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BRIEF REPORT

First Case of 2019 Novel Coronavirus in the United States

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SUMMARY

An outbreak of novel coronavirus (2019-nCoV) that began in Wuhan, China, has spread rapidly, with cases now confirmed in multiple countries. We report the first case of 2019-nCoV infection confirmed in the United States and describe the identification, diagnosis, clinical course, and management of the case, including the patient's initial mild symptoms at presentation with progression to pneumonia on day 9 of illness. This case highlights the importance of close coordination between clinicians and public health authorities at the local, state, and federal levels, as well as the need for rapid dissemination of clinical information related to the care of patients with this emerging infection.

- 本篇為美國第一例確診2019-nCoV感染患者的個案報告，包括診斷、臨床病程以及治療過程，該病患在初期僅為輕微症狀，到病程第9日發展為肺炎。
- 本個案報告強調了臨床醫師與各級公共衛生當局之間密切協作的重要性。

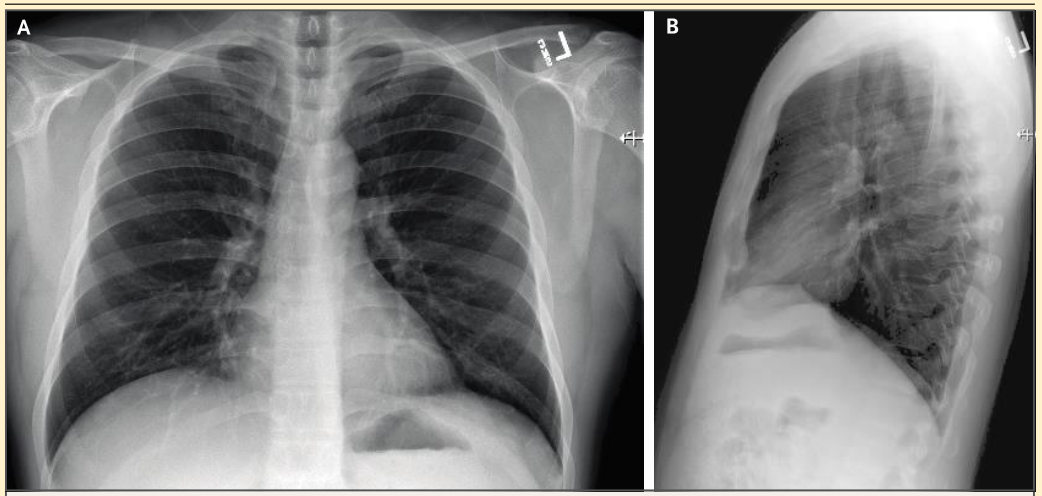


Figure 1. Posteroanterior and Lateral Chest Radiographs, January 19, 2020 (Illness Day 4).
No thoracic abnormalities were noted.

病程第4天：

- 35歲男性，2020/1/19因咳嗽、自覺發燒4天就醫
- 旅遊史：在探望武漢家人後，於2020/1/15返回華盛頓
- 過去史：高三酸甘油脂，不吸菸
- 理學檢查：T/P/R: 37.2°C/110/16, BP: 134/87, SpO2: 96% (ambient air), Lung auscultation: rhonchi
- CXR如右圖無明顯異常
- A及B型流感快速篩檢為陰性
- 鼻腔拭子檢測就診後48小時結果顯示皆為陰性，包括：influenza A and B, parainfluenza, respiratory syncytial virus, rhinovirus, adenovirus, 及四種常見可在人類致病的coronavirus (HKU1, NL63, 229E, and OC43)
- 因病患有武漢旅遊史，診所通報當地衛生部門，後續通報CDC，並決定應進行2019-nCoV病毒檢測

