfamethoxazole and thymosin for treatment. The patient is having fever, possible a sign of merged infection. Prescribe Vancomycin, sulbactam and cefoperazone and Meropenem for infection.

#### Remote Meeting Minute 2

Time: 2012/6/19

Location: First Affiliated Hospital

Expert Attendee: Dr. Zhong Nan Shan, Respiratory department of The First Affliated Hospital, Sun Yat-Sen University

After learning the report of the patient and related information, Dr. Zhong diagnose: 1.Interstitial pneumonia, great possibility for virus infection. 2. Invasive pulmonary aspergillosis (secondary infection). Suggestion: 1. Went to the animal lab in Kun Ming to confirm the type of the bat; 2. Did a throat swab and SARS antibody examination; 3.Prescribe Caspofungin, sulbactam and cefoperazone and Meropenem for treatment; 4. Intensify airway monitor, use fiber bronchoscope to clear out the mucus (do not wash by water). Basically agree with our treatment so far.

After Dr. Qian Chuan Yun, Wang Yun Hui and Liu Rong's discussion, they decided to use Caspofungin, sulbactam and cefoperazone and Meropenem for treatment.

#### Discussion

The patient started to work in the mining filed on April 2, 2012, for up to 14 days.

Day of Admission to the Hospital: 2012/4/27

Discharge Day: 2012/8/13, total of 109 days

Discharge diagnosis: 1. Severe Pneumonia 2.Multiple organs failure 3.ARDS 4. Inhaling Lung Impairment 5. Interstitial pneumonia (Virus related) 6. Invasive pulmonary aspergillosis (secondary infection).

Discharge reason: death

According to Chest film and CT, the illness recurred itself and developed in fluctuation. Finally, the lungs suffered from fibrosis.

The artery blood gas analysis indicated that the patient went through Type I respiration failure, poor oxygenation index. According to the "ARDS Berlin Criteria" in 2012, for sure it was ARDS. Consequentially, one of the causes of death could be respiratory failure.

the T, B, NK Lymphocyte percentage and count of the patients were decreasing. It shows that the immune system of the patient was impaired, had poor resistant to the disease and could easily be infected by hospital-acquired infection. During hospitalization, the patient had deep vein cauterization for four times. The blood culture and mucus culture in the later stage both suggested Acinetobacter baumannii. Before death, the infection related protein PCT reports 92.09ng/ml, therefore, one of the causes of the death could be infectious shock (induced by severe pneumonia).

According to the "Guideline and Diagnosis of invasive fungal infection" published in 2007 by Critical care branch of the Chinese medical association, we should also consider the secondary infection of invasive pulmonary aspergillosis

Prescription: five days after the suspension of Meropenem on 2012/6/28 and sulbactam and cefoperazone on 2012/7/26, the patience started to have high fever while continuously taking Methlyprednisolone and Micafungin. It shows that the possibility of secondary infection is high, the application of antibiotics is necessary.

After the patient passed away, we suggested to do an autopsy surgery to identify actual cause of the death. The families of the patient refused.

Analysis of the death of cause: the immune system was going down. The resistant to the disease was weak. The disease was acute and aggressive. Caught hospital-acquired infection in the later stage.

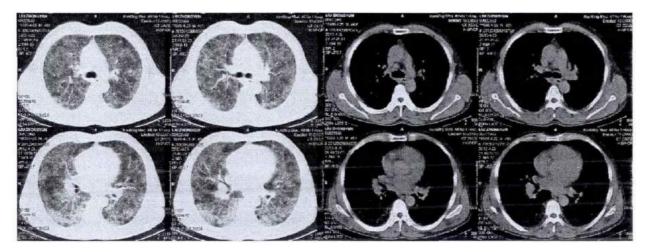
#### Case Four

Patient, Mr. Liu, male, 46 years old. He had sign of coughing, coughing with mucus, fever for 10 days and difficulty in breathing for three days and was admitted to the hospital on 2012/4/26. He worked in the mining well 10 days ago and was exposed to large amount of bats and their feces. He had cough, productive cough and hemoptysis (small amount), fever (highest to 39 Celsius) 10 days ago. He denied chest pain. He started to feel difficulty in breathing three days ago and went to the local hospital for treatment. The actual prescription remained unknown. For further treatment, he was admitted to our hospital. Since the illness started, he lost his appetite and felt drowsy. No significant change in bowel movement and urination. Used to be healthy. Denied high blood pressure, diabetes, heart disease or other chronic illness. He had been to Mo River. Prior to the illness, he worked in the mining well and was exposed to large amount of bats and their feces. Five of his colleagues had similar illness. Denied history of hepatitis, Typhoid or any other contagious disease. No history of blood transmission, allergy, typhoid or Tuberculosis. No other injuries, blood transmission, medical related allergy reaction. The vaccination record remained unknown. Physical examination: Body temperature 37.1 Celsius, Pulse 90 times/ minute, respiratory rate 18 times/ minute, BP 120/80 mmHg, considered poor performance, the pupils are round and dilated with 2.5 mm diameter. Sensitive to light. Softness in neck. The lips and tip of the fingers appear cyanotic, The breathing sound from both lungs were rough. Moist crackle sound from both lower part of the lungs. HR 90 times/ minute, regular, no murmur, rub or gallop. Abdomen soft, non-tender. Bowel sounds: 5 times/ minute. The limbs function okay and so do the muscle strength and stretch. Babinski on both sides. 2012/4/25 CT reports: Increase, thickening and blurring of the lung markings. Large parcel consolidation exudation across both lungs. Initial diagnosis: 1. ARDS; 2. Need more examination on the pathological changes of the bilateral lungs?

#### Method

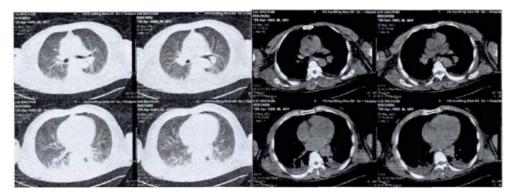
#### Complete examination after hospitalization

2012/4/29 CT reports: increased in lung marking of both lungs and opacity. Multiple patchy opacity and exudative consolidation, especially in the lower lobes. It is recommended to have a second checkup. Pleural effusion found in both lungs (see below).

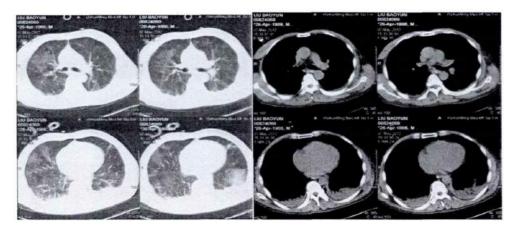


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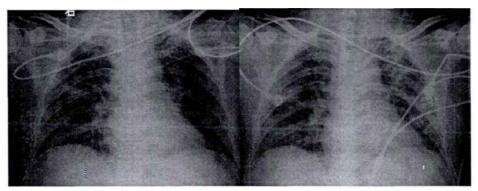
2012/5/3 CT reports: compared to the CT on 2012/4/29, the lung marketing has increased and more opacity. The multiple flaky consolidation exudation seemed to be absorbed in both lungs, so did the effusion (see below).



2012/5/7 Intensified CT reports: screen the artery more, the left and right artery appeared normal. Low density filling defect in bilateral pulmonary arteries, possibly acute pulmonary embolism. Please work with clinical. Multiple glassy exudation and consolidation in both lungs. Little effusion on both sides (see below).



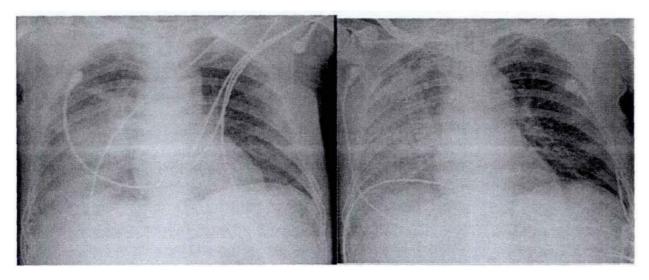
2012/5/8 Chest film: lung marking increased, hila looked normal, more markings in the lower lobe and appear to be blurry and some spotty, flaky and blurry shadow. In the lower lobe of the right lung, there were patchy and blurry shadow (see the left picture below).



