‘Τι είναι ο κορωνοιός’

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Introduction

- At the end of 2019, a novel coronavirus was identified as the cause of a cluster of pneumonia cases in Wuhan, China.
- It rapidly spread, resulting in an epidemic throughout China, followed by an increasing number of cases in other countries throughout the world.
- On March 11, 2020 the WHO declared a pandemic
- Since 31 December 2019 > 1.068.000 deaths have been reported.

Pathophysiology

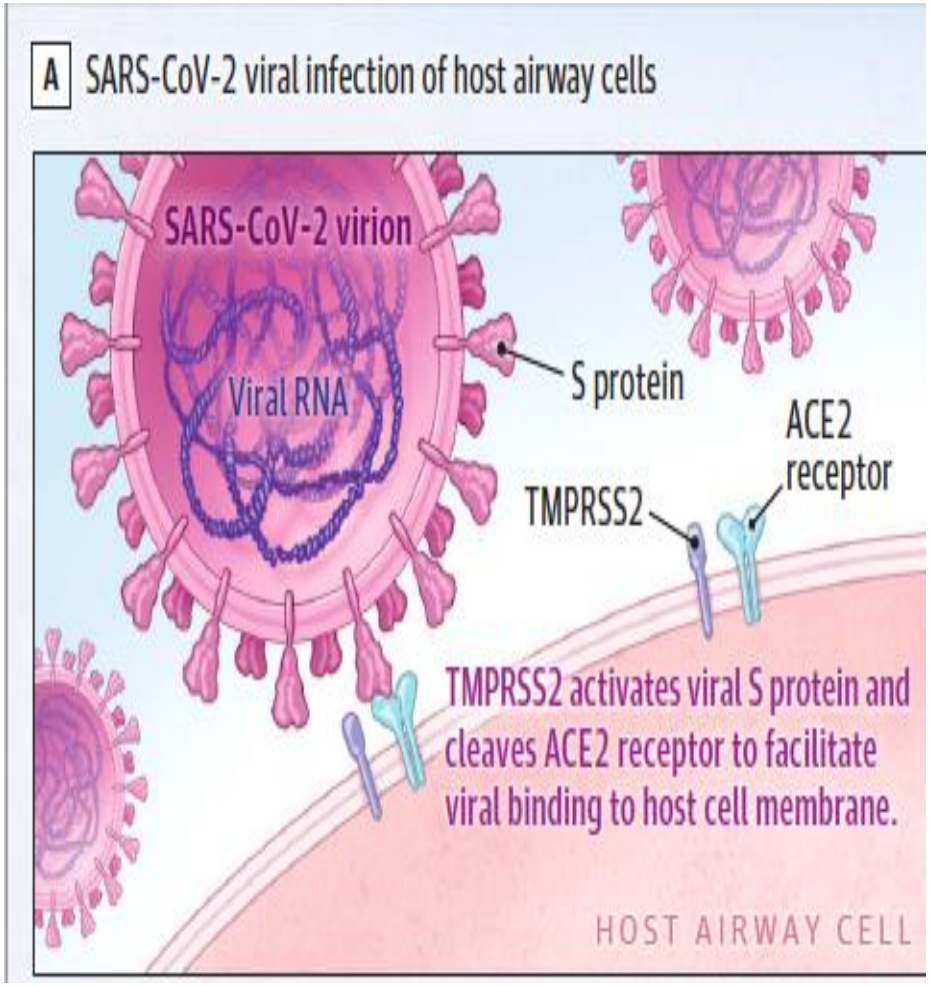
- Single-stranded RNA viruses
- Found in humans and other mammals, such as dogs, cats, chicken, cattle, pigs, and birds.
- Cause respiratory, gastrointestinal, and neurological disease.
- The most common coronaviruses in clinical practice are 229E, OC43, NL63,and HKU1,which typically cause common cold symptoms in immunocompetent individuals.

Pathophysiology

- SARS-CoV-2 is the third coronavirus that has caused severe disease
- The first coronavirus was SARS, which was resulted in the 2002-2003 SARS-CoV pandemic.
- The second was the coronavirus-caused MERS in 2012.
- Bats are thought to be a natural reservoir for SARS-CoV-2, but it has been suggested that humans became infected with SARSCoV- 2 via an intermediate host, such as the pangolin.

The Host Defense Against SARS-CoV-2

- Early in infection
- SARS-CoV-2 targets nasal and bronchial epithelial cells and pneumocytes, through the viral structural spike (S) protein that binds to the angiotensin-converting enzyme 2 (ACE2) receptor.
- The type 2 transmembrane serine protease (TMPRSS2), present in the host cell, promotes viral uptake by cleaving ACE2 and activating the SARS-CoV-2 S protein, which mediates coronavirus entry into host cells



The Host Defense Against SARS-CoV-2

- Profound lymphopenia may occur when SARS-CoV-2 infects and kills T lymphocyte cells.
- Although up regulation of ACE2 receptors from ACE inhibitor and angiotensin receptor blocker medications has been hypothesized to increase susceptibility to SARS-CoV-2 infection, large observational cohorts have not found an association between these medications and risk of infection or hospital mortality due to COVID-19.
  - In a study 4480 patients with COVID-19 from Denmark, previous treatment with ACE inhibitors or angiotensin receptor blockers was not associated with mortality.