2020/1/20 rRT-PCR檢測結果為2019-nCoV陽性

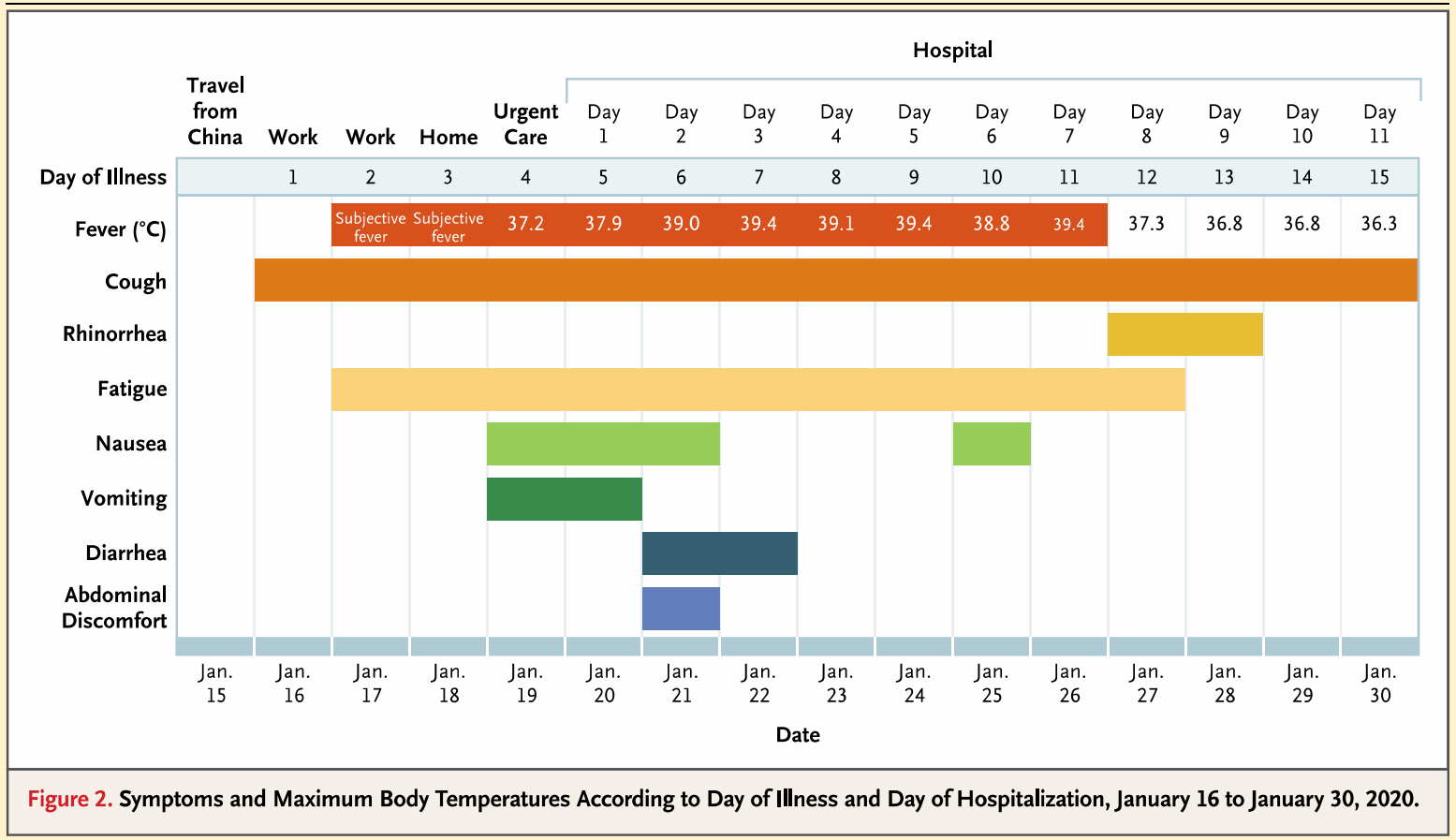


Figure 2. Symptoms and Maximum Body Temperatures According to Day of Illness and Day of Hospitalization, January 16 to January 30, 2020.

- 圖2為病患自病徵出現到入院後的症狀表現
- 病程第6天(入院第2天)開始出現發燒
- 持續性咳嗽(nonproductive)、疲倦
- 病程第4-6天出現噁心、嘔吐
- 病程第6-7天出現腹痛、腹瀉
- 在入院第2天採檢送驗2019-nCoV: **糞便、呼吸道樣本為陽性，血清為陰性**
- 病程第12天(入院第8天)：退燒，出現流鼻水