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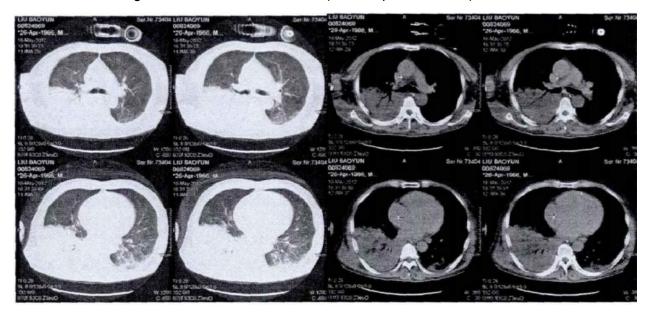
2012/5/12 Chest film: infection in both lungs, work with clinical for periodical checkup (see the right picture above)

2012/5/15 Chest film: Compared to the chest film on 5/13, the exudation on the right lung seemed worse. The left seemed slightly improved (see the left picture below).

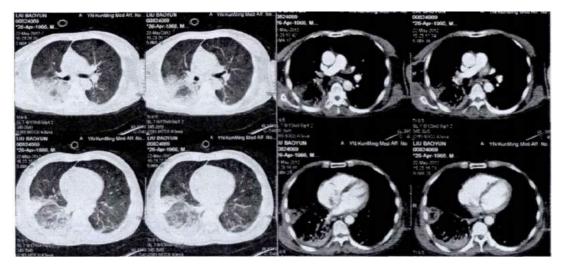


2012/5/18 Chest film: Compared to 2012/5/16, the exudation on both sides had slightly absorbed. Please work with clinical (see the right picture above)

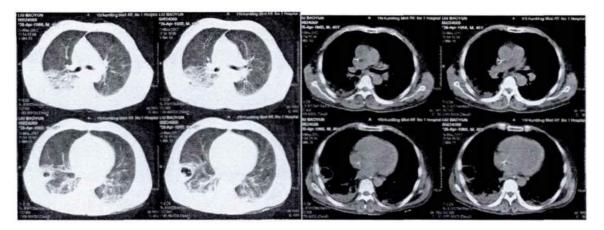
2012/5/18 Intensive CT: The lesion on the left lung decreased substantially. The consolidation exudation on the right need further confirmation (see the picture below).



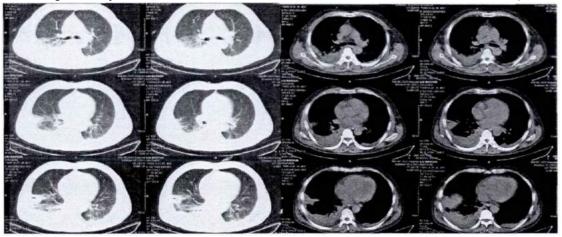
2012/5/22 intensive CT: Compared to 2012/5/18, the consolidation slightly absorbed. Glassy-like dense shadow in both lungs, possibly exudation. The intensive screen did not spot any abnormally (see the picture below ).



2012/5/29 CT film: Compared to the film on 5/22, the consolidation and hollow on the right had slightly absorbed. The glassy-like dense shadow is smaller and less dense. Recommend continue treatment and a follow up checkup (see the picture below).



2012/6/12 CT film: the consolidation on the right become heavier and the hollow seemed absorbed slightly. The glassy-like dense shadow has decreased and less dense. The effusion on the right cavity has increased. The heart and mediastinum remain the same (see below).



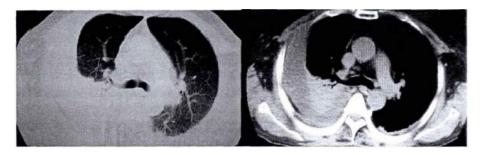
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2012/6/20 CT: Compared to 2012/6/12, the lung markings become blurrier, the consolidation in the right lung is more aggressive, and the area of exudation in the left lung has enlarged. The effusion in the right cavity increased. The shadow of the heart increased. The mediastinum remain the same (see below).



2012/6/27 Chest film: flaky consolidation exudation in the right lung and effusion in the right cavity.

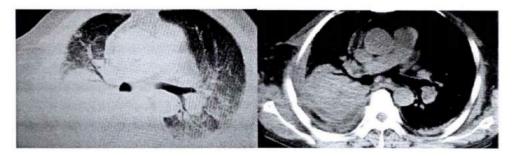
2012/6/28 CT scan: lung marking increased and blurry. Noticed flaky and floccular blurry shadow at the lower part of the lungs. The functioning area in the right lung has decreased. Effusion in both cavities. The widest effusion in the right cavity is 3.1 cm and large patchy dese consolidation shadow in lower right lobe. Sign of air bronchogram inside. Saw the drain in the right cavity (see below).



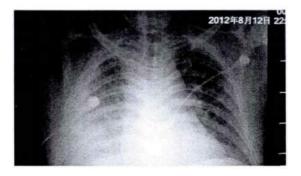
2012/7/6 CT scan: lung marking increased and blurry, ground-glass exudation in both lungs. Consolidation in the upper and lower lobe of the right lung. The airway and bronchus work well. Please work with the clinic. Moderate amount of effusion in the right side and less amount in the left. Multiple big inflamed lymph nodules in mediastinum (see below).



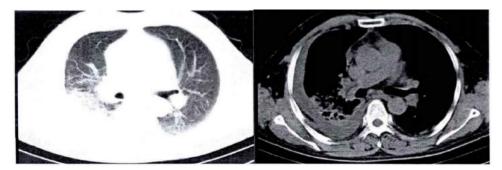
2012/7/11 CT scan: increased lung marking and blurry, ground-glass exudation same as above, the consolidation of the upper and lower right lung remain the same. Moderate amount of effusion in the right side and the left remain the same as before (see below).



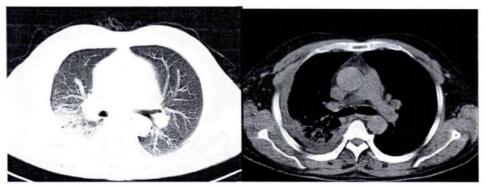
2012/8/12 Chest film: exudation lesion in both lungs have slightly absorb, the right side is more obvious, possible infection. Possibly effusion in right cavity (see below).



2012/8/14 CT scan: large consolidation exudation in the right lung, Sign of air bronchogram inside. Noticed shadow spotty, flaky exudation and stripe exudation. Little amount of effusion in both lungs, atelectasis due to extrinsic pressure. Multiple lymph nodules in mediastinum. The shadow of the heart and the artery remain normal (see below).

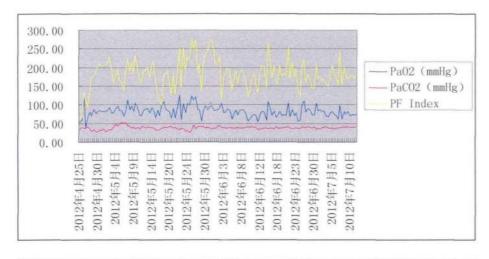


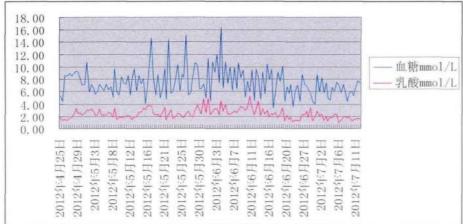
2012/8/23 CT scan: effusion, consolidation and atelectasis remain the same (see below).



