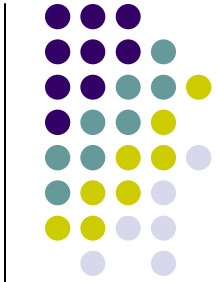
An Invisible Killer

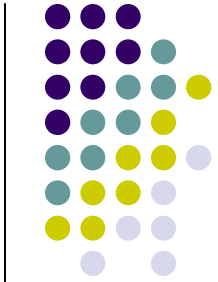
HKSCCM Inter-hospital Meeting
TKOH ICU
Dr. Edward Chung
23 Nov 2010

History



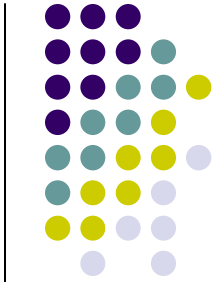
- M/37
- Non smoker
- Good past health
- Owner of optical shop

History of Present Illness



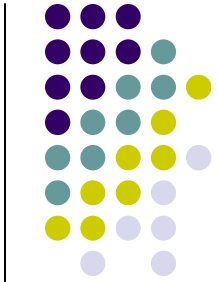
- Increased SOB since evening
- Dry cough
- Minimal sputum
- No runny nose / sore throat
- No hemoptysis
- No chest pain

History of Present Illness



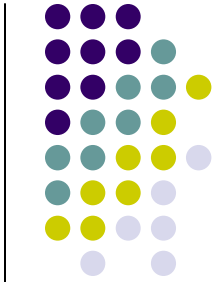
- No avian contact
- No recent travel history
- No recent air travel
- Not on chronic medications
- No habit of recreational drug use

Physical Examination



- T 35.7º
- BP 116/86
- P 120
- RR 36
- SpO2 87% RA
- GCS 15/15

Physical Examination

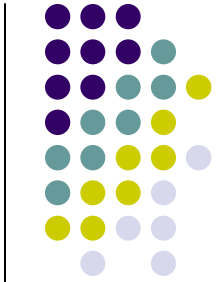


- **Diffuse crepitations over both sides of lungs**
- **HS normal, no murmur heard**
- **No ankle edema**
- **Abodmen soft**

Laboratory

- **WBC 44.3**
  - **Neut 88%**
  - **Lymp 4%**
  - **Eosin 0%**
- **Hb 20.6**
- **Plt 353**
- **Cr 166**
- **LFT normal**
- **Clotting normal**

Progress

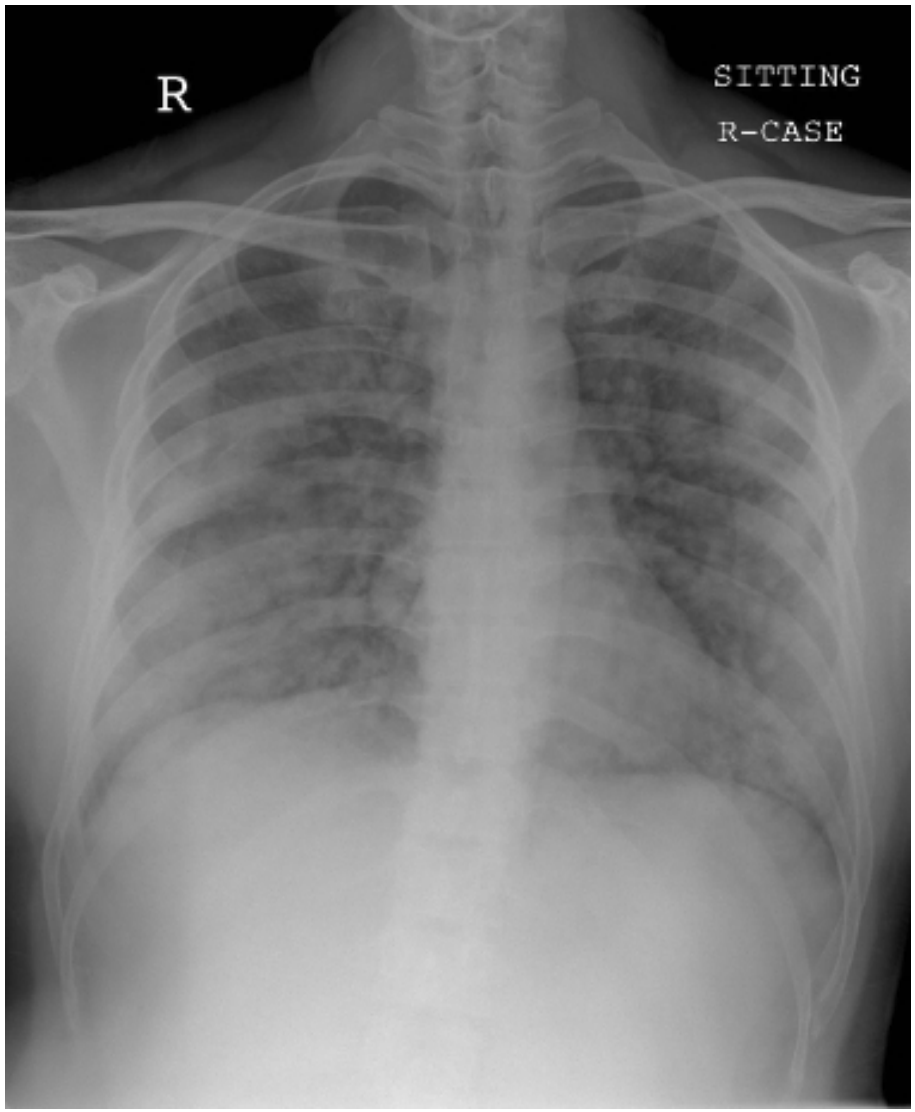


- **Increase in dyspnea**
- **Put on 100% oxygen mask at AED**

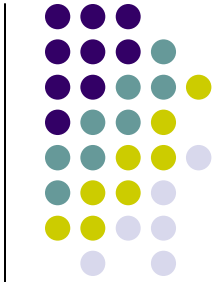
ABG

- pH 7.17
- PaCO2 5.2
- PaO2 9.7
- HCO3 13.8
- BE -13.9
- Cl 96 / Na 136
- AG = 26

CXR (AED)



Progress

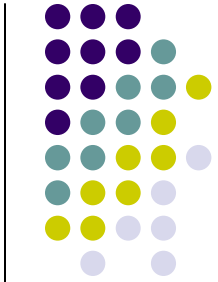


- **ICU consulted**
- **Transferred to ICU for management**

Arrived ICU

- BP 100/70
- Pulse 120
- T 39º
- SpO2 85% on 100% O2 mask
- RR 38
- GCS 15/15

Progress

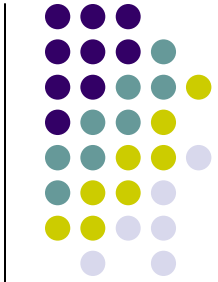


- CPAP
- FiO2 1.0
- SpO2 88%
- ABG
  - pH 7.22
  - pCO2 5
  - pO2 10.3
  - HCO3 15
  - BE -11

