Case 2. 김 O 숙 (F/53)

C.C> 발열 (onset : 2주 전)

P. I>

이전에는 건강하였던 환자로 내원 3주 전 8일간 터키로 여행을 다녀옴. 귀국 당일부터 fever, chill, cough, purulent sputum 발생하여 귀국 다음날 인근 병원 방문하여 감기로 약 복용하였으나 호전 없어 4일 간 입원 치료 시행함. 그러나 38도 이상의 fever, night sweating 지속되어 건국대 병원으로 전원 되어 6일간 IV antibiotics 투여 받았음. Cough, purulent sputum 은 호전 추세였으나 발열 지속되어 본원 응급실 내원함.

PMHx>

DM/HTN/TB/Liver disease (-/-/+/-) : TB lymphadenitis (30YA)

Social Hx>

Non-smoker, alcohol (-)

Drug History>

Omega 3, Vitamin 제제

Systemic review>

G/W (+) E/F (-) Wt loss (-)

F/C (+/+) C/S/R (+/+/-) Sore throat (+)

Chest pain (-) Dyspnea (-) Orthopnea (-) Palpitation (-)

Abdominal Pain (-) A/N/V/D/C (-/-/-/-/-) H/M/H (-/-/-)

Back pain (-) Urinary Sx (-)

Physical Examination>

Initial V/S 117/61 mmHg – 81/min- 20/min- 36.8′C

(after 4hr, 137/63 mmHg – 102/min – 20/min- 39.1′C)

G/A> acute ill-looking, alert, oriented

HEENT>not anemic, anicteric
L/R (++/++) , PI (-), PTH (-/-), not dehydrated tongue
V/E (-/-), Neck LNE (-/-)

Chest > symmetric expansion without retraction
BLLF inspiratory crackle
RHB without murmur

Abdomen> Soft & flat
NABS, T/RT (-/-)
L/S/K (-/-/-)

Back & Ext.> CVAT (-/-) P/C/C (-/-/-)

Initial Lab finding>

CBC 19200 – 10.3 – 362K (seg 88.9%) BUN/Cr 5/0.6 mg/dL

T. Bil 0.9 mg/dL ALP 142 (30~115) IU/L AST/ALT 60/35 (0~40) IU/L

Glucose 125 mg/dL Alb 2.5 (3.3~5.2) g/dL CRP 13.55 (0~0.5) mg/dL

ABGA 7.495 – 32.9 – 81.8 – 26.6 – 97.1%

Sputum culture & Blood culture (-), Sputum AFB smear (-)

Legionella urinary Ag (-) Pnuemococcal urinary Ag (-)

CXR : Bilateral basal lung infiltration

Initial Assessment>

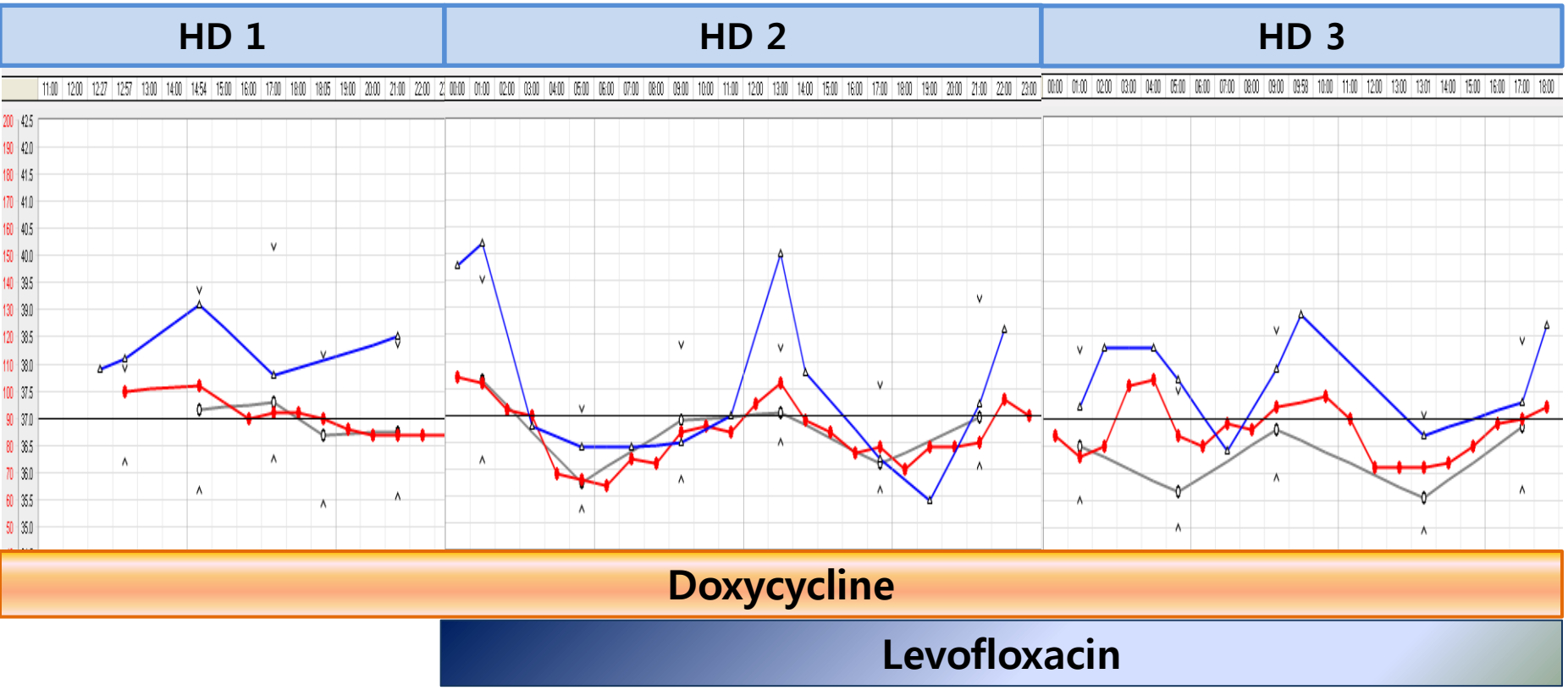
#1. Travel related infection
r/o post-travel Legionella pneumonia
r/o Mediterranean spotted fever
#2. r/o CAP
#3. r/o hidden malignancy