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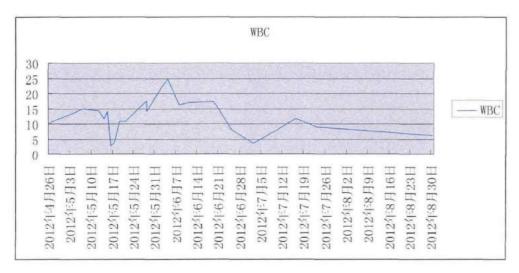
### 2012/4/25 – 2012/7/26 Analysis of Artery Blood gas (see below):





Blood sugar Lactic Acid

2012/4/26 - 2012/8/30 Blood test: line chart of the white blood cell, the rest of the result remain normal (see below)



2012/4/26 - 2012/5/15 CK, AST, LDH, CK-MB and BNP test: normal

2012/4/27 immunoglobulin and complement test: C3 0.76g/L

2012/4/27 Hepatitis Virus and HIV test: negative

2012/5/7 Herpes Simplex virus DNA + Cytomegalovirus DNA + HPV DNA test: Negative

2012/5/9 Implement Picco2

2012/5/19 Conduct Tracheotomy

2012/5/20 Center of Disease Control in Chendu city Army reservation conducted an Aetiology test (swab and blood test): negative

2012/6/27 Ultra sound guided thoracentesis

2012/6/28 effusion test: bloody; Rivalta test: positive, red blood cell 60000 x  $10^6$  / L, White blood cell 2830 x  $10^6$  / L, Percentage of Monocytes - 14%, Percentage of giant cell – 86%

2012/6/28 effusion test: Adenosine deaminase 16.8 U/L, Total protein 39.9 g/L, Glucose 1.3 mmol/ L, Chlorine 101.4 mmol/L

2012/6/29 Cerebrospinal fluid test: increase of Neutrophil

2012/7/2 Cerebrospinal fluid test: Mixed cell reaction

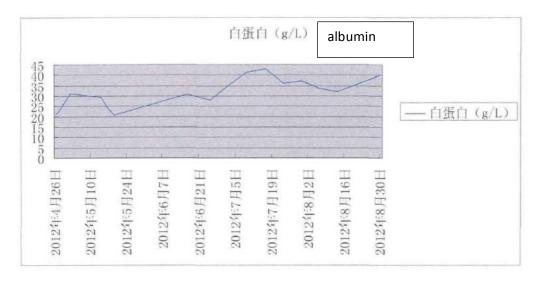
2012/4/26 Urinary test: Ketones1+, Urine Occult Blood 3+

2012/5/12 Urinary test: Urine Occult Blood 3+

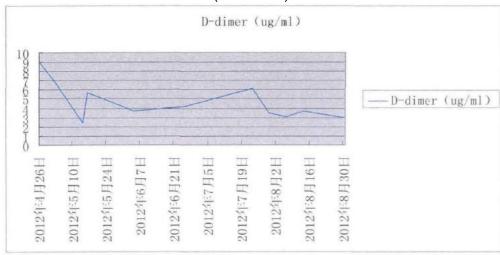
2012/5/29 Stool test: Occult blood positive

2012/6/18 Urinary test: negative

2012/4/26 – 2012/8/30 albumin development (see below), other metabolite index remain normal.

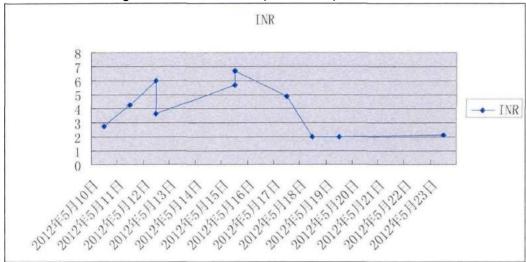


# 2012/4/26 - 2012/8/30 D- dimer (see below):

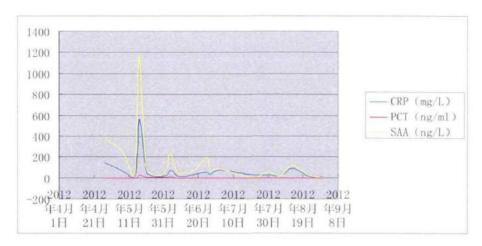


2012/4/26 -

2012/8/30 Anticoagulant treatment INR (see below):



# 2012/4/27 - 2012/8/30 infection related protein (see below):



# Percentage and count of T, B, NK cell (see below):

日期 Date	CD3 阳性 T Positive 淋巴细胞绝	T 抑制细 Suppressor Cell	supporting ce			B 淋巴细 胞 Lymphocyte
	对值	BOX STATE OF STREET	绝对值	阳性细胞 Positvie cell	CD56+ 双	( CD19+
	Aboslute Value of Lymphocyte	8+双阳细 double positive 胞绝对值		绝对值 abosolute value	阳细胞) double positive cell	CD45+)
4-27	4951	1101	20011	1111	1317	4011
5-3	4011	1501	240]]	011	1511	5811
5-11	901	361	471	2↓	102	316↓
6-2	475↓	136↓	308↓	3↓	20↓↓	48↓↓
6-3	1441	1131	3221	011	1411	3811
6-13	1578	669	933	$1\downarrow\downarrow$	84↓	347↓
6-18	1197	417	795	2↓	58↓	438↓

2012/4/27 mucus culture: negative

2012/5/16 blood culture: negative

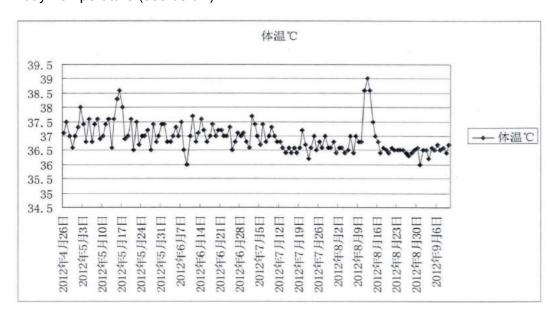
2012/5/18 mucus culture: acinetobacter baumannii

2012/5/18 mucus culture: acinetobacter baumannii, allergic reaction to Amikacin

2012/5/26 mucus culture: acinetobacter baumannii, allergic reaction to Amikacin

2012/5/28 mucus culture: acinetobacter baumannii

2012/5/28 mucus culture: acinetobacter baumannii, E.coli
2012/6/26 mucus culture: acinetobacter baumannii
2012/7/2 blood culture: klebsiella pnuemoniae subsp. Pneumoniae, KPP
2012/8/15 blood culture (Oxygen demand + anaerobic): negative
Body Temperature (see below):



# Prescription after hospitalization:

2012/4/26 – 2012/4/30 (J) Methlyprednisolone injection 80mg, ivgtt, Q12h 2012/4/30 – 2012/5/4 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h 2012/5/4 – 2012/5/10 (J) Methlyprednisolone injection 40mg, ivgtt, Qd 2012/5/10 – 2012/5/17 (J) Methlyprednisolone injection 40mg, ivgtt, Q12 h 2012/5/17 – 2012/5/21 (J) Methlyprednisolone injection 80mg, ivgtt, Q12h 2012/5/21 – 2012/5/25 (J) Methlyprednisolone injection 40mg, ivgtt, Q8h 2012/5/25 – 2012/6/1 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h 2012/6/1 – 2012/6/19 (J) Methlyprednisolone injection 40mg, ivgtt, Qd 2012/6/19 – 2012/6/26 (J) Methlyprednisolone injection 20mg, ivgtt, Qd 2012/6/26 – 2012/6/30 Prednisone Acetate Tablets 10mg, po, Qd 2012/6/30 – 2012/7/4 Prednisone Acetate Tablets 5mg, po, Qd