Progress

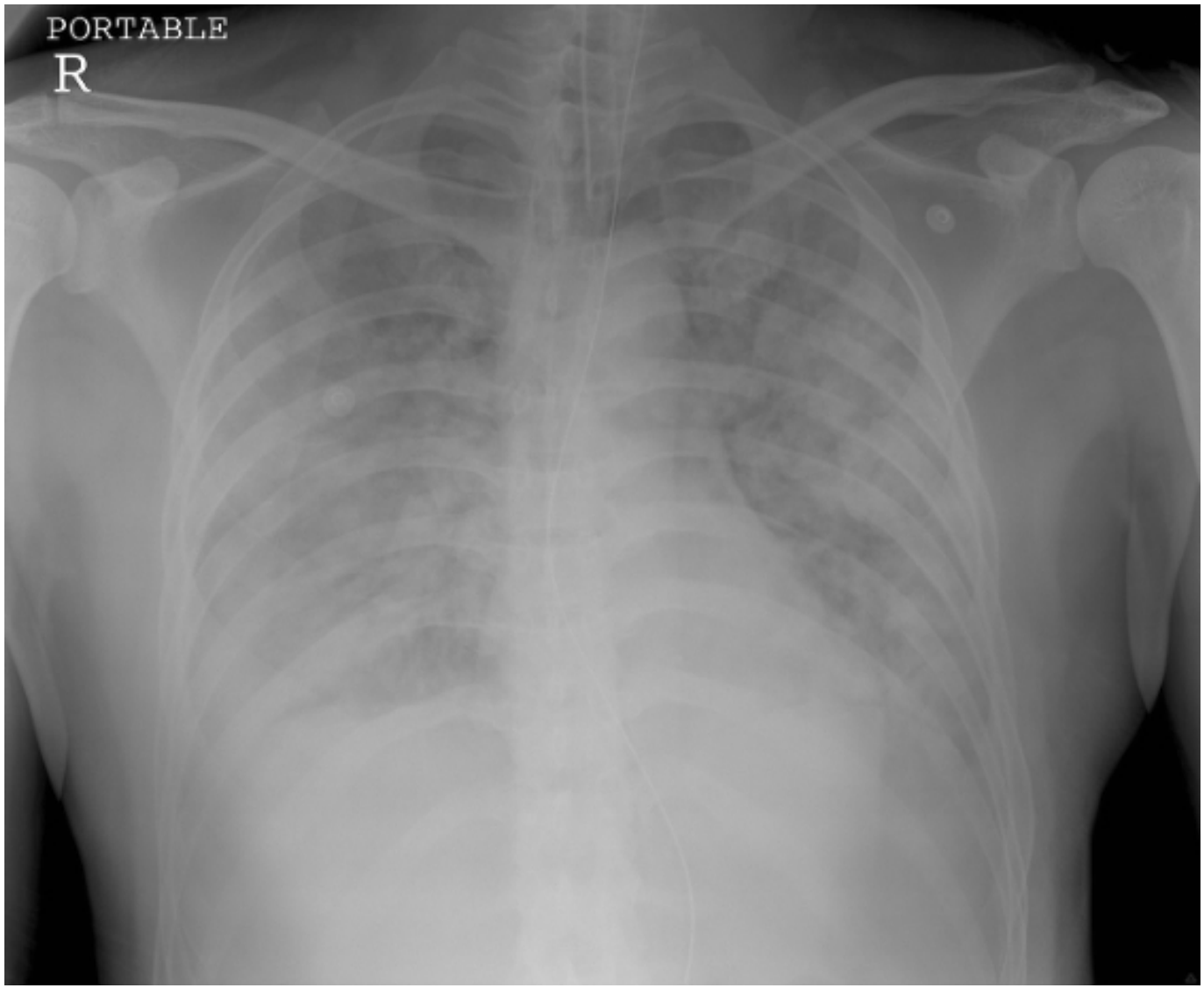
- **Patient agreed to intubation**

Mechanical Ventilation



- Intubated and sedated
- ACPC mode
- FiO2 1.0
- Pi 20
- PEEP 12

CXR (Post-intubation, Day 1)



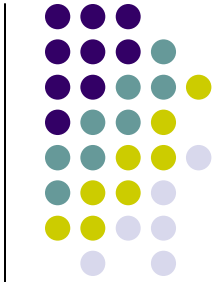
Laboratory

- **WCC 31**
  - **Neut 90%**
- **Hb 19**
- **RLFT normal**
- **Troponin T –ve**

ABG

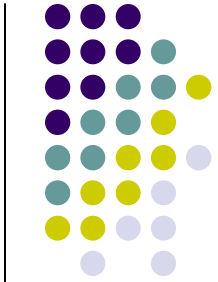
- pH 7.03
- pCO2 12
- pO2 8.5
- HCO3 23.4
- BE -10

Short Summary



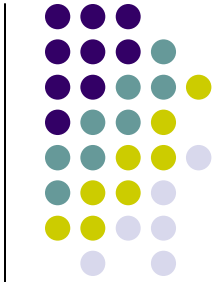
- Young man with good past health
- Sudden onset of severe respiratory failure
- Fever
- Leucocytosis with neutrophil predominance
- Diffuse bilateral lung infiltrates in pulmonary edema pattern

Acute Pulmonary Edema



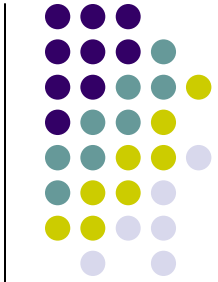
- Cardiogenic
  - Left ventricular dysfunction
    - Acute myocarditis
    - Ischemic disease
    - Arrhythmia
    - Valvular disease
    - Constrictive pericarditis or acute tamponade
  - Hypertensive emergency
  - Volume overload
  - High output state
    - Intracardiac or extracardiac shunt
    - Anemia
    - Sepsis
    - Thyrotoxicosis
  - Substances abuse
- Non cardiogenic (ARDS)
  - Sepsis
    - Pneumonia
    - Extrapulmonary source
  - Trauma
  - TRALI
  - Aspiration

Echocardiogram



- **EF 60% (by four chambers view)**
- **No RWMA**
- **No Pericardial effusion / Cardiac tamponade**
- **No significant valvular lesion**
- **No intra-cardiac shunt**
- **No dilated RV / significant TR**

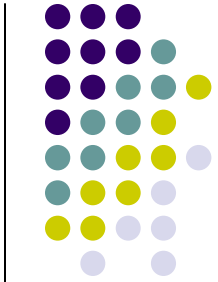
Progress



- **Bronchoscopy**
  - **Airways clear**
  - **No sputum retention**
  - **No pulmonary hemorrhage**
  - **No endobronchial lesion**

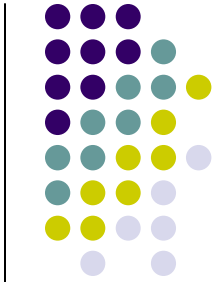
- **Bronchoscopic lavage done**

Preliminary diagnosis



- **ARDS**
- **?underlying cause**

Treatment



- **Rocephin + Azithromycin**
- **Noradrenaline for hypotension**
- **Hydrocortisone**

Progress

	Day 1	Day 2	Day 3	Day 4	Day 5
WBC	44.3	24.1	18.8	11.5	10.5
FiO2	1.0	0.7	0.5	0.45	0.4
PEEP	12	15	15	8	6
PaO2	8.5	11.0	12.5	11.8	12.4

TEMPERATURE PULSE & RESPIRATION CHART

NOTES

ADM at: 0514 E/C, CC, T/I

BP: 142/114 mm Hg HT: cm (%)

BW: 83.9 (kg./lb. OFC: cm (%)

Urine : Alb +ve Sugar +ve

Temperature

☐ oral

☐ rectal

☑ ear

X=APICAL RATE

I.D.

Dept.:

DATE 20/11/08 21 22 23

TIME AM PM 3 7 11 3 7 11

41°C 40° 39° 38° 37° 36°

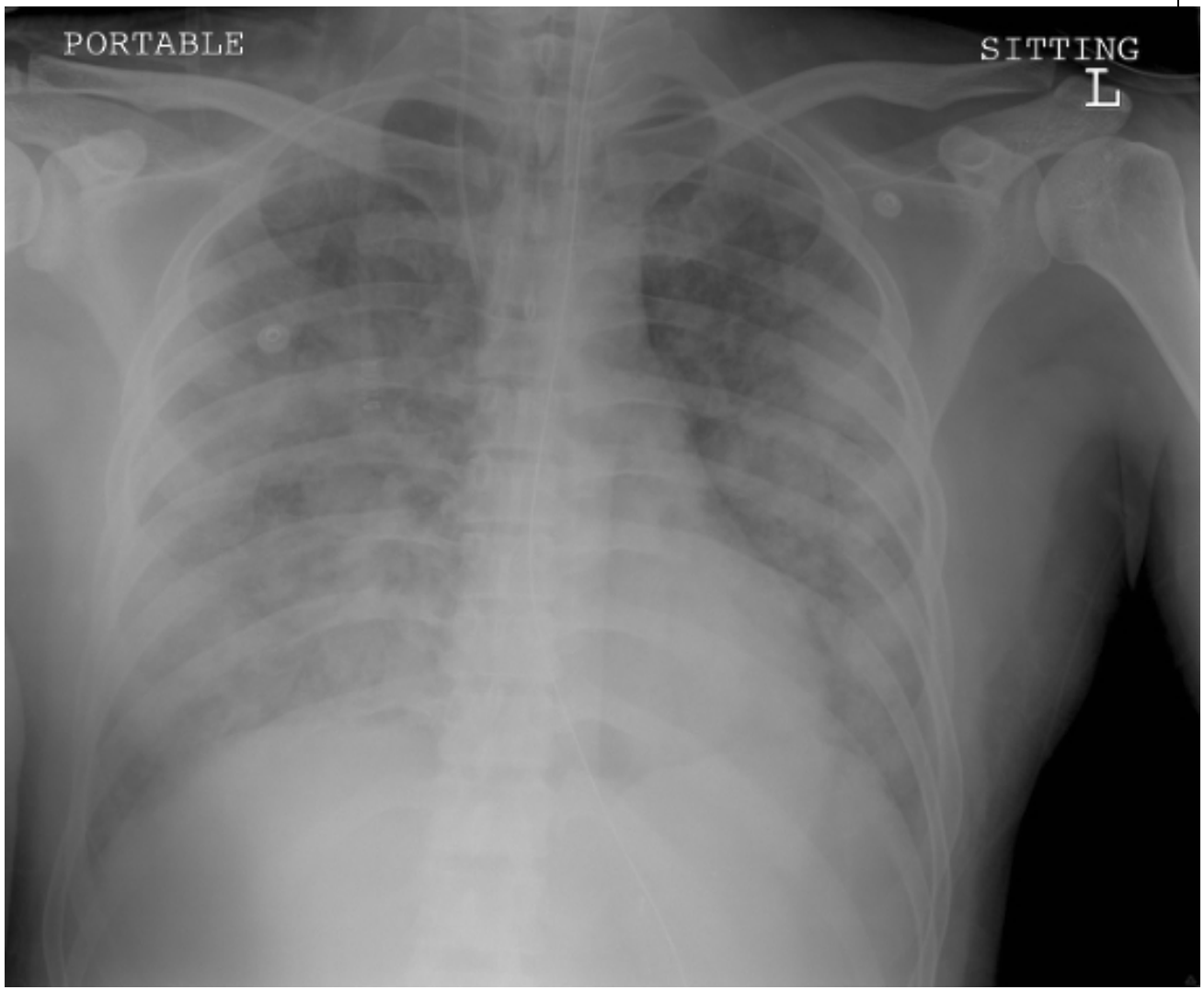
160 150 140 130 120 110 100 90 80 70 60

Pulse Rate

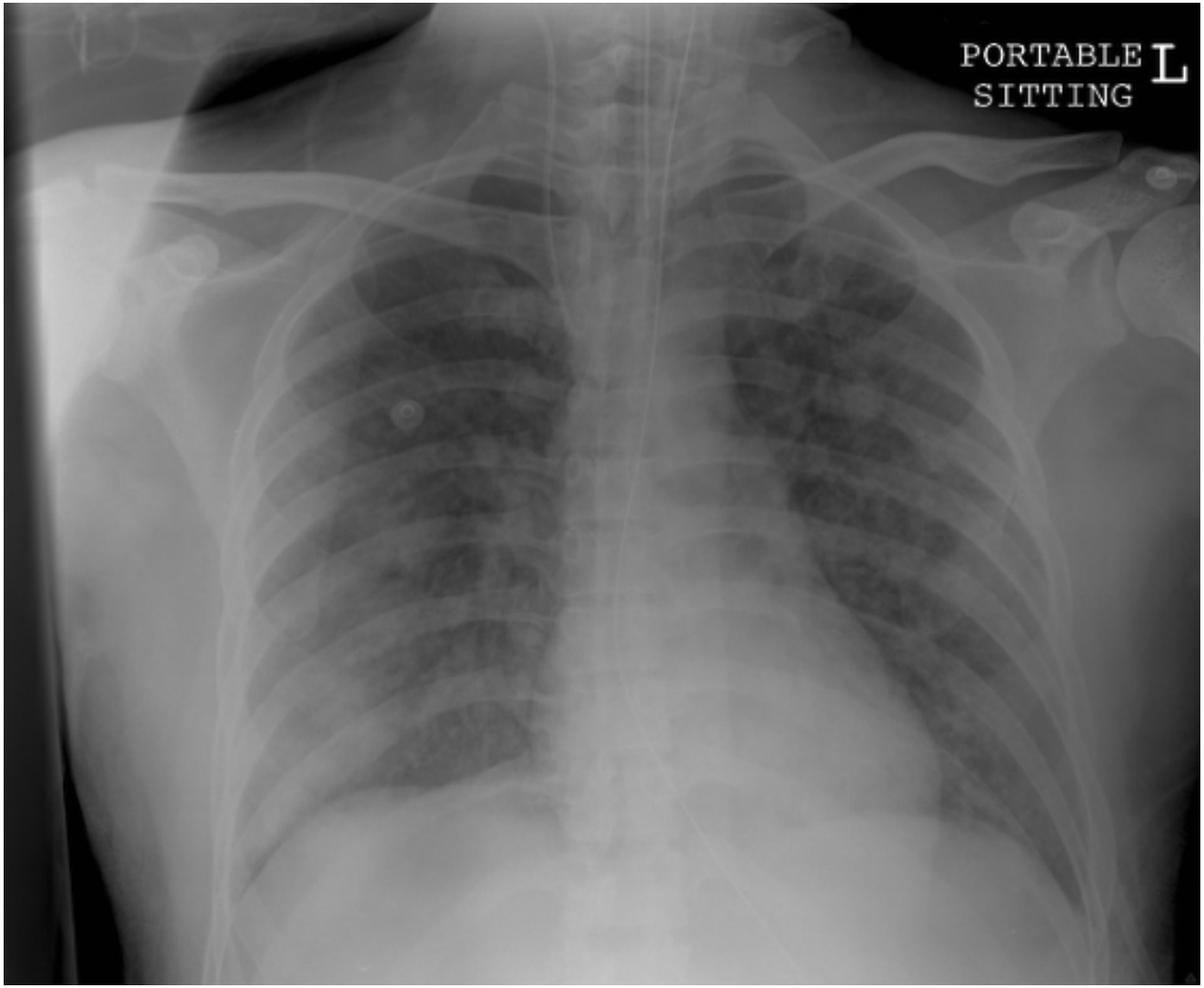
Bowels

Resp.