Initial Plan>

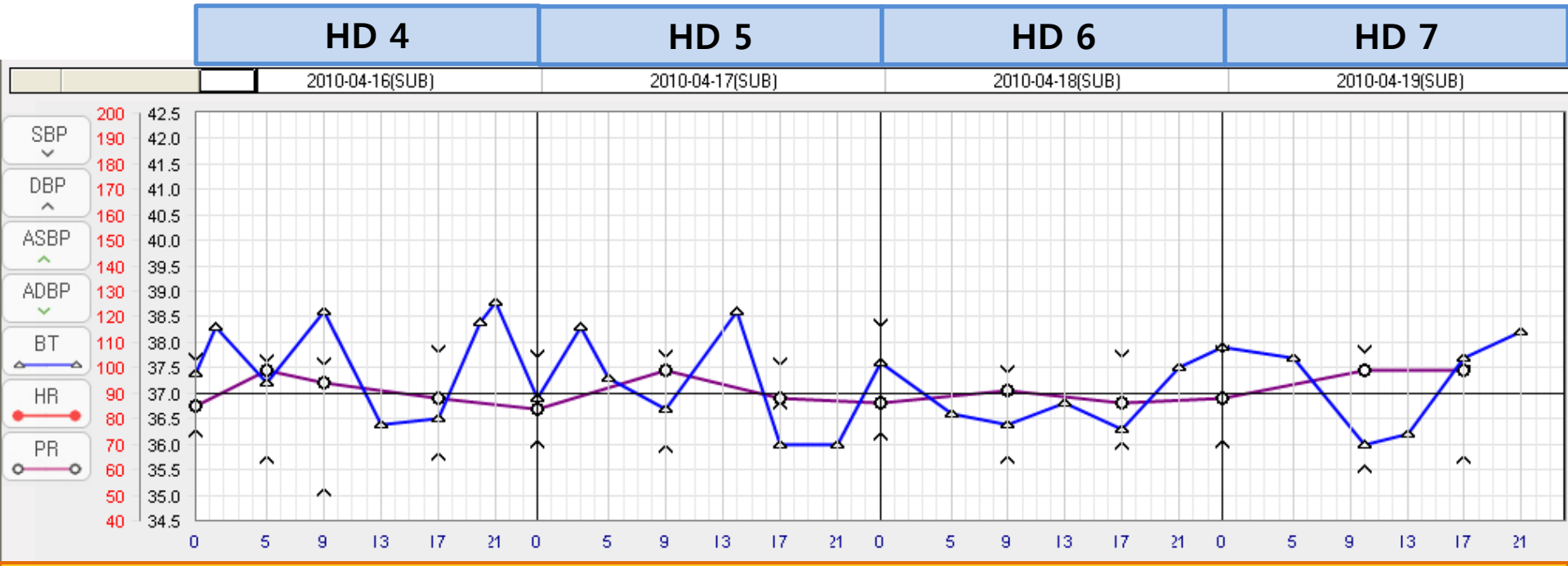
#1. #2. doxycycline, levofloxacin start
serology check