#### 2012/4/26 - 2012/5/2 Ganciclovir 0.3g, jvgtt, Q12h

2012/5/7 - 2012/5/10 Aciclovir 0.25g x 3, ivgtt, Q8h

2012/5/10 - 2012/5/21 Ganciclovir 0.3g, ivgtt, Q12h

2012/4/26 - 2012/5/14 L - Voriconazole, 0.4g, ivgtt, Q12h

2012/6/2 - 2012/6/4 (J) Itraconazole capsule 600 mg, po, Qd

2012/6/5 – 2012/6/19 Fluconazole 400mg (double the initial intake), ivgtt, Qd

2012/6/5 - 2012/6/6 Caspofungin 70mg, ivgtt, Qd

2012/6/6 - 2012/7/12 Caspofungin 50mg, ivgtt, Qd

2012/7/12 - 2012/8/16 Itraconazole tablet 100 mg, po, Bid

2012/7/17 -2012/9/5 Fluconazole 0.2g, po, Bid

2012/4/26 - 2012/5/7 Moxifloxacin 0.4g, ivgtt, Qd

2012/5/17 - 2012/6/2 Meropenem 0.5g x 2, ivgtt, Q8h

2012/5/17 - 2012/5/30 Linezolid 0.6g, ivgtt, Q12h

2012/5/21 - 2012/6/2 Cefoperazone sulbactam 1.5g x 2, ivgtt, Q12h

2012/6/2 – 2012/6/5 Cefoperazone sulbactam 2.25g, ivgtt, Q8h

2012/6/5 - 2012/6/28 Cefoperazone sulbactam 1.5g x 2, ivgtt, Q12h

2012/6/19 - 2012/6/28 Meropenem 0.5g x 2, ivgtt, Q8h

2012/8/14 – 2012/8/22 Z- Piperacillin tazobactam 4.5g, ivgtt, Q8h

2012/8/14 – 2012/8/27 Levofloaxacin tablets 0.5g, po, Qd

2012/5/7 – 2012/5/8 low molecular weight heparin 0.4 ml, ih, Qd

2012/5/8 - 2012/5/11 Warfarin Tablet 6mg, po, Qd

2012/5/11 - Discharge Warfarin Tablet 3mg, po, Qd

2012/5/18 - Discharge low molecular weight heparin 0.6 ml, ih, Qd

2012/5/16 VitKI 10mg, im, st

2012/5/24 Haloperidol 50mg, im, st

2012/6/4 - 2012/6/26 a - Thymosin injection 1.6mg, im, Qod

English translation of the MSc: "The Analysis of Six Patients With Severe Pneumonia Caused By Unknown Viruses" By Li Xu of Kunming Medical University, 2013. Translation completed: Jun 23rd 2020 (https://www.independentsciencenews.org/)

#### Discussion

The patient started to work in the mining well since 2012/4/2 for up to 14 days.

The day the patient was admitted: 2012/4/26, day of discharge: 2012/9/10, total of 107 days.

Discharge diagnose: 1. Interstitial pneumonia 2. Severe Pneumonia, ARDS 3. Low Proteinuria

Discharge reason: recovery

According to the analysis of the artery blood gas line chart, the beginning of the hospitalization is Type I respiratory failure, oxygenation index is low. According to the "ARDS Berlin Criteria" in 2012, it was confirmed as ARDS.

The illness was more severe at the beginning. It started to get better after the tracheal intubation and the aid from ventilation. However, the oxygenation index dropped again on May 4. Correspondently, the parameter of the ventilation was adjusted, yet the oxygenation index was still low. The D-dimer was 8.9 ug/ml on April 26, 6.9 ug/ml on May 2. The reason for the drop remained unknown. Therefore, did an emergency intensive CT on May 7 and it suggested that the artery and branches on the top and the bottom part of the lungs were in low density and filling defect, considering acute pulmonary embolism. We immediately prescribe low molecular weight heparin and Warfarin for two days. The breathing has improved significantly, indicated that anticoagulation and antithrombosis treatment were effective. During the treatment of anticoagulation, according to INR, we adjusted the amount of warfarin. During the adjustment, we noticed a INR 6.03 and immediately used VItkl for treatment.

On May 16, the oxygenation index dropped again and the body temperature rose sharply. Since the admission on April 26, the patient kept taking Fluconazole, Ganciclovir and Methlyprednisolone for treatment. On May 7, the patient stop taking Moxifloxacin and did not take any antibodies afterward. So we suspected that the malfunctioning of the breathing was caused by the intensifying lung infection. On May 17, PCT reports 24.05 ng/ml, so the patient took Meropenem and Itraconazole right away. As suggested by the CT on May 18, there was consolidation in large area in the right lung. On May 18, the mucus culture came back with acinetobacter baumannii positive twice. The blood culture was also positive. After prescription, the body temperate has dropped. On May 21, PCT was 1.63ng/ml. Indicated by the Intensive CT on May 22, the consolidation of the right lung has absorbed and the breathing was getting better.

2012/5/29 CT reports: There were frosty glass like density increased and hollows in both lungs. The temperature fluctuate between 36.8 – 37.4 Celsius. Possibly having secondary infection caused by Invasive pulmonary aspergillosis. On June 2, PCT reports 5.38 ng/ml, added Itraconzaole capsule, oral treatment. On 6/3, the oxygenation index dropped again, Since the diagnoses of acute pulmonary embolism on May 7, we apply anticoagulation treatment every day. Based on the report on 6/4, the D-dimer is 3.7 ug/ml and PCT is 14.02ng/ml, we predict the likelihood of having another acute pulmonary embolism is low, yet the possibilities of having severe pneumonia infection is bigger. Because the patient has been in critical medical condition and the diagnosis remain unclear, we sought out advice from Dr. Xie.

On 2012/6/4, Dr. Xie Can Mao, Chief Physician, Respiratory department of The First Affliated Hospital, Sun Yat-Sen University, gave us some suggestions in a remote meeting. He diagnosed: 1. Interstitial pneumonia, great possibility for fungal infection. 2. Invasive pulmonary aspergillosis (secondary infection). 3. pulmonary embolism. The patient could take a more complete G examination and and fiber bronchoscope checkup. If the circumstances allow, we should also consider conducting biopsy of lung. However, the patient is on noninvasive ventilator, the biopsy is not appropriate. Treatment wise, Dr. Xie agrees with what we have done so far. He suggested that we should also prescribe 2 tablets of compound Sulfamethoxazole (oral), 3 times/ day. Fluconazole for the fungus and Thymosin for boosting up immune system. Our department agree with using Fluconazole for 14 days. For the antifungal medicine, we agreed to switch to Caspofungin and Fluconazole for treatment. On 6/8, PCT was 0.61ng/ml and on 6/11 was 0.11 ng/ml. The CT scan on 6/12, the hollows in the right lungs were slightly absorbed. The frosty glass like density has decreased and less dense. The improvement reflects on the effectiveness of fungal treatment.

During hospitalization, the body temperature of the patient fluctuate between 37 – 37.3 Celsius. With the help of increasing nutrients, prone position and treatment for swollen lung, the patient still couldn't get rid of the ventilation machine. On June 19, we had Dr. Zhong Nan Shan from the Respiratory department of The First Affiliated Hospital, Sun Yat-Sen University to join our team remotely. He diagnosed: 1. Interstitial pneumonia, great possibility for virus infection. 2. Invasive pulmonary aspergillosis (secondary infection). He suggested 1. Visit the Animal lab in Kun Ming to confirm the species of the bat. 2. Conduct a swab test and SARS antibody examination. 3. Prescribe Caspofungin, Cefoperazone sulbactam and Meropenem for tratement. 4. Intensify airway monitoring, use fiber bronchoscope to clear out the mucus (do not wash by water), try to suspend the usage of ventilation machine. He basically agreed with our treatment so far.

2012/6/20 Chest CT plain scan, the lung marking become blurry, the consolidation in the right lung is more aggressive, and the area of exudation in the left lung has enlarged. The effusion in the right cavity increased. On 6/27, we conducted ultrasound assisted thoracoscopic thymectomy and extracted some pink effusion for further examination. It was exudate (nontuberculous or tumorous). Continue the treatment from the remote meeting. On 7/6 and 7/11, CT reports: consolidation in the upper and lower lobes of the right lung, average amount of effusion in right cavity and less effusion in left cavity. Continuously envelope pleural effusion drainage. At the same time, keep close attention to the hyoalbuminemia.

On 7/6, the oxygenation index was around 200. The blood flow is steady and can breathe on his own. After the breathing and airway evaluation, we successfully remove the metal tube.