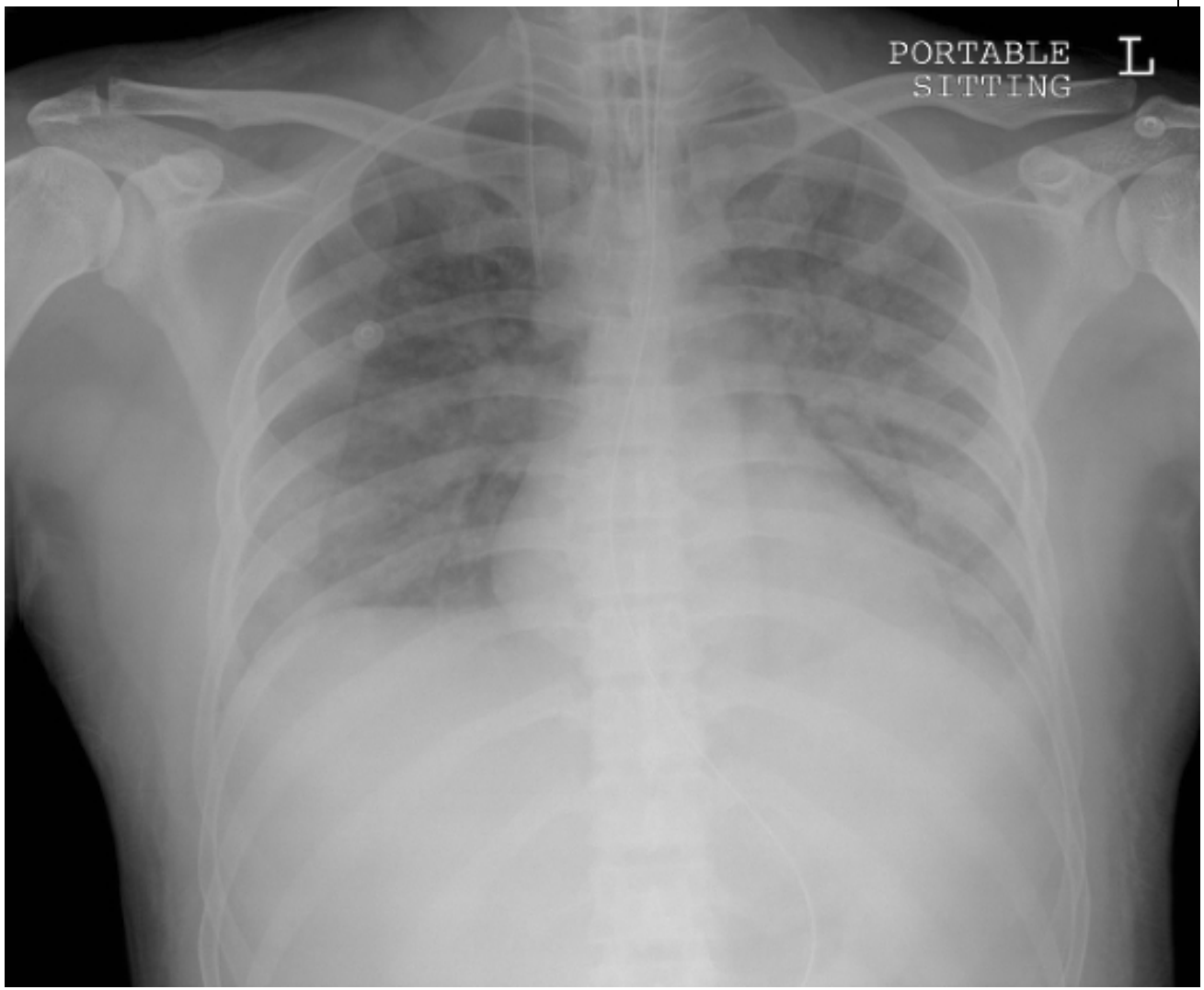
CXR (Day 2)



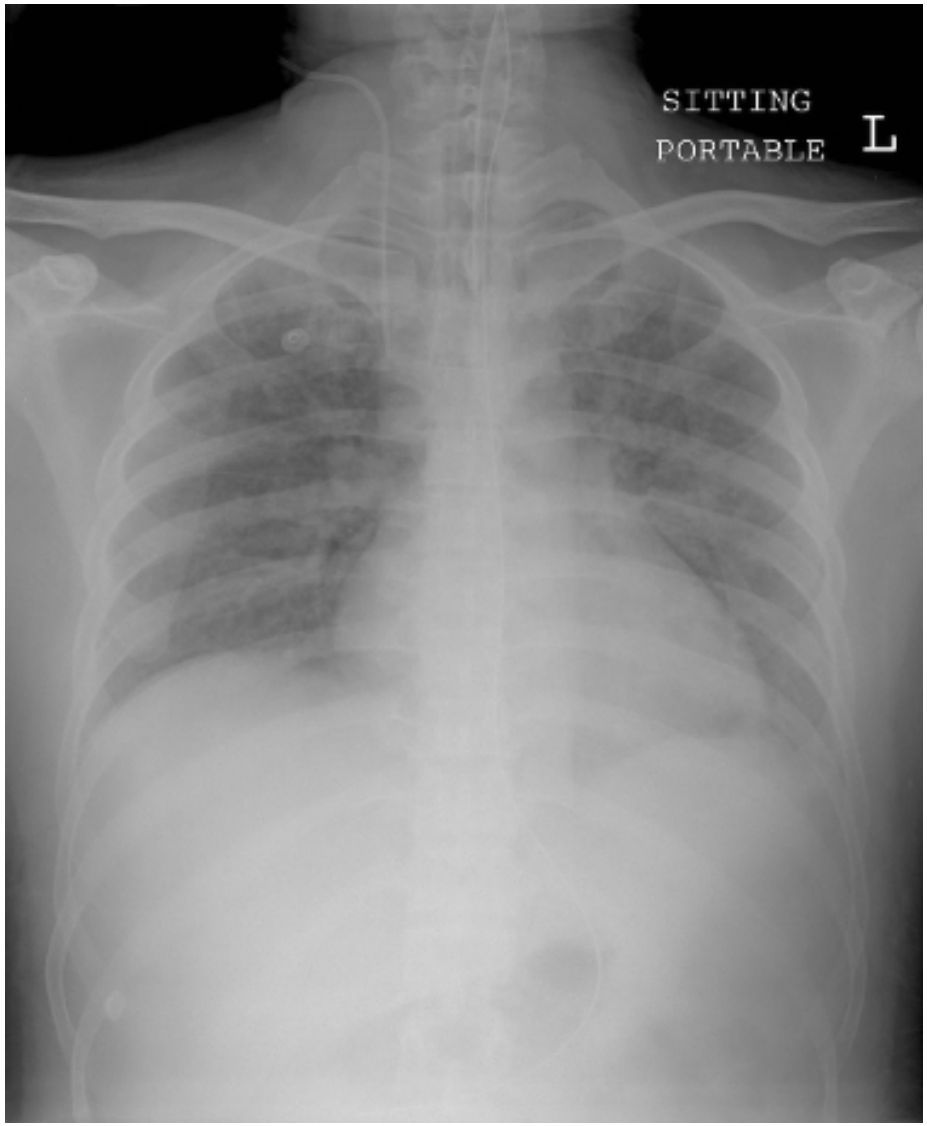
CXR (Day 3)



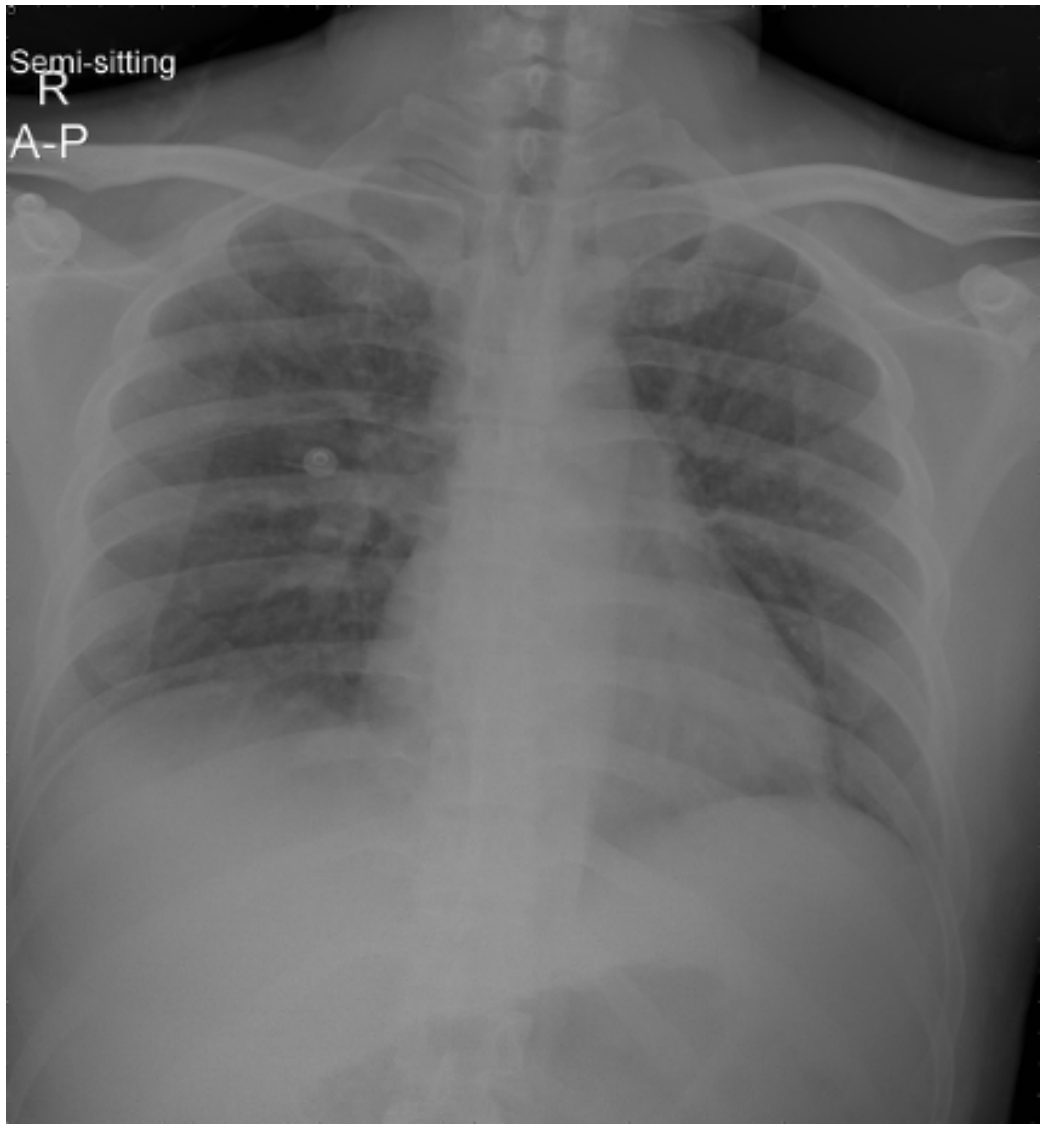
CXR (Day 4)