#3. consider VATS

Hospital Course>



Hospital Course>



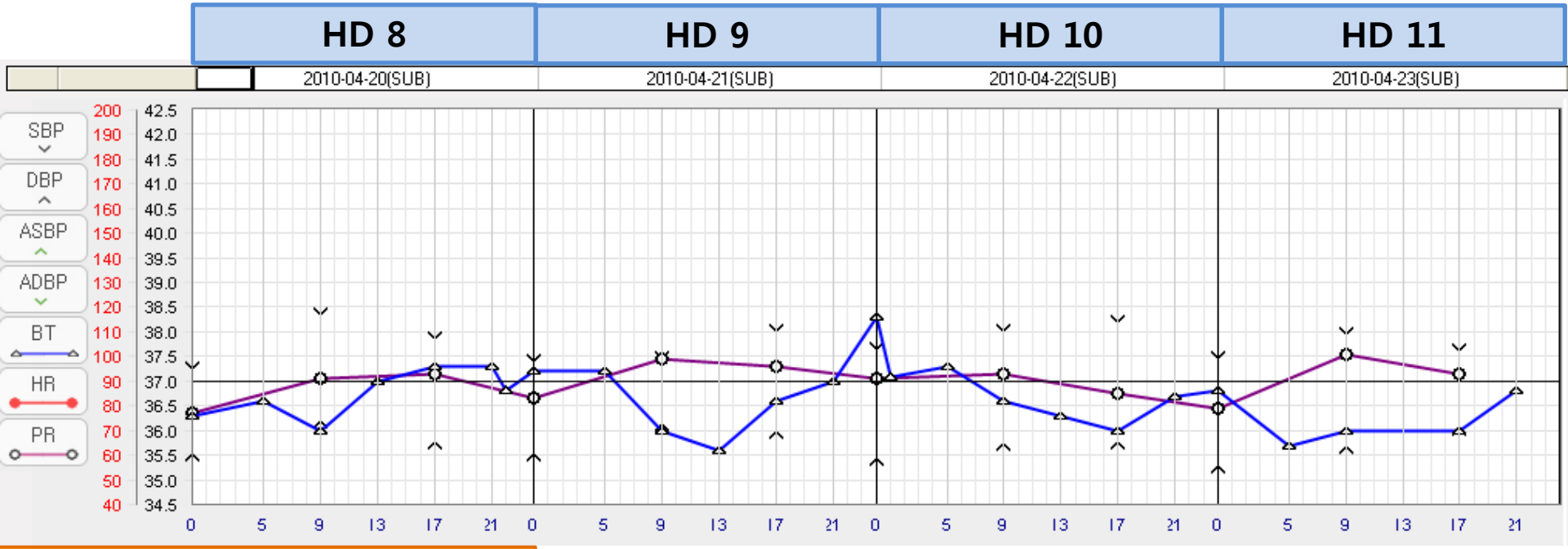
Doxycycline

Levofloxacin

Hold Levofloxacin due to AST/ALT elevation

Bronchoscopy & BAL 시행함.

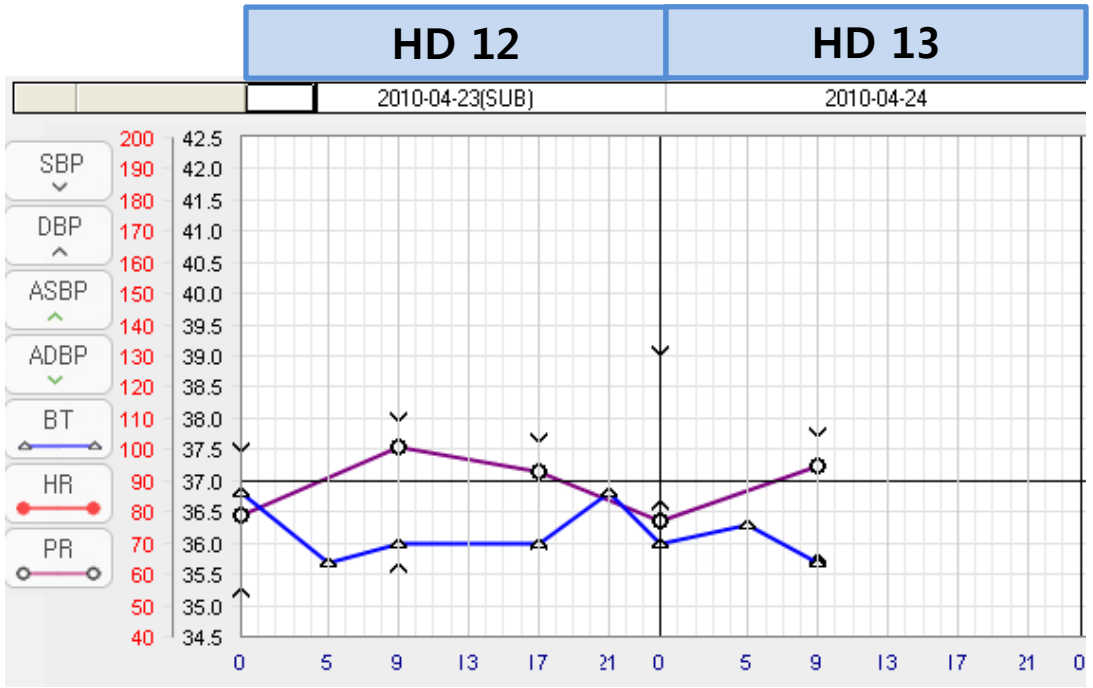
Hospital Course>



Doxycycline

- BAL resp. virus PCR : human coronavirus OC43/HKU1 positive
- Cytospin: RBC 10 WBC 554 (seg 8%, lympho 41%)