On 8/12, the temperature of the patient spiked but could not find the cause. On 8/13, the infection related protein reports: CRP 90.8 mg/L, PCT 0.72 ng/ml. Given the patient was on the antifungal med, we did not prescribe any antibiotics. Instead, we prescribed Z- Piperacillin tazobactam and Levofloxacin tablets. After 2 days treatment, his body temperature went back to normal. In the later stage, CT plain scan suggested the consolidation, atelectasis and effusion in the right lung were slightly absorbed, yet on the back of the left lung.

There were still parts of consolidation exudation.

The percentage and counts for T, B, NK lymph cells is lower in the early and middle stage of the illness. Because of the treatment, the immune system of the patient has improved. In the later stage, the index went back to normal.

During hospitalization, we carefully monitor patient's random blood sugar in between 6-10 mmol/L. We tried to minimize the blood sugar variation.

On 8/15, blood culture (oxygen demand and anaerobic) reports negative. On 8/30, the infection related protein test: CRP 12.5 mg/L, PCT 0.04 ng/ml, SAA 3.22ng/L, the upper part of the lungs basically back to normality. The body temperature remained around 36.5 Celsius. Besides, the symptom of coughing, coughing with mucus, difficulty in breathing and soreness in limbs is gone. We decided to suspend every other medicine besides the anticoagulation one. The patient was discharged on 2012/9/10.

#### Case Five

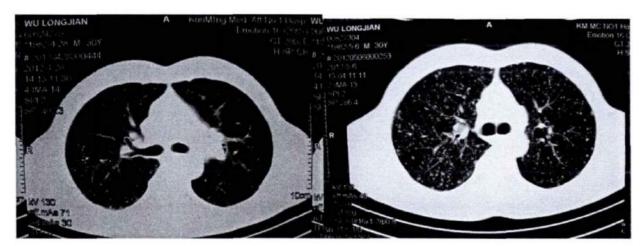
Patient, Mr. Wu, male, 30 year old, was admitted to the hospital on May 2, 2012. He had signs of coughing, coughing with mucus, fever, chest tightness and shortness of breath for five days. Dry cough most of the time, sometimes with white slimy mucus and the mucus came out easily. Chills and fever. There was no observable pattern for the fever. The highest is 39.0 Celsius, accompany with headache, soreness in limbs, chest tightness and short of breath after some light exercise. No symptom of hemoptysis, dizziness and palpitation. Sweating, dizziness, loss of strength, sign of paroxysmal dyspnea at night and edema. No specific treatment after onset of illness. Admitted to our ER last night for further treatment. Exudation and shadow of nodules found in the initial diagnosis. Sleeps and eats well. Normal bowel movement and urination. Used to work in the mining field for about 20 years. He has been to a big cave (about 150 meters deep) to work and was exposed to feces of bats for 4 days. No record of special diseases. No history of allergic reaction. Physical examination: temperature – 36.4 Celsius, Pulse 78 times/ minute, Respiration rate 19 times/ minute, BP 118/60mmHg, alert, No sign of cyanosis on the tip of the fingers or lips; the outline of the chest remains normal. No pain in the chest when pressured. Without inhaling, the oxygenation in the blood is 88%. No white spots in oral mucosa. Resonant to percussion over bilateral lung. Rough breathing sound. Little moist crackles sound from the lower left lung. Did not heard any dry crackle sound from both lungs. The heart rate is 78 times/ minute. No murmurs. No cardiomegaly. The abdominal is soft and flat. No pain when pressure or reflex. The examination did not involve liver, spleen and ribs. No edema in the legs. CT on 2012/4/28: chestnut shaped nodules in both lungs, shadow of multiple exudation.

Initial diagnosis after admission: Further confirmation on the exudation and shadow of the nodules in the lungs (possibly inhaling pneumonia, check with pneumoconiosis)

#### Method

Assisted examination after admission:

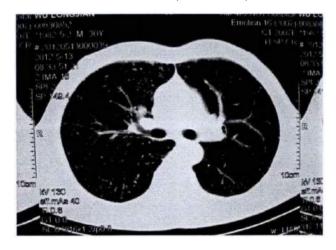
2012/4/28 CT: multiple chestnut shaped nodules, shadows of exudation in both lungs. Multiple inflamed big lymph nodules in mediastinum (see below).



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2012/5/6 CT: found chestnut-shaped nodules in both lungs, the exudation is more apparent in the lower lungs (see the upper right picture)

2012/5/13 CT: diffusive lesion in both lungs seemed to improved. The lymph nodules in the mediastinum decreased (see below)



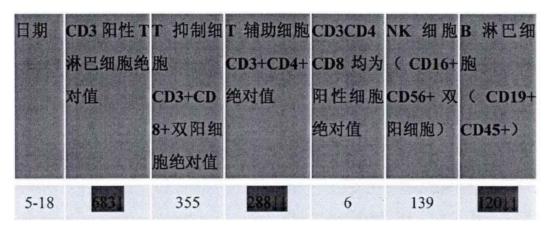
2012/5/2 – 2012/5/24 regular blood test, blood biochem test and artery gas analysis, CK, AST, LDH, CK-MB test, PT, APTT, TT, FIB test, BNP and D-dimer: Normal.

2012/5/2 PPD test: negative.

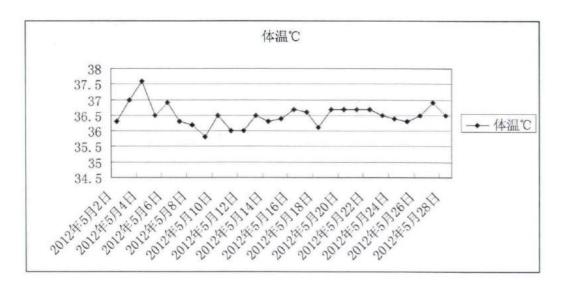
2012/5/2 ECG test reports sinus bradycardia and others were normal

Infection related protein: CRP 21.3 mg/L (May 2), PCT 0.67 mg/ml (May 3), PCT 0.75 mg/ml (May 7), CRP 12.6 mg/L, PCT 0.04 ng/ml, SAA 44.10 mg/L (May 9), PCT reports < 0.1 ng/ml (May 18), CRP 0.8 mg/L, PCT 0.04 ng/ml, SAA 2.82 mg/L (May 21).

Percentage and count of cell T, B, NK (see below):



Body temperature (see below):



### Prescription after hospitalization:

2012/5/2 – 2012/5/10 Sulbencillin 1.0 g x 4 shots, ivgtt, Q8h

2012/5/7 – 2012/5/27 L – Fluconazole 0.2 g x 1, ivgtt, Q12h

2012/5/7 – 2012/5/9 (J) Methlyprednisolone injection 40mg x 1 shot, ivgtt, Qd

2012/5/9 – 2012/5/14 Prednisolone 10mg x 3 shots, ivgtt, Qd

2012/5/14 - 2012/5/15 Prednisolone 10mg x 2 shots, ivgtt, Qd

2012/5/15 – 2012/5/21 Prednisone Acetate tablet 20mg, po, Qd

2012/5/21 - Discharge, Prednisone Acetate tablet 15mg, po, Qd

2012/5/22 - Discharge, Thymosin, 1.0 mg x 2 shots, ivgtt, Qd

#### **Discussion**

The patient started to work in the mining cave on 2012/4/22 for up to 4 days.

First day of hospitalization: 2012/5/2; Day of Discharge: 2012/5/28, total of 26 days

Discharge diagnosis: Multiple nodules in the lungs, need further confirmation for the exudation (possibly Histoplasmosis also need to check for the possibility for pneumoconiosis)

Discharge reason: recovery

The patient is young adult. After taking anti-infection and antifungal treatment, the disease was under control while hospitalization. No reoccurrence of fever, coughing, coughing with mucus, tightness of chest and short in breath. The patient did not take any anti-virus medicine during rehabilitation, yet he has recovered. It indicates that his own immune system play a big role in fighting the disease.