Table 1. Clinical Laboratory Results.*

Measure	Reference Range	Illness Day 6, Hospital Day 2†	Illness Day 7, Hospital Day 3	Illness Day 9, Hospital Day 5	Illness Day 11, Hospital Day 7	Illness Day 13, Hospital Day 9	Illness Day 14, Hospital Day 10
White-cell count (per μl)	3800–11,000	"Slight decrease"	3120‡	3300‡	5400	5600	6500
Red-cell count (per μl)	4,200,000–5,700,000	—	4,870,000	5,150,000	5,010,000	4,650,000	5,010,000
Absolute neutrophil count (per μl)	1900–7400	—	1750‡	1700‡	3700	3800	3200
Absolute lymphocyte count (per μl)	1000–3900	—	1070	1400	1400	1400	2100
Platelet count (per μl)	150,000–400,000	"Adequate"	122,000‡	132,000‡	151,000	150,000	239,000
Hemoglobin (g/dl)	13.2–17.0	12.2‡	14.2	14.8	14.8	13.5	14.2
Hematocrit (%)	39.0–50.0	36.0‡	42.0	43.0	43.0	39.3	42.0
Sodium (mmol/liter)	136–145	134‡	136	138	138	135‡	138
Potassium (mmol/liter)	3.5–5.1	3.3‡	3.6	3.4‡	3.6	4.1	3.9
Chloride (mmol/liter)	98–107	99	101	105	106	100	103
Calcium (mg/dl)	8.7–10.4	—	8.5‡	9.3	9.0	8.6‡	9.3
Carbon dioxide (mmol/liter)	20–31	—	26	24	25	23	36§
Anion gap (mmol/liter)	5–16	—	9	9	7	12	9
Glucose (mmol/liter)	65–140	104	103	120	96	148§	104
Blood urea nitrogen (mg/dl)	9–23	15	10	13	13	22§	18
Creatinine (mg/dl)	0.7–1.3	1.0	1.06	1.06	0.88	1.08	0.84
Total protein (g/dl)	5.7–8.2	—	6.9	7.1	6.8	6.9	6.8
Albumin (g/dl)	3.2–4.8	—	4.2	4.7	4.5	2.9‡	4.4
Total bilirubin (mg/dl)	0.3–1.2	—	1.0	1.1	1.5§	0.8	1.0
Procalcitonin (ng/ml)	<0.05	—	—	<0.05	<0.05	—	—
Alanine aminotransferase (U/liter)	10–49	—	68§	105§	119§	219§	203§
Aspartate aminotransferase (U/liter)	≤33	—	37§	77§	85§	129§	89§
Alkaline phosphatase (U/liter)	46–116	—	50	68§	88§	137§	163§
Fibrinogen (mg/dl)	150–450	—	477§	—	—	—	—
Lactate dehydrogenase (U/liter)	120–246	—	250§	465§	—	—	388§
Prothrombin time (sec)	12.2–14.6	—	11.9‡	11.9‡	—	—	12.7
International normalized ratio	0.9–1.1	—	0.9	0.9	—	—	1.0
Creatine kinase (U/liter)	62–325	—	353§	332§	—	—	—
Venous lactate (mmol/liter)	0.4–2.0	—	1.3	1.7	—	—	—

* To convert the values for calcium to millimoles per liter, multiply by 0.250. To convert the values for blood urea nitrogen to millimoles per liter of urea, multiply by 0.357. To convert the values for creatinine to micromoles per liter, multiply by 88.4. To convert the values for total bilirubin to micromoles per liter, multiply by 17.1.
† Results are from point-of-care blood analyzer (iStat) testing.
‡ The value in the patient was below normal.
§ The value in the patient was above normal.

血液檢查：

- 病程第7天和第9天(住院第3天和第5天)：
  - Leukopenia
  - mild thrombocytopenia
  - elevated CK
- ALP (68 U/l), ALT (105 U/l), AST (77 U/l), LDH (465 U/l) 在病程第9天(住院第5天)皆上升
- 在住院第4天因為反復發燒所做的血液培養皆為陰性

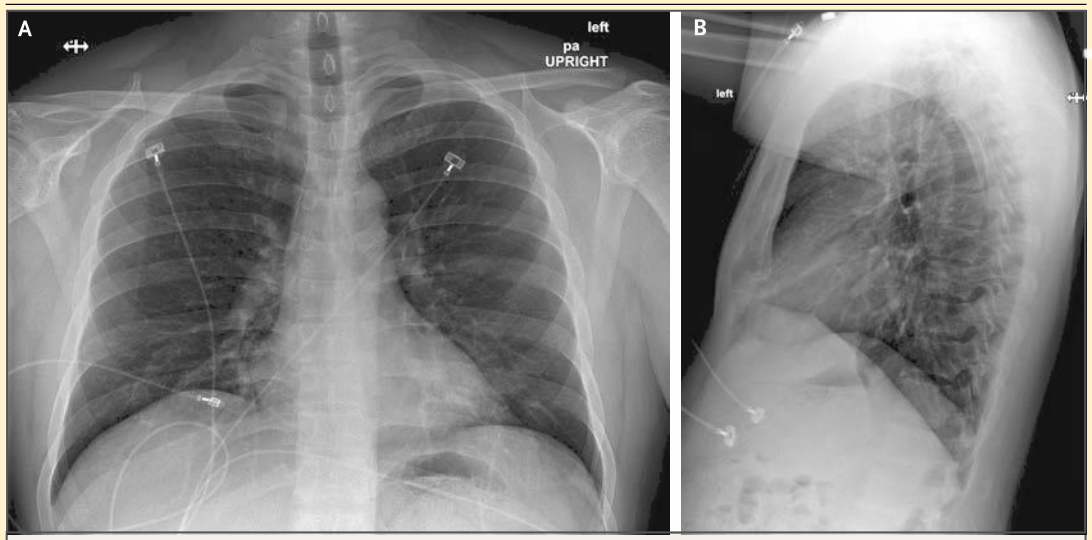


Figure 3. Posteroanterior and Lateral Chest Radiographs, January 22, 2020 (Illness Day 7, Hospital Day 3).
No acute intrathoracic plain-film abnormality was noted.