Hospital Course>

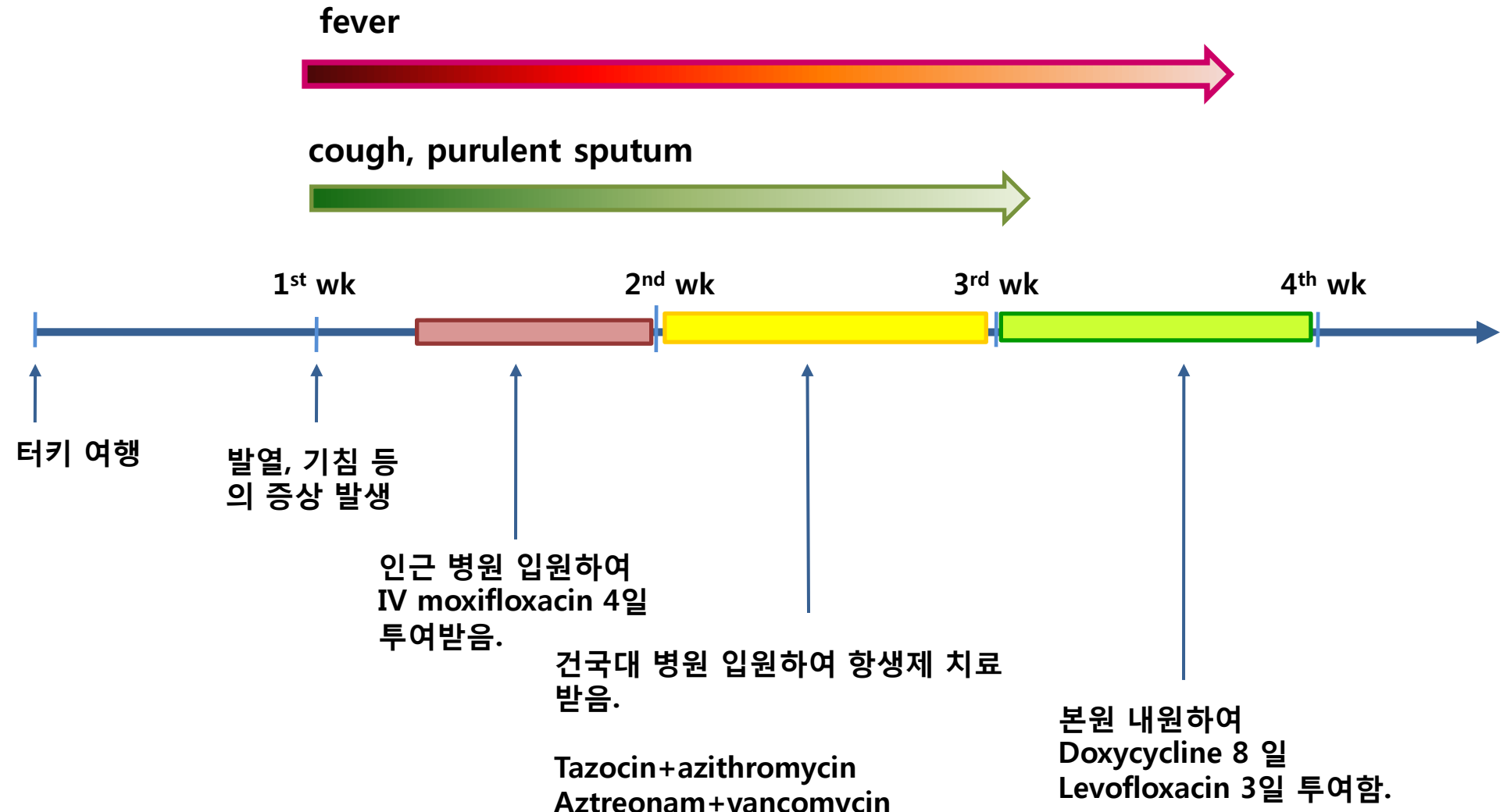


• 퇴원 후 외래에서 확인한 sputum AFB culture 1쌍과 BAL 검체로 시행한 AFB culture 에서 M. Tuberculosis 가 동정 되었음. (약 3 주 후)

• Mild cough 이외 다른 증상 및 검사 소견 모두 호전되어 퇴원함.

• CBC 12290 – 12.1 – 678 (seg 75.2%), CRP 1.52

Clinical Course>



Human Coronaviruses (HCoV)

- enveloped RNA viruses
- the family *Coronaviridae*, genus *coronavirus*
- **HCoV-229E**, **HCoV-OC43** : since the mid-1960s, the cause of common cold
- SARS-CoV : affected > 8000 people with 750 deaths in 2002 and 2003
- **HCoV-NL63** : from a 7month-old infant in Nethelands, 2004
- **HCoV-HKU1** : from an adult who had chronic pulmonary disease in Hong Kong, 2005

Diagnosis of viral pneumonia

1. Viral culture

- Gold standard
- Limitations : lower sensitivity
  - ✓ shedding low titers of viruses for a short period from adults with CAP
  - ✓ thermolabile
  - ✓ take between 3 and 14 days to yield results
  - ✓ require specific technical expertise, labor-intensive, expensive
  - ✓ Human novel coronaviruses (NL63, HKU1) grow poorly in viral cultures.