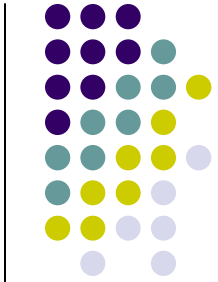
CXR (Day 5)



CXR (Day 6)

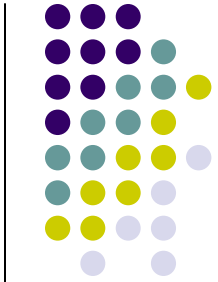


Progress



- **To General ward on Day 6**

Autoimmune Markers

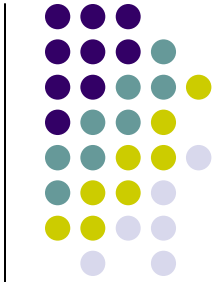


- ANA -ve
- ANCA -ve
- Anti-GBM <2
- RF -ve
- C3/4 normal

Microbiology

- **Streptococcus pneumoniae Ag -ve**
- **Legionella Ag -ve**
- **Influenza A/B -ve**
- **Anti-HIV -ve**
- **Sputum c/st -ve**

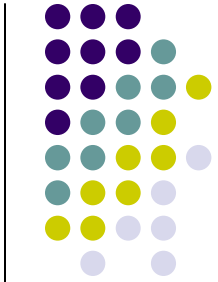
Bronchoscopic Lavage



- WBC trace
- Bacterial c/st -ve
- AFB -ve
- No PCP
- Viral c/st -ve
- Cytology -ve

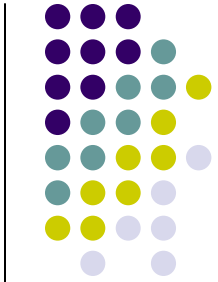
Clues?

The Hint



- **Patient is owner of an optical shop**
- **“I broke a glass of nitric acid which is for cleaning the metal parts of glasses in the afternoon”**

Internet Search……



- **Three young men died of rapidly progressive pulmonary edema of delayed onset after inhalation of fumes from an accidental nitric acid explosion.**

Chest 1990;97;487-89

- **A case of acute inhalation injury of nitric acid in a 56-year old white male. The patient presented conscious and dyspneic at the emergency department after cleaning a copper chandelier with nitric acid. He had to be intubated 2 h after admission and mechanically ventilated because of fulminant respiratory insufficiency**

Resuscitation35 (1997) 33-36

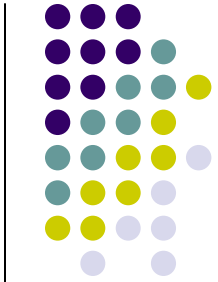
- **As all sources of mechanical ventilation failed, ECMO had to be established 7 h after admission. With the additional use of surfactant, patient could be stabilised for 3 days and lung function improved temporarily. Despite all efforts the patient died at the fourth day from refractory respiratory failure.**

Resuscitation35 (1997) 33-36

- **A rare case of survival following inhalation of nitric acid fumes and its decomposition products, which resulted in severe pulmonary edema and ARDS. Successful outcome followed ventilatory support and use of steroids.**

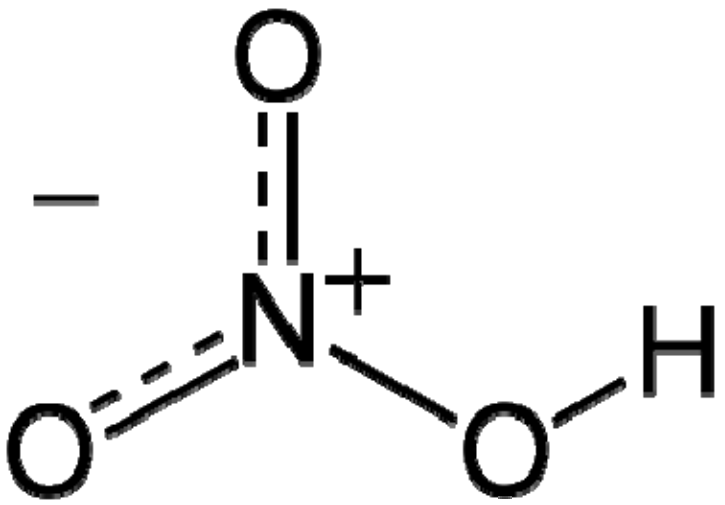
IJCCM 2005;9;244-7

Diagnosis



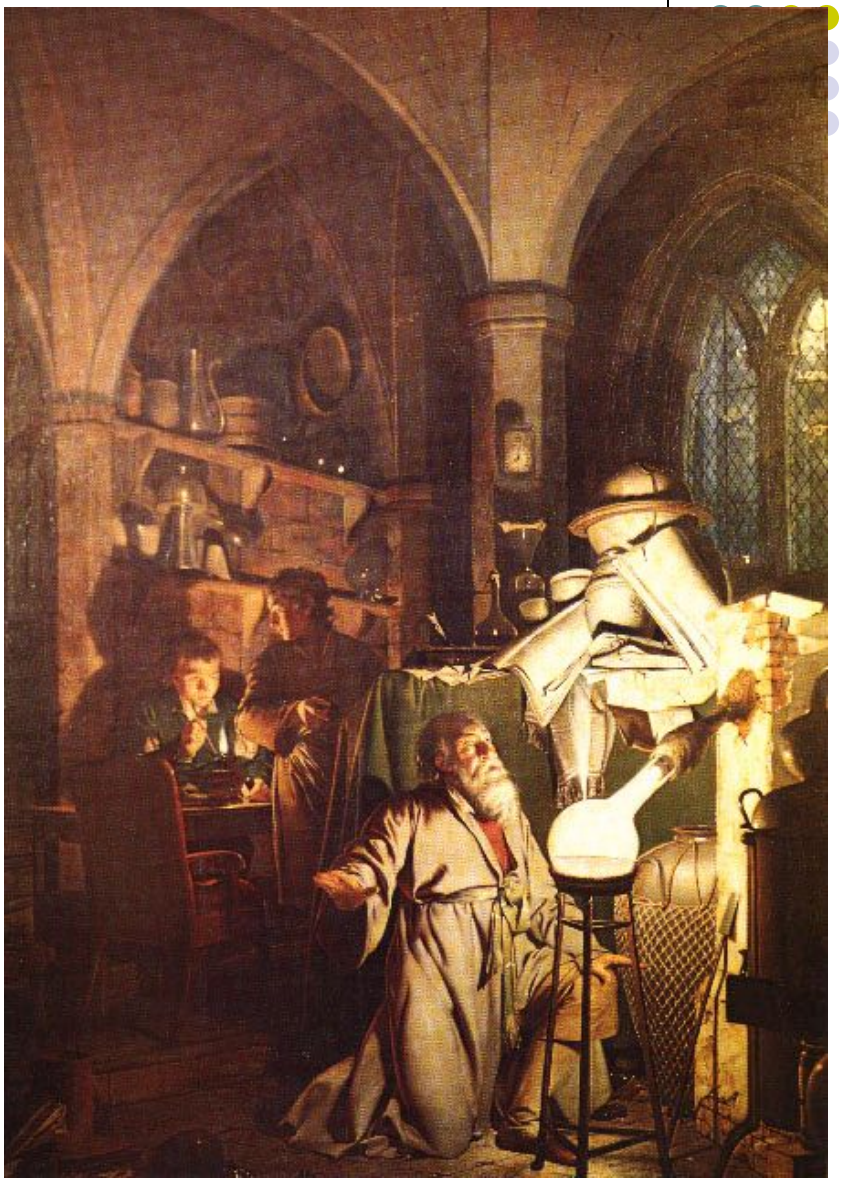
- **Acute pulmonary edema induced by nitric acid fume inhalation**