病程第7天(入院第3天)：CXR顯示肺部無浸潤或其他異常

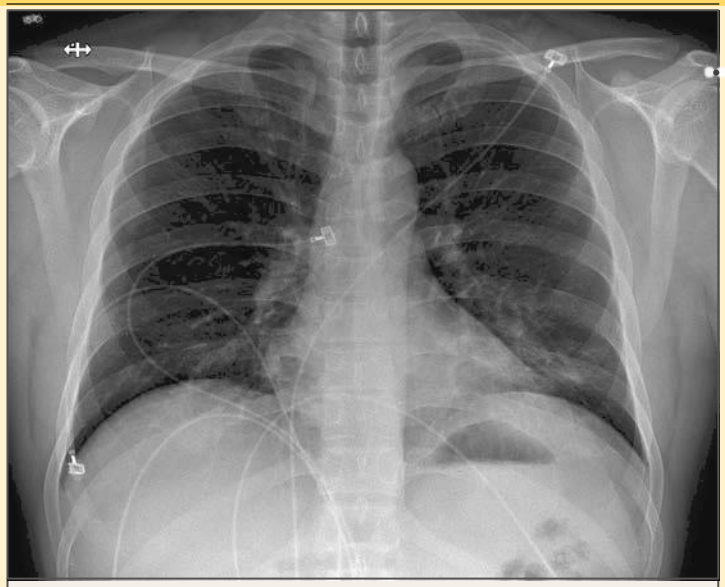


Figure 4. Posteroanterior Chest Radiograph, January 24, 2020 (Illness Day 9, Hospital Day 5).
Increasing left basilar opacity was visible, arousing concern about pneumonia.

病程第9天(入院第5天)：

- CXR顯示左下肺葉肺炎
- 病患SpO2下降至90% (ambient air)

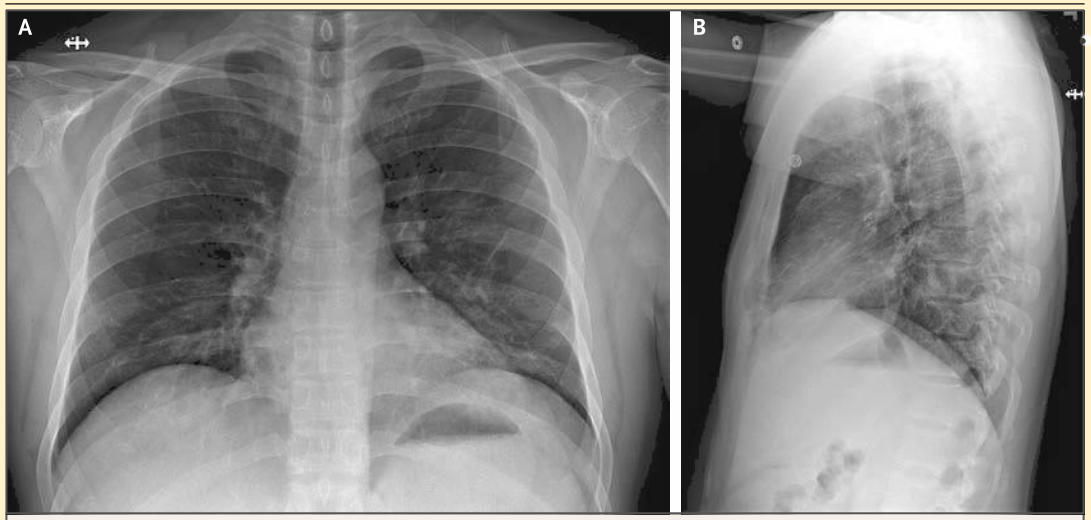


Figure 5. **Anteroposterior and Lateral Chest Radiographs, January 26, 2020 (Illness Day 10, Hospital Day 6).**
Stable streaky opacities in the lung bases were visible, indicating likely atypical pneumonia; the opacities have steadily increased in density over time.