On May 6, according to the CT plain scan, the illness was getting worse. Therefore, we prescribed the antifungal medication and some hormone. The consolidation exudation in the upper lung has improved five days after. The temperature has dropped to normal. It indicates that antifungal med and hormones were effective.

The cause of recovery: The patient is younger with stronger immune system. In addition, he did not spend a long time in the mining field, The treatment was immediate and effective.

### Case Six

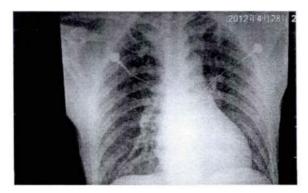
Patient Li, male, 32 year old, has been admitted to the hospital on 2012/4/26. He had sign of coughing, coughing with mucus, fever and difficulty in breathing for four days. He worked in the mining well four days ago. There were many bats and their feces in the well. Four days ago, he started to show sign of coughing, coughing with mucus (white and slimy) and fever. It smelled really bad in the well. His temperature went up to 39 Celsius. When he coughed, he had difficulties in breathing. No chest pain or coughing up blood. No sign of paroxysmal dyspnea at night. No stomach ache or diarrhea. He went to the local hospital for treatment but no documentation. His symptom had improved but wanted further treatment. He was healthy. No history of high blood pressure, diabetes, heart disease or any other chronic illness. He worked in the mining well before and was exposed to big amount of bats' feces. He had inhaled much irritating gas. No history of hepatitis, Typhoid or any other contagious disease or in contact with such diseases. No medical or food allergy. The vaccination report remained unknown. Physical checkup: temperature: 37 Celsius, pulse 74 times/minute, respiration rate 24 times/ minute, blood pressure 137/72 mmHg. In moderate health. No yellowing of skin and mucous membranes. Did not feel any lymph nodules on the superficial level. No abnormality in the head structure. The pupils were round and equal sized. Sensitive to the light. No sign of cyanosis on the tip of the fingers or lips. No resistance in the neck. The airway was in the middle. The thyroid was normal. The outline of the chest looked symmetric. The breathing sound from the lungs was rough. Did not hear any moist or dry crackle. Did not see any abnormality in heart and abdominal checkup. No sign of edema in legs. No abnormality in spine and limbs. Regular active and normal muscle strength. React to reflex and no any pathological reflex. Assistive checkup: CT reports: lung markings thickening and increased. Noticed multiple chestnut-shaped nodules. Need further confirmation on possibilities for Pneumoconiosis, acute pulmonary tuberculosis or other illnesses. Noticed multiple inflamed lymph nodules in mediastinum.

Initial diagnosis: 1. Cause of fever (possibly lung infection). 2. Inhaling lung impairment 3. Hypokalemia.

#### Method

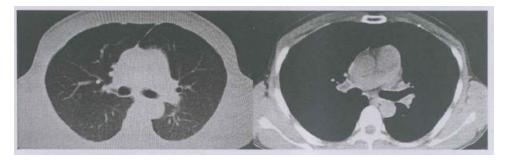
After hospitalization, a complete examination:

2012/4/28 Chest plain film: lungs marking messy and murky. Chest-nut shaped nodules all over bilateral lungs. Please work with the clinical for further confirmation. The heart and diaphragm remained normal (see below).

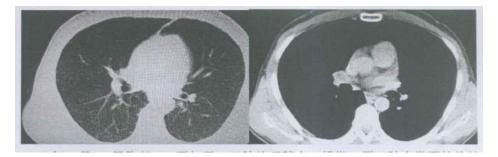


English translation of the MSc: "The Analysis of Six Patients With Severe Pneumonia Caused By Unknown Viruses" By Li Xu of Kunming Medical University, 2013. Translation completed: Jun 23rd 2020 (https://www.independentsciencenews.org/)

2012/4/29 CT chest plain scan: lung markings have increased and become blurrier in both lungs. Decrease amount of chestnut-shaped nodules shadows in both lungs. Noticed few strip shadows at the bottom part of the lower lobes in both lungs. Thickening on the left back side of the pulmonary pleurae.

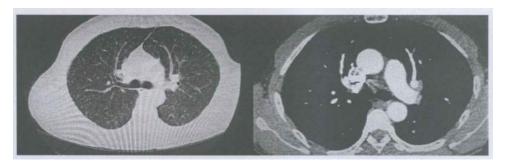


2012/5/7 CT plain scan: Compared to the scan on 2012/4/29, the lung marking has increased and blurry. The shadow of chestnut-shaped nodules has decreased. Less strip at the bottom of the lower lobes. The local emphysema, and bullae on the ring remained the same as before. The shadow of the heart looked normal. Noticed multiple inflamed lymph nodules in mediastinum (see below).



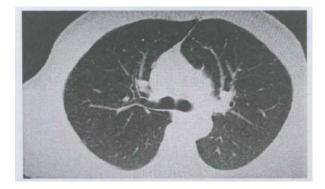
2012/5/14 CT plain scan: lung marking has increased and blurry. The chestnut shaped nodules remain the same. Noticed few strip shadow at the bottom of the lower lobes, local emphysema and bullae on the ring.

2012/5/18 intensive CT: 1. Diffuse pulmonary lesions (tuberculosis?) in both lungs, the change of the lesions was not as apparent as before. 2. The lung artery has thickened (see below).



2012/5/28 CT plain scan: the lung marking has slightly increased and blurry. Fewer shadow of chestnut-shaped nodules. Noticed few strip shadow at the bottom of the lower lobes, local emphysema and bullae on the ring.

# (see below)



2012/4/26 Regular blood test, bio-Chem blood test, PT, APTT, TT, FIB and CK, AST, LDH, CK-MB: normal

2012/4/27 Bio-Chem blood test: CRP 34.2 mg/L, SAA 79.00 ng/L

2012/4/27 Hepatitis virus examination, regular urinary test, PT, APTT, TT, FIB: normal

2012/5/7 NK and PCR: normal

2012/5/17 Regular blood test, Bio-Chem blood test, CK, AST, LDH, CK-MB, blood culture: normal

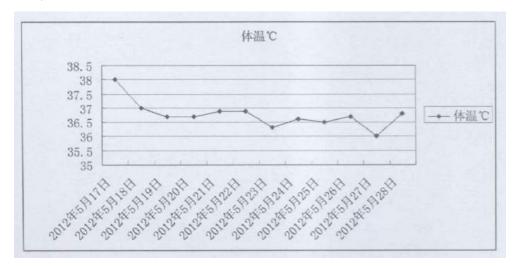
2012/5/18 Artery blood gas analysis: PaO2 56.9mmHg, PaCO2 32.9 mmHg, Oxygenation Index (PF index) 270.8, Blood sugar 5.7 mmol/ L, Lactic Acid 1.4 mmol/L

2012/5/19 Artery gas Analysis:  $PaO_2$  76.2 mmHg,  $PaCo_2$  36.7 mmHg, Oxygenation Index (PF index) 363.0, Blood sugar 7.9 mmol/ L, Lactic Acid 3.0 mmol/L

2012/5/18 Blood test: EDP 5.3 ug/ml, Antithrombin III 146.5 %, D-dimer 3.9 ug/ml

2012/5/18 Infection related protein: CRP 66.3 mg/L, PCT 0.04 ng/ml, SAA 230.00 ng/L

Body temperature chart (see below):



Prescription during hospitalization:

2012/5/17 - 2012/5/21 Ganciclovir 150 mg x 2 shots, ivgtt, Q12h.

2012/5/17 – 2012/5/24 Piperacillin Sodium and Tazobactam Sodium 4.5g, ivgtt, Q8h

2012/5/17 – 2012/5/21 (J) Methlyprednisolone injection 40mg, ivgtt, Q12h

2012/5/21 – 2012/5/26 (J) Methlyprednisolone injection 20mg, jvgtt, Q12h

#### **Discussion**

The patient started to work in the mining cave since 2012/4/22 and a total of 4 days.