Curr Opin Infect Dis 22;143-147

Diagnosis of viral pneumonia

2. Rapid viral antigen detection

- by immunofluorescence or enzyme immunoassay
- Limitations : lower sensitivity
  - ✓ require relatively higher viral load
  - ✓ lack of reagents (rhinovirus, coronavirus, bocavirus)
  - ✓ lower sensitivity in detecting dual infections

3. Serology

- Single serum Ig G antibody titer is not useful.
- detection of Ig M in acute-phase serum
- Demonstration of a more than four-fold increase in virus-specific Ig G
  - ✓ most reliable
  - ✓ retrospective nature

Curr Opin Infect Dis 22;143-147

Diagnosis of viral pneumonia

4. Nucleic acid amplification test

- Improved sensitivity and specificity
- Very rapid results compared with conventional methods
- Multiplex PCR : simultaneously detect a large number of viral agents usinf a single test

Curr Opin Infect Dis 22;143-147

Incidence of viral community-acquired pneumonia

Population	Cause	Clinical findings	Reference
Consecutive immunocompetent patients admitted to hospital with CAP (N=193)	Overall microbiologic diagnosis 39%; bacterial 20%;**viral 15%**;**mixed 8%** **(coronavirus OC43,2%)**	Older and more frail; more heart disease; less chest pain;less leukocytosis	Johnstone *et al.* Chest 2008;134
Consecutive patients admitted to hospital with CAP (N=225)	Overall microbiologic diagnosis 58%; bacterial 48%;**viral 30%**;**mixed 15%** **(coronavirus OC43 & 229E ,1%)**	More myalgia; fewer rigors; fewer smokers; fewer neutrophils in nonrhinovirus infection	Jennings *et al.* Thorax 2008;63
Consecutive immunocompetent and immunosuppressed patients admitted to hospital with CAP (N=198)	Overall microbiologic diagnosis 57%; bacterial 33%;**viral 13%**;**mixed 10%** **(coronavirus,2%)**	Fewer leukocytosis; less CRP	Marcos et al. Antivir Ther 2006;11
Consecutive patients admitted to hospital with CAP (N=92); with CAP not hospitalized (N=13)	Overall microbiologic diagnosis 76%; bacterial 44%;**viral 50%**;**mixed 27%** **(coronavirus OC43 & 229E ,14%)**	87% of patients more than 60 years of age	Templeton et al. Clin Infect Dis 2005;41

Clinical features of coronavirus pneumonia

Characteristic	Description or value for patient[b]:					
	1	2	3	4	5	6
Sex/age (yr)[a]	F/2	F/7	M/84	M/3	M/87	F/4
Ethnic origin	Chinese	Chinese	Chinese	Chinese	Chinese	Chinese
Underlying condition(s)		Prematurity, cerebral palsy, epilepsy	COPD, old PTB, IHD, BPH, ex-smoker	Recurrent febrile exanthema, SMA carrier	MVP, AF, HT, hypercholesterolemia, ex-smoker	Febrile convulsion
Presenting symptoms						
Fever	+	+	+	+	+	+
Chills			+	+	+	
Rigor			+	+	+	
Cough			+		+	+
Sputum			+		+	
Dyspnea			+			
Rhinorrhea	+	+	+	+		
Vomiting					+	+
Convulsion	+	+				+
Other symptom(s)	Diarrhea	Skin rash	Myalgia	Skin rash, joint swelling		Abdominal pain
Physical examination finding(s)	Congested throat, shotty generalized lymphadenopathy	Generalized maculopapular rash, shotty cervical lymphadenopathy		Limb and joint swelling, generalized rash, shotty cervical lymphadenopathy	Bilateral basal crackles	Congested throat
Chest radiograph finding(s)	Not taken	Clear	Old tuberculosis	Not taken	Bilateral lower-zone haziness	Clear
Diagnosis	URTI, febrile seizure	URTI, epilepsy	URTI	URTI, angioedema	Pneumonia	URTI, febrile seizure
Duration of hospitalization (no. of days)	3	5	7	2	5	3

Clinical features of coronavirus pneumonia

Table 3 Characteristics of patients with community-acquired pneumonia associated with specific respiratory viruses