Nitric Acid



History

- First synthesised at 8th century
- Described as “Aqua Fortis” (Strong Water)
- Obtained by calcining a mixture of niter, alum and blue vitriol

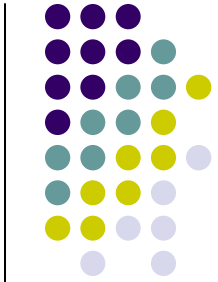


Nitric Acid

- **Nitric acid is a potent oxidant and corrosive agent**

- **Used in various industries**
  - **Metal refining and cleaning**
  - **Electroplating**
  - **Production of explosives**
  - **Production of dyes**
  - **Oxidizer in rocket fuel**

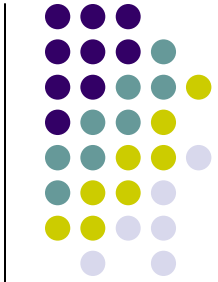
Nitric Acid



- **Nitric acid (HNO_3) is colourless**

- **Commercially used nitric acid is typically a solution of 52-68% HNO_3 in water**

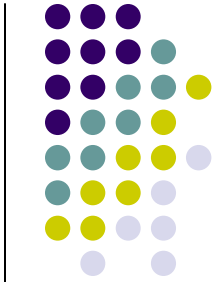
Nitric Acid



- **Fumes of HNO3 contain a mixture of HNO3, nitric oxide (NO) and nitrogen dioxide (NO2)**

- **Depends on temperature, humidity, or contact with organic materials or metals**

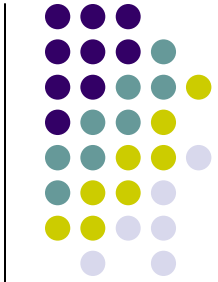
Nitric Oxides



- **NO and NO2 are naturally occurring products of biological metabolism**

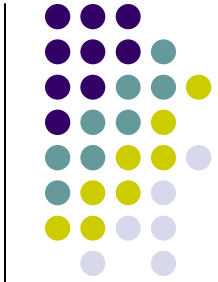
- **Created by fires, volcanoes, fossil fuel combustion and lightning**

Nitric Oxides



- **In small amounts, oxides of nitrogen (NO/NO2) are harmless**
- **NO is beneficial in improving oxygenation in refractory ARDS**
- **Significant exposure to nitrogen oxides is fatal**

Nitrogen Dioxide



- **NO_2 is liberated when HNO_3 contacts with organic materials or metals**
- **NO_2 is a reactive free radical**
- **Causes extensive damage to mucous membranes and the surface lining of lungs**

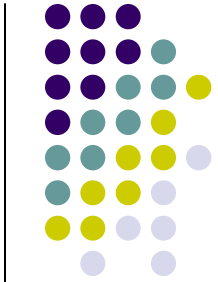
Nitric Acid Inhalation

Toxic standards

NO	**25 ppm**
NO2	**5 ppm**

Toxic

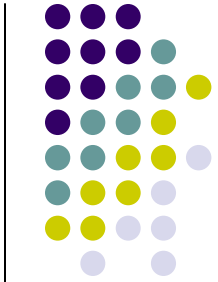
Nitric Acid Inhalation



- **At levels of 100-150 ppm**
  - **toxicity occurs within 30-60 min**

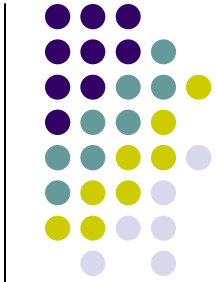
- **At levels of 200-700 ppm**
  - **fatalities result shortly after exposure**

Clinical Presentation



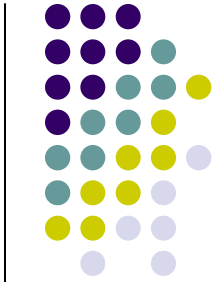
- **Depends on duration and intensity of exposure**
- **From mild irritation of upper respiratory tract to fulminant pulmonary edema**

Triphasic Pattern



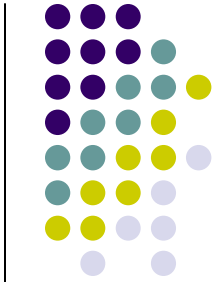
- **Phase 1**
  - **Mild irritation of the upper respiratory tract**
  - **Within several hours mild cases may stay asymptomatic**

Triphasic Pattern



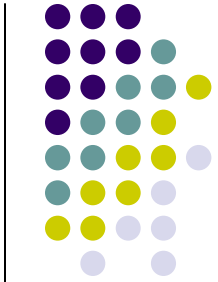
- **Phase 2**
  - **After a latency of 3-24 h, typical symptoms of pulmonary edema may appear, resulting in acute respiratory failure**

Triphasic Pattern



- **Phase 3**
  - **In severe exposures, progressive pulmonary edema develops instantaneously and the patients may not survive for more than 24 h**

Fulminant Pulmonary Edema



- **Our patient developed fulminant pulmonary edema after accidental nitric acid inhalation**

- **Toxicity of nitric acid (HNO3) on the respiratory tract is mediated by nitrogen oxides (NO, NO2)**

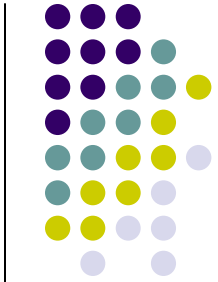
Pathogenesis

- **Nitrogen oxides (NO, NO2) are insoluble in water**
- **Less irritating to conjunctiva and oropharynx**
- **Victims may be unaware of exposure**

Pathogenesis

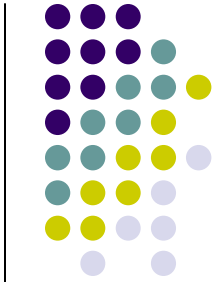
- **NO and NO2 are potent oxidants**
- **Local tissue inflammation**
- **Damage distal airways**

Pathogenesis



- **Form free radicals**
- **Initiate lipid peroxidation and oxidation of cellular proteins**
- **Inhibit cellular metabolism**

Pathogenesis



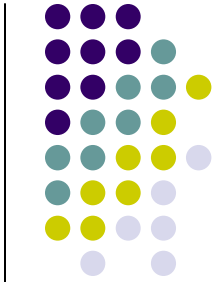
- **Increase membrane permeability**
- **Lead to swelling and disintegration of intracellular organelles**
- **Impair lung surfactant activity**
- **Induce collagen degradation**

Pathogenesis

- **Type I and type II alveolar cells are affected**

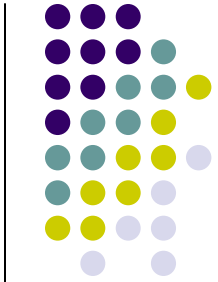
- **Type I cells at the junction of the terminal airways and gas exchange tissue being affected the greatest**

Symptoms



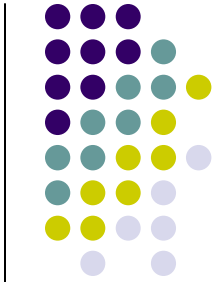
- **Symptoms can be generalized into three phases**
  - **Acute**
  - **Subacute**
  - **Delayed**