Day admitted to the hospital: 2012/4/26; Day of discharge: 2012/5/28, total of 24 days

Discharge diagnose: 1. Lung infection 2. Inhaling lung impairment 3. Hypokalemia

Discharge reason: recovery

The patient is a young adult. After receiving the anti-infection, anti-inflammation and antivirus treatment, the patient has started to recover. The body temperature was kept in the normal range. No reoccurrence of coughing, coughing with mucus or any difficulty in breathing. The patient did not receive any anti-fungal medicine for treatment, yet still recovered. This suggested that the possibility of the illness being triggered by fungal infection is slim.

Compared the CT at the beginning and in the end, it showed that the treatment was effective.

The cause of recovery: the patient was young and with a stronger immune system. He did not spend a long time in the mining well. The treatment was immediate and effective.

### **Comprehensive Analysis**

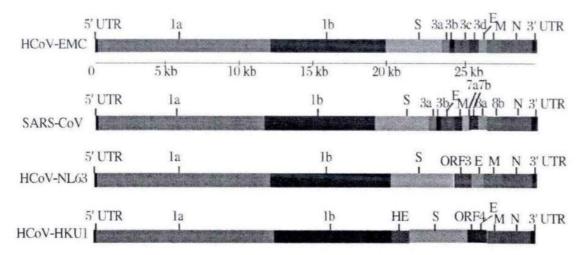
## I. Etiology

Virus is a small, simple structure non-cellular life with only one type of Nucleic acid (DNA or RNA). To multiply itself, it has to parasite with a live cell. According to the type and the structure of Nucleic acid, virus is sorted into two kinds: DNA and RNA. Among RNA virus, based on different shapes, it can be categorized into: Paramyxoviridae, Orthomyxoviridae, Retrovirus, Picornaviridae, Coronaviridae, Arenavirus, Rhabdovirida, Filoviridae and so forth.

Based on the categorization, coronavirus belongs to Coronaviridae. One of its varieties is what caused SARS. According to the analysis on the sequence of the nucleic acids, in the ninth report from the International committee on taxonomy of viruses (ICTV), corona virus has four categories: a,  $\beta$ ,  $\gamma$  and a presumably new one.  $\beta$  -coronavirus mainly includes severe acute respiratory syndrome (SARS), SARS-like CoV and Chinese rufous horseshoe bat virus Rf1, HKU3, HKU4, HKU5, leopard cat virus and so forth.

#### About SARS-like-CoV:

In November, 2002, as a new corona virus, SARS had a first outbreak in Guang Dong Province and had spread out in a short timeframe. Because the main symptom is severe acute respiratory illness, it is named SARS-CoV or contagious non-traditional pneumonia. The real host of SARS-CoV had not been found. However, in the process of tracing SARS-CoV, scientists have dissected multiple corona viruses from different kinds of bats. The genetic structure and feature of the corona virus from the Chinese rufous horseshoe bat is similar to SARS-CoV. They have the comparable similarity in Nucleotide, it was between 82 % - 92 %. Hence, this virus was named SARS-like CoV or Bats kind SARS-like Corona Virus reference 3.



In the previous research, SARS-like CoV reference 4 was found in the Chinese rufous horseshoe bat in Hong Kong (by bio-chemistry scientist Yuan Guo Yong, Chinese Hong Kong Univeristy), Greater horseshoe bat and Big-eared horseshoe bat in Tian Jing (Li Wen Dong), Rhinolophus Pearsonii in Guang Xi Nan Ning by using RT-PCR examination. If the bats carry SARS-CoV or SARS-like CoV, then very likely they can transmit the disease to human and other animals. In that way, the virus is transferred across different species. However, from other researches, it indicates that when compared the genetic sequence, the SARS-CoV from SARS patients and other animals is more advanced than the SARS-like CoV from the bat. The figures suggested that SARS – CoV, which caused SARS in 2002-2003, is from the evolution group related bats virus Reference 4. Therefore, bats corona virus has become the hot topic of international virus study.

#### II. "Horizontal" Analysis:

- 1. All 6 patients worked in the same mining cave in different times. The main duty was "cleaning the bats' feces inside the cave", then they all immediately have the illness with "similar syndrome in different degrees".
- 2. After five patients were admitted into our department in different times (Mr. Wu was admitted to respiratory department), the doctor on duty immediately reported to the medical office about the circumstance in case of an outburst of disease.
- 3. Four patients were in severe condition when they got admitted to our department. They were in Type I respiration failure, meaning gas exchange function was failing. Hence the reflection of interstitial lung disease and alveoli lesion.
- 4. After admitted to the hospital, the percentage and count for T, B, NK cells were all substantially low, which means the immune system of the patients were in severe impairment and created chances for multiple infections. In 2011, a scholar mentioned the importance of low CD4 + T lymph in virus infection reference 5. Therefore, presume that all 6 patients were infected by the virus.
- 5. After admission, Patient Guo and Liu did test for etiology (swabs and blood) for SARS-CoV, hemorrhagic fever, Dengue fever, Japanese encephalitis, Influenza A virus and other related virus by Chen Du army reserved Center for Disease Prevention and Control, the result were all negative. A negative on a onetime etiology test could not exempt other related virus.
- 6. According to Table 1: The major clinical syndrome of the six patients was "coughing, coughing with mucus and fever", some other accompanied syndromes were "difficulty in breathing, soreness in limbs, cough up blood and headache".
- 7. According to Table 2: The longer the time spent in the mining cave, the likelihood of death is higher. At the same time, the older patient died sooner. In terms of recovery, the fewer the working hours, the younger the patient, the better the recovery. They spend less time in the hospital.
- 8. According to Table 3: In the first infection related protein test of all 6 patients, SAA were noticeably increasing,

PCT remained in the normal range. It suggested that the six patients possibly had virus infection.

	表格』 Table 1			The syndromes of the six patients 6 位患者入院主诉及伴随症状						
	症状患者	咳嗽	咳痰	发热 ≥39°C	呼吸困难	四肢酸痛	血性痰	头痛	胸痛	
		Coughi	Coughi	Fever	Difficulty	Soreness	Bloody	Headac	Chest	
Patient Zhou	周xx	+	+	•	+	+	-	+	+	
Patient Lu	吕XX	•			+	+	+	-	-	
Patient Guo	郭XX	+	+	•	•		+		-	
Patient Liu	刘xx	+	+		+	+	+	-		
Patient Wu	吴xx	+	+		+	+	-		-	
Patient Li	李XX	+	+	+	-	-	-	-	-	

	表格 2 Table 2			相 <b>关重要</b> Related Impo				
· ·	情况患者	入院时 间	住院天数	出院情况	下洞穴工作天数	性别	年龄 (岁)	
		Date admitted to Hospital	Total days of hospitalization	Discharge reason	Number of days spend in the cave	Sex	Age	
Patient Zhou	周 XX	4-26	12	死亡	14	男	63	
Patient Lu	吕XX	4-25	48	死亡	14	男	42	
Patient Guo	郭XX	4-27	109	死亡	14	男	45	
Patient Liu	刘 XX	4-26	107	好转	14	男	46	
Patient Wu	吴 XX	5-2	26	好转	4	男	30	
Patient Li	李XX	4-26	24	好转	4	男	32	

	姓名	时间	CRP mg/L	PCT ng/ml	SAA mg/L
Patient Zhou	周XX	4-27	82.1	0.40	198.00
Patient Lu	呂 XX	4-26	117.0	0.04	398.00
Patient Guo	郭 XX	4-28	23.8	0.04	434.00
Patient Liu	刘XX	4-27	145.0	0.47	380.00
Patient Wu	吴 XX	5-9	12.6	0.04	44.10
Patient Li	李XX	4-27	34.2	0.04	79.00

( 現院 PCT 用胶体金比色法(B.R.A.H.M.SPCT-Q-半定量快速实验)测得,结果分为四级:正常<0.5ng/mL;

入院后首次感染相关蛋白

Initial infection related protein test

轮度升高>0.5ng/mL; 明显升高>2ng/mL; 显著升高>10ng/mL。)