	Aetiological agent						
	Rhinovirus (n = 31)	Influenza A (n = 23)	Influenza B (n = 6)	RSV (n = 12)	Adenovirus (n = 11)	Parainfluenza virus (n = 6)	Coronavirus (n = 6)
Male	15 (48)	15 (65)	2 (33)	8 (67)	6 (55)	3 (50)	4 (67)
Age (years) (median (IQR))	66 (42–78)	66 (55–76)	72 (68–83)	79 (70–81)	51 (30–71)	81 (73–86)	71 (55–78)
Duration symptoms (days) (median (IQR))	7 (3–7)	7 (3–21)	6 (4–14)	6 (4–18)	3 (2–7)	6 (4–7)	6 (4–14)
Symptoms							
Cough	29/31 (94)	21/22 (96)	5/6 (83)	12/12 (100)	9/11 (82)	6/6 (100)	6/6/(100)
Sputum	23/31 (74)	16/22 (73)	4/6 (67)	10/12 (83)	8/11 (73)	2/5 (40)	4/6 (67)
Pleuritic pain	18/31 (58)	8/23 (35)	3/6 (50)	4/12 (33)	6/10 (60)	2/5 (40)	4/6 (67)
Rigors	14/29 (48)	5/11 (46)	1/3 (33)	2/8 (25)	1/4 (25)	2/3 (67)	2/2 (100)
Lethargy	26/30 (87)	15/15 (100)	4/4 (100)	7/9 (78)	5/6 (83)	2/2 (100)	3/3 (100)
Anorexia	23/30 (77)	13/14 (93)	3/3 (100)	6/9 (67)	6/6 (100)	0/2 (0)	2/2 (100)
Diarrhoea	5/30 (17)	5/12 (42)	3/4 (75)	4/8 (50)	2/6 (33)	0/2 (0)	–
Headache	12/29 (41)	5/9 (56)	1/2 (50)	1/7 (14)	1/4 (25)	0/2 (0)	–
Myalgia	7/27 (26)	5/10 (50)	2/2 (100)	2/7 (29)	2/5 (40)	0/2 (0)	–
Any comorbidity	18/31 (58)	13/23 (57)	3/6 (50)	10/12 (83)	7/11 (64)	3/6 (50)	4/6 (67)
COPD	6/31 (19)	8/23 (35)	1/6 (17)	4/12 (33)	3/11 (27)	2/6 (33)	3/6 (50)
Asthma	8/31 (26)	3/23 (13)	0/6 (0)	1/12 (8)	3/11 (27)	0/6 (0)	1/6 (17)
Cardiac failure	2/31 (7)	3/23 (13)	1/6 (17)	5/12 (42)	3/11 (27)	2/6 (33)	0/6 (0)
Diabetes	3/31 (10)	3/23 (13)	1/6 (17)	6/12 (50)	1/11 (9)	0/6 (0)	1/6 (17)
Cerebrovascular disease	4/31 (13)	3/23 (13)	0/6 (0)	5/12 (42)	1/11 (9)	2/6 (33)	0/6 (0)
Renal disease	1/31 (3)	1/23 (4)	1/6 (17)	1/12 (8)	1/11 (9)	0/6 (0)	0/6 (0)
Current smoker	7/31 (23)	7/23 (30)	1/6 (17)	1/12 (8)	4/11 (36)	1/6 (17)	0/6 (0)
Influenza vaccine within 1 year	16/31 (52)	7/23 (30)	2/5 (40)	8/12 (67)	5/11 (46)	5/6 (83)	2/6 (33)
CURBage >2	7/31 (23)	2/23 (9)	1/6 (17)	4/12 (33)	3/11 (27)	3/6 (50)	2/6 (33)
PSI class IV and V	12/31 (39)	15/23 (65)	3/6 (50)	9/12 (75)	4/11 (36)	5/6 (83)	3/6 (50)

Clinical features of coronavirus pneumonia

Parameter	Value for patients infected with:			
	CoV-HKU1	HCoV-NL63	HCoV-OC43	HCoV-229E
Total no. of patients	13	17	53	13
Male-to-female ratio	8:5	8:9	28:25	1:3
Age				
Range	19 mo–87 yr	6 mo–86 yr	1 mo–88 yr	2 yr–75 yr
Median (yr)	4	2	9	8.5
Duration of fever (days)				
Range	1–4	1–7	1–8	1–4
Median	1	1	1	2.5
Duration of hospitalization (days)				
Range	2–7	1–9	1–20	3–14
Median	3	3	3	3
No. (%) of patients with underlying diseases	8 (62)	10 (59)	34 (64)	2 (50)
No. (%) of patients with diagnosis of[a]:				
URTI[c]	11 (85)	12 (71)	41 (77)	2 (50)
Asthma/COPD exacerbation[c]	1 (8)	2 (12)	4 (8)	0 (0)
Acute bronchiolitis	1 (8)	1 (6)	3 (6)	0 (0)
Pneumonia	1 (8)	3 (18)	8 (15)	2 (50)
Croup	0 (0)	2 (12)	0 (0)	0 (0)
Febrile convulsion	5 (38)[b]	3 (18)	3 (6)[b]	0 (0)
Breakthrough seizure	2 (15)[b]	1 (6)	0 (0)[b]	0 (0)
Aseptic meningitis	0 (0)	0 (0)	1 (2)	0 (0)
Kawasaki disease	0 (0)	0 (0)	1 (2)	0 (0)
No. (%) of patients who died	0 (0)	0 (0)	1 (2)	0 (0)

Table 2. Epidemiological, clinical, and radiological characteristics of patients with community-acquired pneumonia associated with coronavirus HKU1. (N=418)