Acute Symptoms



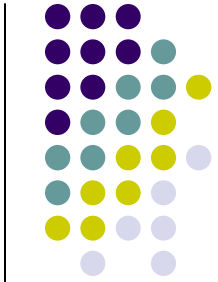
- **Related to HNO_3 exposure**
  - **Cough**
  - **Dyspnea**
  - **Chest tightness**
  - **Nausea and vomiting**
  - **Laryngospasm**
  - **Bronchospasm**

Subacute Symptoms



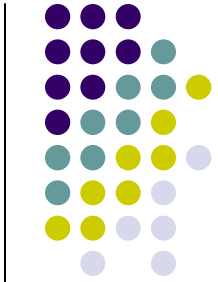
- **Non-specific**
- **Dyspnea, cough, headache, fatigue, somnolence, and nausea**
- **Can persist for up to 2 weeks**

Delayed Symptoms



- **Can begin from 4 to 12 h after exposure**
- **Include dyspnea, tachypnea, cyanosis, bronchospasm, hemoptysis, tachycardia, and substernal chest pain**
- **Associated with development of chemical pneumonitis or ARDS**

Delayed Symptoms



- **A 66-year-old white man developed delayed-onset pulmonary edema, ARDS, and fatal circulatory collapse 53 h after occupational exposure to HNO3. He was put on mechanical ventilator and inotropes support. Methylprednisolone was also started.**

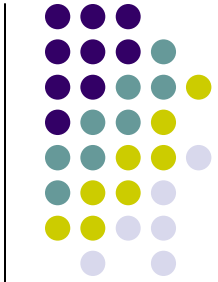
The journal of emergency medicine Vol.39, pp. 39-43, 2010

Delayed Symptoms

- **He expired on hospital day 3. Autopsy examination revealed edematous lungs with stiff parenchyma. Microscopic evaluation demonstrated congestion of alveolar capillaries and larger vessels and focal areas of intra-alveolar proteinaceous debris and mononuclear cells. Cause of death was determined to be pulmonary edema due to inhalation of nitric acid.**

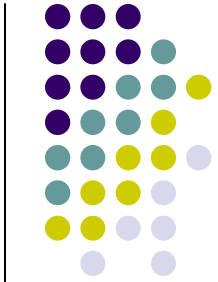
The journal of emergency medicine Vol.39, pp. 39-43, 2010

Treatment



- **Few case reports published**
- **No RCT**
- **Mainly supportive**
- **Observe for at least 24 h even if initially asymptomatic**

Treatment



- **Support respiratory failure**
  - **Mechanical Ventilation**
  - **ECLS**

ECLS

- **Two Koreans presented with potentially fatal pulmonary edema after accidental exposure to nitric and hydrofluoric acid fumes during electroplating. Despite aggressive respiratory support, one succumbed 3.5 h after inhalation. The other patient also rapidly progressed to respiratory failure. Extracorporeal life support (ECLS) was started 5 h after exposure at the ED. During ECLS, hypoxia improved, but pulmonary edema shown by radiography became aggravated.**

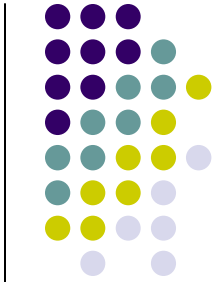
Resuscitation volume 75, Issue 1, October 2007, Pages 184-188

ECLS

- ***N*-Acetyl cysteine was given i.v. on the first day of admission and nebulised for 48 h after exposure. Pulmonary secretions were significantly reduced 24 h after the nebulising therapy began. Ultimately, the patient was discharged without serious pulmonary or neurological complications after 28 days of hospitalisation. In this case, early ECLS, nebulised antioxidant and antidote were available to treat potentially fatal pulmonary edema after exposure to nitric and hydrofluoric acid fumes.**

Resuscitation volume 75, Issue 1, October 2007, Pages 184-188

Treatment



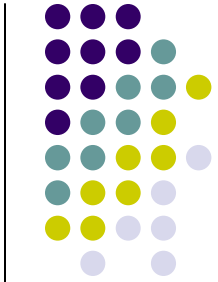
- **Steroids, surfactants and nebulised anti-oxidants have been mentioned in case reports**

Steroids in HNO3 inhalation

- **Patients with exposure to high level of nitrogen dioxide have been reported to develop bronchiolitis obliterans**

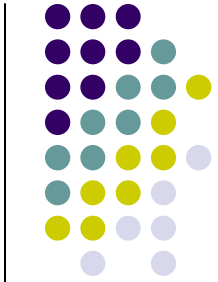
- **Steroids reduce inflammation in bronchiolitis obliterans**

Prognosis



- **The long-term sequelae not fully understood**
- **Bronchiolitis obliterans can occur up to 1 month after acute illness**
- **Patients with minor upper airway symptoms recover completely**

Risky Occupation

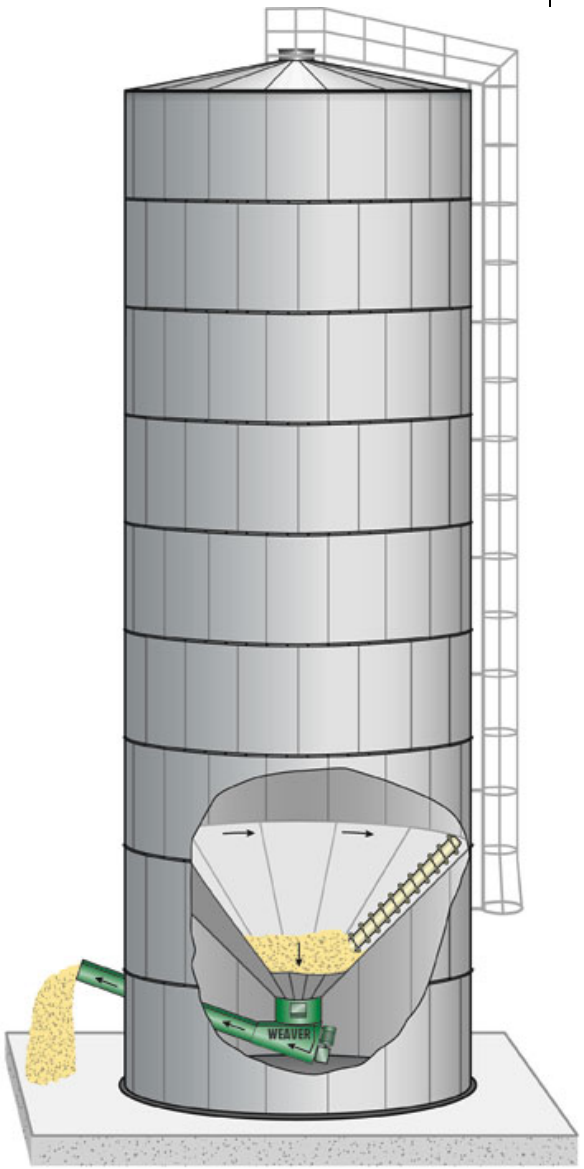


- Manufacturer of dyes
- Fertilizers
- Lacquers
- Welding
- Glass blowing
- Food bleaching
- Firemen
- Farmers

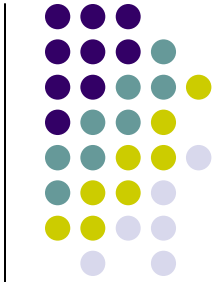
Silo Filler's Disease

- A silo is a structure for storing grain

- Occupational disease resulting from exposure to nitrogen oxides produced in silos



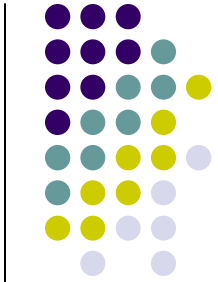
Silo Filler’s Disease



- **First recorded incidence of death was in 1914 when 3 men fell into a silo and were asphyxiated by an unknown gas**

- **The term silo filler's disease was coined in 1956**

Silo Filler's Disease



- **Toxic level of nitrogen dioxide forms in farm silos filled with fresh organic material (eg, corn, grains)**
- **Prevalent during the harvest months**
- **Associated with ARDS/ bronchiolitis obliterans**

Safety Precautions

Eyes: Wear appropriate protective eyeglasses or chemical safety goggles as described by OSHA's eye and face protection regulations in 29 CFR 1910.133. Wear face shield.