病程第10天(入院第6天)：

- 開始給予氧氣治療
- 考量到hospital-acquired pneumonia, 開始給予Vancomycin及Cefepime治療
- 再追蹤CXR顯示雙側肺部basilar streaky opacities的非典型肺炎表現
- 持續發燒，肺部聽診兩側rales

病程第11天(入院第7天)：

- 考量病況持續進展，醫師決定給予研發中的抗病毒藥物**Remdesivir**
- 給予Remdesivir當天晚上停用Vancomycin，隔天停用Cefepime

病程第12天(入院第8天)：

- 病患臨床症狀改善，不再發燒
- 停止氧氣治療後，SpO2可達94-96% (ambient air)
- 雙側肺部rales消失
- 食慾改善，除了間歇性咳嗽和流鼻水，沒有其他症狀

至2020/1/30，患者仍住院中：

- 沒有發燒
- 咳嗽症狀減輕。除了咳嗽外，沒有其他症狀。

不同病程日各部位檢體之rRT-PCR檢測結果

Table 2. Results of Real-Time Reverse-Transcriptase–Polymerase-Chain-Reaction Testing for the 2019 Novel Coronavirus (2019-nCoV).*

Specimen	Illness Day 4	Illness Day 7	Illness Day 11	Illness Day 12
Nasopharyngeal swab	Positive (Ct, 18–20)	Positive (Ct, 23–24)	Positive (Ct, 33–34)	Positive (Ct, 37–40)
Oropharyngeal swab	Positive (Ct, 21–22)	Positive (Ct, 32–33)	Positive (Ct, 36–40)	Negative
Serum	Negative	Negative	Pending	Pending
Urine	NT	Negative	NT	NT
Stool	NT	Positive (Ct, 36–38)	NT	NT

* Lower cycle threshold (Ct) values indicate higher viral loads. NT denotes not tested.

＊ Cycle threshold (Ct)值越低，Viral loads越高

- 在病程第4天：
  - 鼻咽及口咽檢體結果皆為2019-nCoV陽性
  - **低Ct值，表示此時的viral loads高，雖然病患只有輕微症狀**
- 在病程第7天：
  - 鼻咽及口咽檢體結果仍為2019-nCoV陽性
  - **鼻咽檢體仍為高viral loads**
- 在病程第11天及12天：
  - 鼻咽及口咽檢體病毒量呈現下降趨勢
  - 口咽檢體於第12天顯示2019-nCoV陰性
- 血清檢體
  - 在病程第4天及第7天為2019-nCoV陰性
  - 其他病程日檢體仍在等待結果中
- 糞便檢體：
  - 在病程第7天為2019-nCoV陽性

Discussion

- 此個案有武漢旅遊史，但在武漢期間，沒有去過華南海鮮市場、醫療院所，或與其他患者接觸。雖然此患者的感染來源未明，但2019-nCoV可在人與人之間傳播已有實證。

- 在病程第4天和第7天，上呼吸道檢體檢測 2019-nCoV RNA結果顯示低 Ct值，代表**高病毒量以及潛在可傳播性**。
- 此個案在病程第7天於糞便檢體可測得2019- nCoV RNA，在病程第4天和第7天的血清檢體則為陰性。然而，在肺部外測得2019-nCoV RNA 並不一定表示感染此病毒，**呼吸道以外檢體測得2019-nCoV RNA的臨床重要性目前仍未明**。

- 目前對於2019-nCoV感染臨床表現的了解仍非常有限。其併發症如：嚴重肺炎、呼吸衰竭、ARDS、心臟損傷、死亡等，被報導在中國的個案。然而值得重視的是這些病例是根據肺炎的診斷確定為2019-nCoV感染的，因此可能會使報告偏向更嚴重的結果。

- 此篇文章的案例，最初出現輕度咳嗽和低度間歇性發燒，在病程第4天CXR沒有肺炎跡象，在病程第9天才發展為肺炎。**在2019-nCoV感染的早期臨床過程中，輕度的非特異性徵象和症狀，在臨床上可能與許多其他常見傳染病沒有明顯區別**，尤其是在冬季呼吸道病毒季節。

- 雖然此篇文章案例，在臨床狀況惡化的情況下使用Remdesivir抗病毒藥物治療後病況改善，但**仍需要進行隨機對照試驗來確定Remdesivir和其他任何研究藥物對於2019-nCoV感染治療的安全性和有效性。**

- 透過此篇個案報告，強調了**臨床醫師面對任何出現急性症狀的患者，應注意患者近期旅遊史或接觸史的重要性**，以確保對可能處於2019-nCoV感染危險中的患者進行適當的辨識和即時隔離，並有助於減少進一步傳播。