Characteristic	Patient									
	1	2	3	4	5 [19]	6	7	8	9	10
Month/year	Mar/2003	Apr/2003	May/2003	Jan/2004	Jan/2004	Jan/2004	Jan/2004	Jan/2004	Mar/2004	Mar/2004
Sex/age, years	F/35	M/66	M/13	M/75	M/71	F/96	M/78	M/68	F/83	M/72
Ethnic origin	Chinese	Arabian	Chinese	Chinese	Chinese	Chinese	Chinese	Chinese	Chinese	Chinese
Underlying disease(s)	–	Diabetes mellitus, old myocardial infarction, gastric lymphoma	Asthma, situs inversus, dextrocardia	Hypertension	Chronic obstructive airway disease, hyperlipidemia, abdominal aortic aneurysm	Hypertension	Chronic obstructive airway disease, diabetes mellitus	–	Chronic obstructive airway disease, parathyroid adenoma, dementia	Prostate carcinoma, cerebrovascular accident, diabetes mellitus
History of travel within 2 weeks of disease onset	–	–	Shenzhen, China	Guangdong, China	Shenzhen, China	–	–	Guangdong, China	–	–
History of smoking	–	–	–	+	+	–	+	–	+	+
Clinical feature										
Fever	+	–	+	–	+	+	+	+	+	+
Chills	–	–	–	–	+	–	–	–	–	–
Rigor	–	–	–	–	–	–	–	–	–	–
Myalgia	–	–	–	–	–	–	–	–	–	–
Headache	–	–	–	–	+	–	–	–	–	–
Cough	+	–	+	+	+	–	+	+	–	+
Sputum production	–	–	+	+	+	–	+	+	–	+
Dyspnea	–	+	–	+	–	–	+	+	+	+
Pleurisy	–	–	–	–	–	–	–	–	–	–
Rhinorrhea	–	–	–	–	+	–	–	–	–	–
Sore throat	+	–	–	–	+	–	–	–	–	–
Oxygen saturation level on room air, %	99	83	100	99	99	97	97	95	99	88
Chest radiograph features	RLZ airspace shadows	Bilateral airspace shadows	LMZ and LLZ airspace shadows	LLZ airspace shadows	LLZ airspace shadows	RLZ airspace shadows	LLZ airspace shadows	RMZ airspace shadows	RLZ airspace shadows	Bilateral airspace shadows
Outcome	Survived	Died	Survived	Survived	Survived	Survived	Survived	Survived	Survived	Died
Duration of hospitalization, no. of days	2	Died on day 12	3	7	5	7	13	5	6	Died on day 6

NOTE. +, present; –, absent; LLZ, left lower zone; LMZ, left middle zone; LUZ, left upper zone; RLZ, right lower zone; RMZ, right middle zone; RUZ, right upper zone.

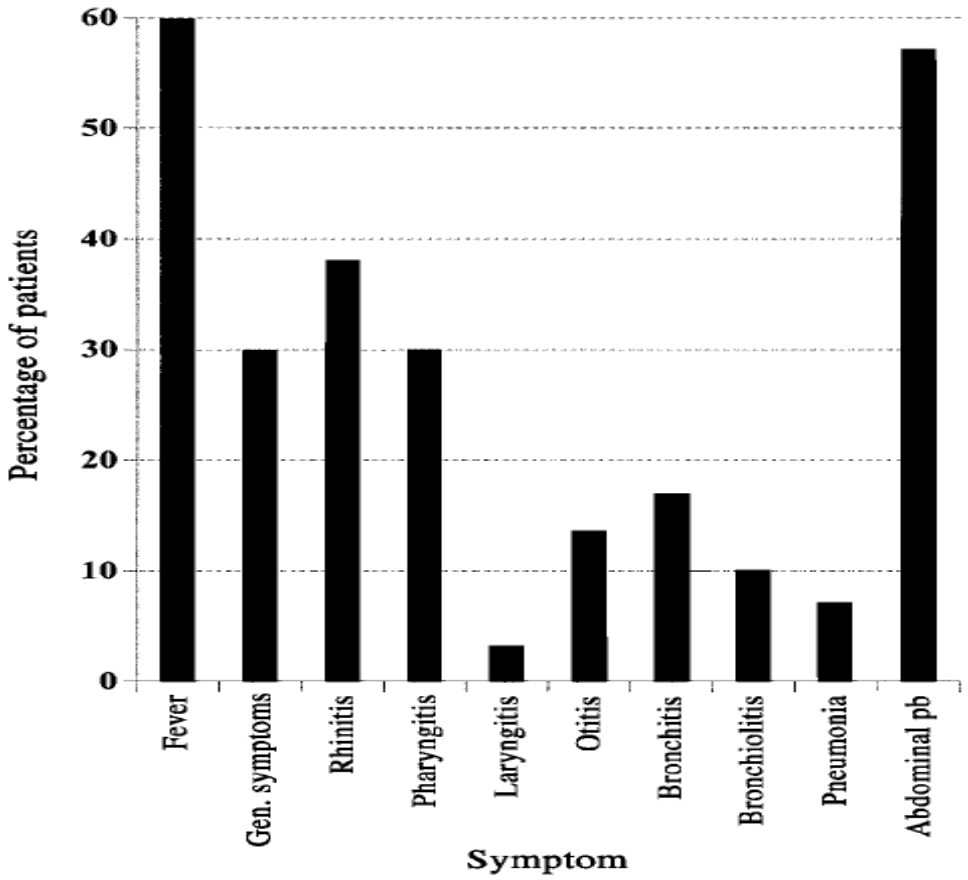
JID 2005;192

Table 4. Comparison of clinical, laboratory, and radiological characteristics of patients who survived and those who died of coronavirus HKU1–associated pneumonia.