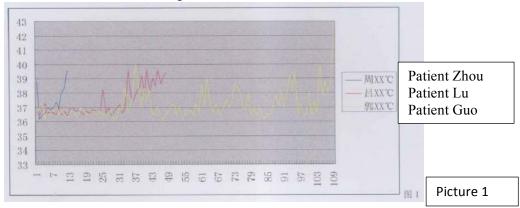
Table 3

(For PCT, we used colloidal gold colorimetric (B.R.A.H.M. SPCT-Q Semi-quantitative speedy exam). There are four levels: normal < 0.5 ng/ml; slightly higher > 0.5 ng/ml, substantial higher > 2ng/ml; noticeably higher > 10 ng/ml)

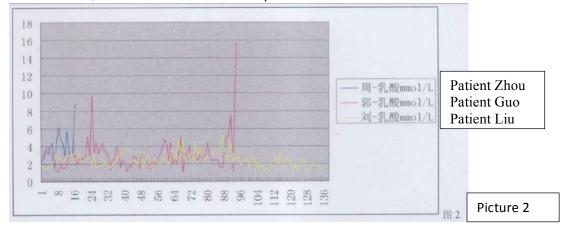
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9. Picture 1 shows the temperature line chart of the three dead patients. It suggested three of them were all in high fever.



10. Picture 2 shows the lactic acid of the three patients in critical stage (Because some of the Lu's information was missing, I wasn't able to do the comparison). According to international and domestic researches, lactic acid is a critical index for monitoring the illness of the patients in critical stage. It is useful in evaluating the severity of hypoxia during shock, tissue hypoperfusion and so forth. It can also predict the possibility of recovery reference 6. In our case, the level of lactic acid is related to the rate of death, which resonates with the previous researches.



- 12. Phone counselling after the discharge: Patient Liu, has been discharged for 240 days, he was still resting at home. He said his immune system is weak, which makes him catch a cold very easily. He worked out at home to boost up his immune system. The two young adult patients, Patient Wu and Li, both were doing fine after discharge, but also have poor body resistant.
- 13. Patient Liu was the only recovery case for critical condition patient, we conclude the success of the treatment is: This is a comprehensive treatment as we provided supports in breathing, circulation and nutrients. At the same time, closely monitored the functions of each organs and kept the balance of PH and electrolyte. We

- prepared for and immediately took care of any complication, especially any hospital acquired infections.
- 14. Gaps and failings: (1) Initially, the patients were tested for etiology (swabs and blood) by Chen Du army reserved Center for Disease Prevention and Control and the result was negative. However, a negative on a onetime etiology test could not exempt the possibility of infections caused by other related viruses. In the later stage, we worked with Dr. Zhong Nan Shan and did some sampling. The patient tested positive for Serum IgM by the WuHan Institute of Virology. It suggested the existence of virus infection. Therefore, in the future, if there is any more unknown virus related severe pneumonia or severe group lung infection cases in clinical, we need to be alert to the possibilities of contagiousness and work closely with local center for disease control. That way, we can ensure the prevention, clinical and research for similar kinds of disease. (2) We had three patients died this time. We had considered a lung biopsy before, but we did not do one in the end for various reasons. Currently, diagnosis rate done by biopsy is around 94%. For patients in critical condition, the risk of doing a biopsy with the assistance of ultrasound or CT is very high. Doctors should consider doing fiberoptic bronchoscopy instead. The diagnosis rate is not as high as biopsy but is worth trying. (3) The work of preventing hospital acquired infection should be the priority of ICU. (4) Given all six patients had the same disease but to different degrees, it is important to do autopsy on those who died. Autopsy and Etiology are important for the advancement in medical field. The reluctance of patients' families stands in the way of better understanding the disease. In the future, for unknown and possibly contagious disease, there should be a law which allows immediate autopsy for further examination. (5) For the first two dead patients, we failed to take any blood sampling when they died for the purpose of related examination and scientific research. (6) Given all of the six patients were exposed to huge amount of bats and their feces, also inhaling the smell of the feces, it is important to go sampling the live bats and their feces in the same cave.

#### III. Future Research

- 1. About SAA: Recently, there were many researches, internationally and domestically, indicate the increment of SAA during virus or bacterial infection, however, CRP does not increase or the increment is not noticeable in virus infection reference 7. Testing for both SAA and CRP can increase the rate of diagnosis for virus infection in the early stage. The testing is also valuable for determining the kinds of virus or bacterial infection and treatment reference 8-9. At recent years, the pervasiveness of PCT and its credible application shows that PCT has become the critical index in determining severe bacterial infection reference 10-11.
- About Bats: The research on SARS is still ongoing. In the international arena, scholars from Hong Kong are highly respected. They have discovered that the Chinese rufous horseshoe bat plays an important role in understanding the transmission of SARS-CoV.

3. With the Kunming Institute of Zoology, we confirmed that the six patients were exposed to Chinese rufous horseshoe bat, which caused the disease. However, a paper published in *Science* magazine in 2005 by Scientist Shi Zheng Li and Zhang Shu Yi from Wuhan Institute of Virology under Chinese Academy of Science, concluded that the SARS-like-CoV carried by bats is not contagious to humans. This contradiction indicates the importance of these six cases: the severe pneumonia caused by the unknown virus and the bats in the cave merit further investigation and research.

#### IV. Conclusion

Based on the above mentioned cases and related researches, the unknown virus lead to severe pneumonia could be: The SARS-like-CoV from the Chinese rufous horseshoe bat or Bats kind SARS-like CoV.

# 参考文献

- [1] Virus taxonomy, classification and nomenclature of viruses: ninth report of the International Committee on Taxonomy of Viruses. San Diego, CA: Academic Press, 2012.
- [2] World Health Organization(WHO).WHO final summary SARS, 15 August 2003: Summary table of SARS cases by country, 1 November 2002-7 August 2003. Geneva, WHO, 2003.
- [3] Lau S K, Woo P C, Li K S, et al. Severe acute respiratory syndrome coronavirus-like virus in Chinese horseshoe bats[J]. Proc Natl Acad Sci, USA, 2005, 102:14040-14045.
- [4] Li W, Shi Z, Yu M, et al. Bats are natural reservoirs of SARS-like coronaviruses Science, 2005, 310(5748): 676-679.
- [5] Fahey LM, Wilson EB. Viral persistence redirects CD4 T cell differentiation toward T follocular helper cells [J]. Exp Med, 2011, 208(5):987-99.
- [6] 蒋文中, 汤彦. 危重病乳酸增高机制及其在预后中价值[J]. 临床荟萃, 2004, 19(7): 405-407.
- [7]Urieli-Shoval S,Linke RP,Matzner Y.Expression and function of serum amyloid A, a major acutephase protein, in normal and disease states[J].Curr Opin Hematol,2000,7(1):64-69.
- [8]Lannergard A,Larsson A,Friman G,et al. Human serum amyloid A (SAA) and high sensitive C-reactive protein (hsCRP) in preterm newborn infants with nosocomial infections[J]. Acta Paediatr, 2008, 97(8):1061-1065.
- [9]Lannergard A,Larsson A,Cars O,et al.The time course of body temperature, serum anyloid A protein,C-reactive protein and interleukin-6 in patients with bacterial infection during the initial 3 days of antibiotic therapy[J].Scand J Infect Dis,2009,41(9):663-671.
- [10] Schuetz P, Christ-Crain M, Thomann R, et al. Effect of procalcitonin-based guidelines vs standard guidelines on antibiotic use in lower respiratory tract infections: the ProHOSP randomized controlled trial [J]. JAMA, 2009, 302(10): 1059-1066.
- [11]Ricdel S, Melendez JH, An AT, et al. Procalcitonin as a marker for the detection of bacteremia and sepsis in the emergency department[J]. Am J Clin Pathol, 2011, 135(2): 182-189.

# 攻读硕士学位期间发表文章情况

李旭, 钱传云, 吴海鹰. PiCCO 监测血管外肺水对 ARDS 的指导性治疗[J]. 昆明医科大学学报, 2012, (2B): 387-389.

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