Skin: Wear appropriate protective neoprene gloves to prevent skin exposure. Wear acid-resistant PVC or neoprene jacket, trousers and boots sufficient to protect skin.

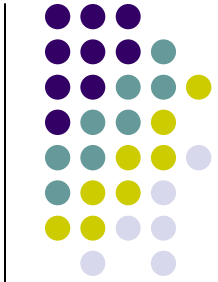
Clothing: Wear appropriate protective clothing to prevent skin exposure.

Respiratory Protection: Wear appropriate OSHA/MSHA approved chemical cartridge respirator. Regulations found in 29CFR 1910.134. If more than TLV, do not breathe vapour. Wear self-contained breathing apparatus. Always use an NIOSH-approved respirator when necessary.

Ventilation: Use only in a chemical fume hood. Adequate ventilation to maintain vapour/dust below TLV.

Other Protective Equipment: Make eye bath and emergency shower available.

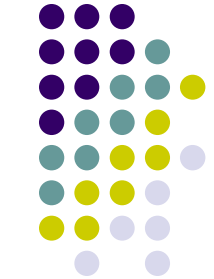
NO In ARDS



- **Inhaled NO (INO) was first used in clinical practice in 1991**

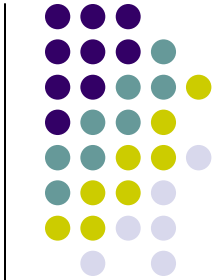
- **Suggested dose of NO => 5 to 10 ppm**

Theorectical Benefits



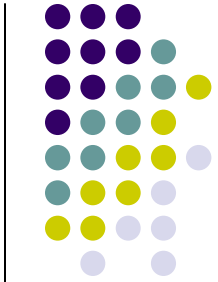
- **Selective pulmonary vasodilatation in well-ventilated lung units**
- **Improving ventilation-perfusion mismatch**
- **Reducing pulmonary hypertension**

Potential Harm



- **NO is rapidly converted to active intermediates, e.g. nitrogen dioxide**
- **Accumulation of its degradation products result in lung tissue damage**
- **High dose NO (> 80 ppm) not recommended due to risk of production of toxic level of nitrogen dioxide (NO2)**

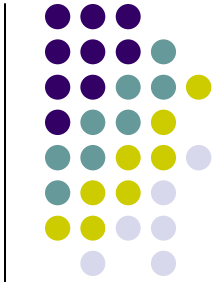
NO In ARDS



- A systematic review of 14 trials with 1303 patients with acute hypoxaemic respiratory failure (AHRF)
- Found no benefits of NO on survival
- Transiently improve oxygenation for the first 24 hours
- Increases the risk of renal failure

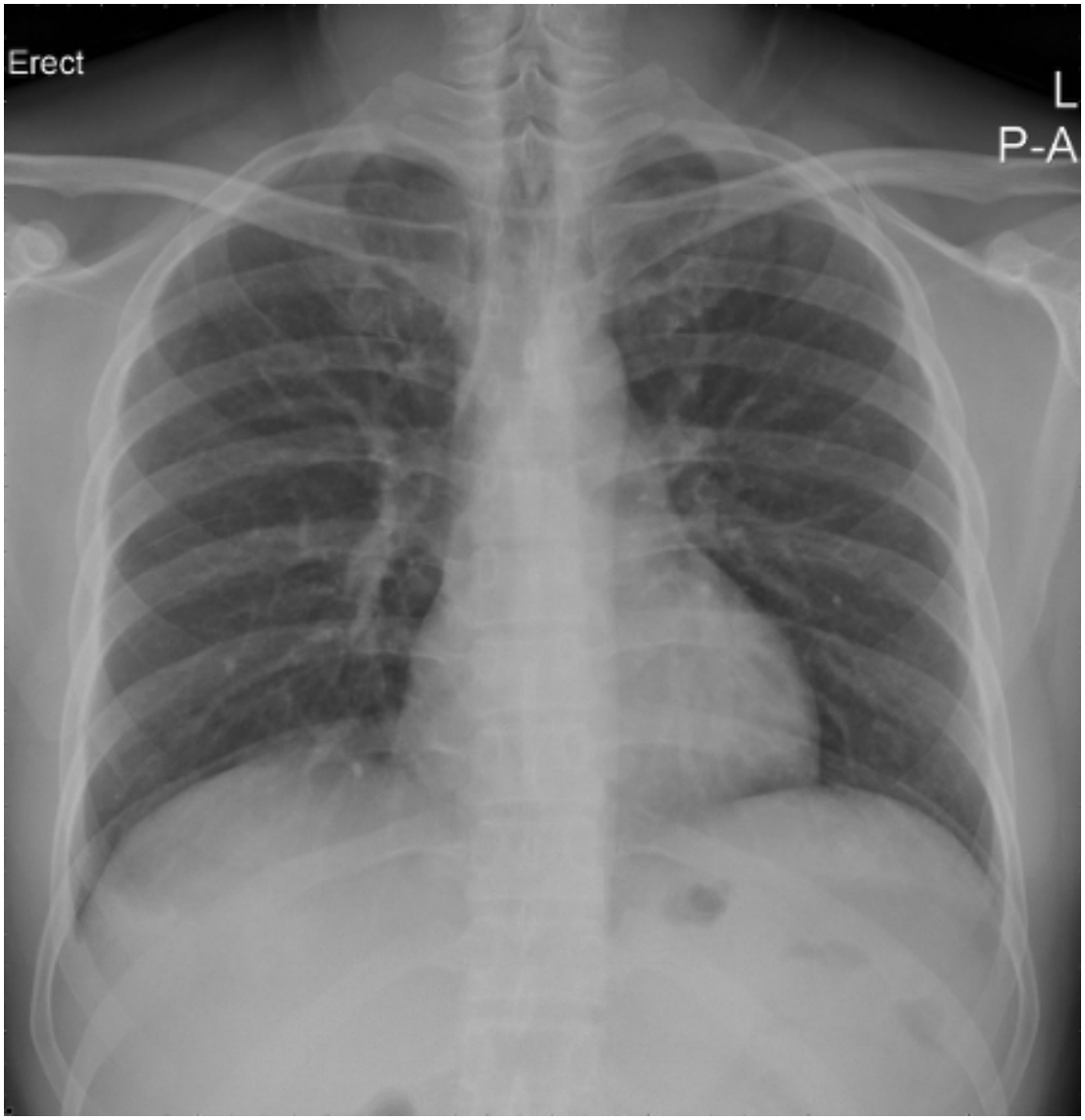
Cochrane Database of Systematic Reviews Issue: Volume (8), 2010

Our Patient

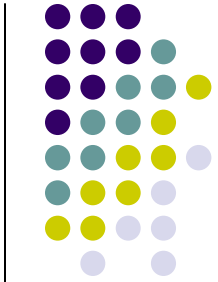


- **Discharged from general ward on Day 9**

CXR (Day 9)

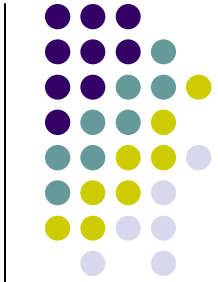


Follow Up

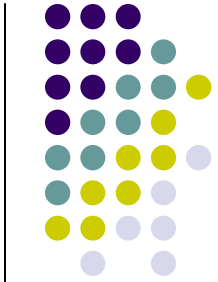


- HRCT showed complete resolution of pulmonary edema
- Blood test results were completely normal
- Totally asymptomatic
- Exercise tolerance back to normal
- Resume his work

Take Away Messages



- Occupational history is important
- Observe at least 24 h in toxic fume inhalation cases
- Early ICU care and supportive treatment
- Consider ECLS if failed mechanical ventilator support
- Consider steroid if HNO_3 inhalation injury suspected



Thank You