Characteristic	Outcome[a]		P
	Survived ($n = 8$)	Died ($n = 2$)	
Sex, M:F	5:3	2:0	1.00
Age, years	73	69	.60
Underlying diseases	6	2	.45
History of travel within 2 weeks of disease onset	4	0	.24
History of smoking	4	1	1.00
Clinical features			
Fever	7	1	.26
Cough	6	1	.51
Sputum production	5	1	.76
Dyspnea	4	2	.22
Rhinorrhea	1	0	.62
Sore throat	2	0	.45
Hematological feature			
Hemoglobin concentration, g/dL	13.4	9	.04[b]
Leukocyte count, $\times 10^9$ leukocytes/L	9.7	7.85	.43
Neutrophil count, $\times 10^9$ neutrophils/L	7.4	6.9	.79
Lymphocyte count, $\times 10^9$ lymphocytes/L	1.35	0.55	.15
Monocyte count, $\times 10^9$ monocytes/L	0.7	0.3	.04[b]
Platelet count, $\times 10^9$ platelets/L	292	200.5	.79
Serum biochemical feature			
Sodium concentration, mmol/L	137.5	134	.11
Potassium concentration, mmol/L	3.9	4.5	.06
Creatinine concentration, μmol/L	79	76.5	.69
Urea concentration, mmol/L	4.6	10.75	.19
Albumin concentration, g/L	38.5	26	.04[b]
Globulin concentration, g/L	30	30	1.00
Bilirubin concentration, μmol/L	10	30.5	.79
ALT concentration, U/L	16.5	30.5	.36
Alkaline phosphatase concentration, U/L	86	190.5	.07
Oxygen saturation level on room air, %	99	85.5	.03[b]
Radiological feature			
Bilateral involvement	0	2	.003[b]
No. of zones involved	1	6	.01[b]

JID 2005;192

Clinical features of coronavirus pneumonia



30 patients who tested positive for human coronavirus OC43 by RT-PCR hybridization, February and March 2001,Lower Normandy, France.

Clinical Infectious Diseases 2003; 36:985–9

Clinical value of a positive result by respiratory virus PCR

• HCoV 229E and HCoV OC43 were not found by RT-PCR of nasopharyngeal aspirated from children without respiratory symptoms in Finland.

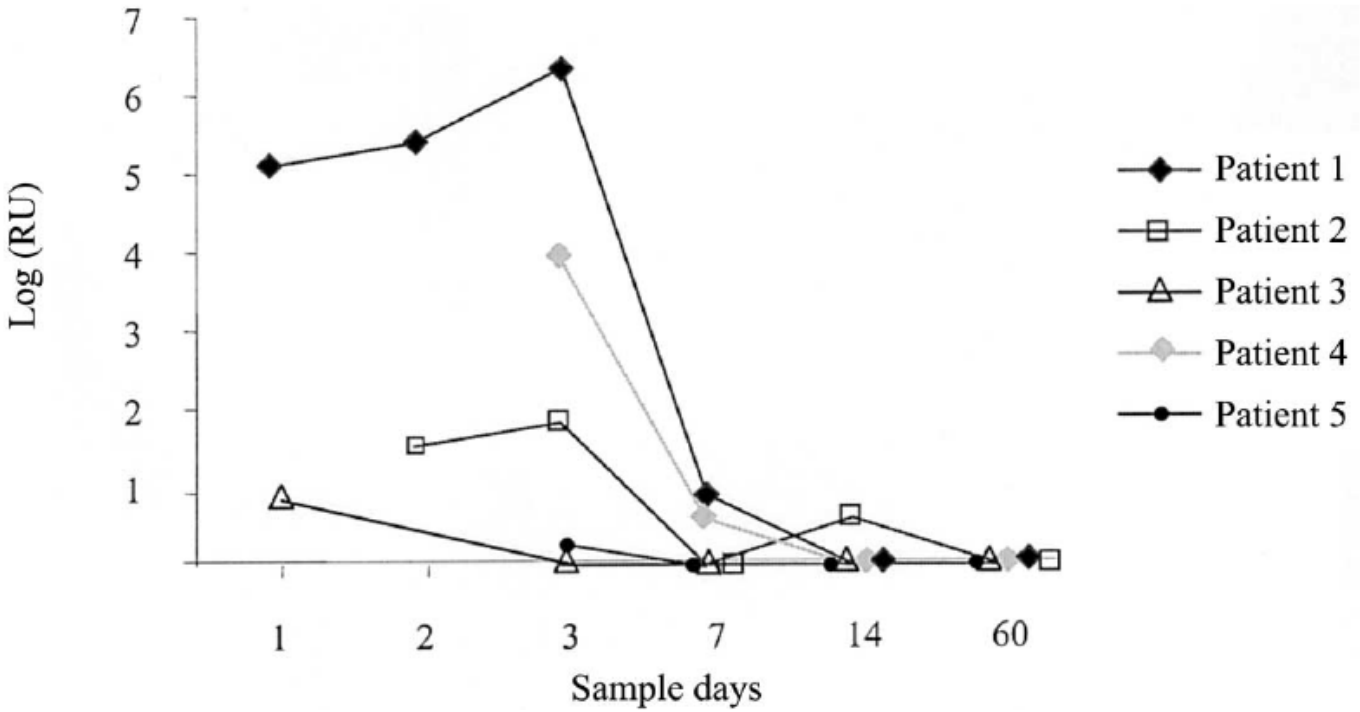
J Med Virol 2002;66:417-20

• 2 (15.4%) of 13 nasopharyngeal swabs from patients with pneumonia : positive RT-PCR for HCoV.

• HCoV RNA was detected in only 1 (0.4%) of 243 nasopharyngeal swabs from patients without symptoms of respiratory tract infection.

J Infect Dis 189;652-7

Clinical value of a positive result by respiratory virus PCR



J Infect Dis 189;652-7

Clinical value of a positive result by respiratory virus PCR

•HCoV-positive finding by RT-PCR in a specimen from a symptomatic patient might have diagnostic significance.