The Host Defense Against SARS-CoV-2

In severe COVID-19, fulminant activation of coagulation and consumption of clotting factors occur

- High incidence of thrombotic complications
  - such as deep venous thrombosis, pulmonary embolism, and thrombotic arterial complications (eg, limb ischemia, ischemic stroke, myocardial infarction) in critically ill patients
- The development of viral sepsis, defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, may further contribute to multiorgan failure.

Transmission of SARS-CoV-2 Infection

- **Droplets** during talking, coughing, or sneezing is the most common mode of transmission.
  - Higher risk for transmission in
    - Prolonged exposure to an infected person (6 feet for at least 15 min)
    - Briefer exposures to individuals who are symptomatic (eg, coughing)
  - Less likely to result in transmission in
    - Brief exposures to asymptomatic contacts
- Via **aerosols** (smaller droplets that remain suspended in air)
  - Existence of aerosols in physiological states (eg, coughing) or
  - Detection of nucleic acid in the air does not mean that small airborne particles are infectious.

Touching a surface with virus on it is another possible mode of transmission

- The clinical significance of SARS-CoV-2 transmission from in animate surfaces is difficult to interpret without knowing the minimum dose of virus particles that can initiate infection.
- Viral load persist at higher levels on impermeable surfaces, such as stainless steel and plastic, for up to 3 to 4 days after inoculation than permeable surfaces, such as cardboard.
- Widespread viral contamination of hospital rooms has been documented.
- However, it is thought that the amount of virus detected on surfaces decays rapidly within 48 to 72 hours.

The effect of temperature on persistence of SARS-CoV-2 on common surfaces

Shane Riddell*, Sarah Goldie, Andrew Hill, Debbie Eagles and Trevor W. Drew

Abstract

Background: The rate at which COVID-19 has spread throughout the globe has been alarming. While the role of fomite transmission is not yet fully understood, precise data on the environmental stability of SARS-CoV-2 is required to determine the risks of fomite transmission from contaminated surfaces.

Methods: This study measured the survival rates of infectious SARS-CoV-2, suspended in a standard ASTM E2197 matrix, on several common surface types. All experiments were carried out in the dark, to negate any effects of UV light. Inoculated surfaces were incubated at 20 °C, 30 °C and 40 °C and sampled at various time points.

Results: Survival rates of SARS-CoV-2 were determined at different temperatures and D-values, Z-values and half-life were calculated. We obtained half lives of between 1.7 and 2.7 days at 20 °C, reducing to a few hours when temperature was elevated to 40 °C. With initial viral loads broadly equivalent to the highest titres excreted by infectious patients, viable virus was isolated for up to 28 days at 20 °C from common surfaces such as glass, stainless steel and both paper and polymer banknotes. Conversely, infectious virus survived less than 24 h at 40 °C on some surfaces.

Conclusion: These findings demonstrate SARS-CoV-2 can remain infectious for significantly longer time periods than generally considered possible. These results could be used to inform improved risk mitigation procedures to prevent the fomite spread of COVID-19.

Keywords: Environmental stability, SARS-CoV-2, COVID-19, Survivability

Riddell et al. Virol J 2020; 17:145

Transmission of SARS-CoV-2 Infection

- Viral load in the upper respiratory tract
  - Viral shedding begins 2 - 3 days prior to the onset of symptoms
  - Peak at the time of symptom onset
- Pharyngeal shedding is high during the first week of infection at a time in which symptoms are still mild
- Asymptomatic and presymptomatic carriers can transmit SARS-CoV-2
- Infections transmitted from a presymptomatic individual is ranging between 48% - 62%.

Transmission of SARS-CoV-2 Infection

- Viral nucleic acid can be detectable in throat swabs > 6 weeks
- Viral cultures are negative 8 days after symptom onset.
- Studies have shown that transmission did not occur 5 days after the onset of symptoms.
- This suggests that individuals can be released from isolation based on clinical improvement.
- The Centers for Disease Control and Prevention recommend
  - Isolating for at least 10 days after symptom onset and 3 days after improvement of symptoms.
  - Uncertainty whether serial testing is required for specific subgroups
    - immunosuppressed patients or critically ill patients or older adults residing in short or long-term care facilities.

Clinical features

Spectrum of illness severity

- Asymptomatic
- Mild
  - mild clinical symptoms without pneumonia
- Ordinary
  - fever and other respiratory symptoms with pneumonia
- Severe
  - respiratory distress
  - hypoxia (oxygen saturation, ≤93%), or
  - abnormal results of blood gas ($PaO_2 < 90$ mm Hg or $PaCO_2 > 50$ mm Hg)
- Critical
  - respiratory failure requiring mechanical ventilation,
  - shock, or other organ failure requiring intensive care unit monitoring and treatment.

Spectrum of illness severity

The spectrum of symptomatic infection ranges from mild to critical; most infections are not severe

Box. Key Findings From the Chinese Center for Disease Control and Prevention Report

72 314 Cases (as of February 11, 2020)
- Confirmed cases: 44 672 (62%)
- Suspected cases: 16 186 (22%)
- Diagnosed cases: 10 567 (15%)
- Asymptomatic cases: 889 (1%)

Age distribution (N = 44 672)
- ≥80 years: 3% (1408 cases)
- 30-79 years: 87% (38 680 cases)
- 20-29 years: 8% (3619 cases)
- 10-19 years: 1% (549 cases)
- <10 years: 1% (416 cases)

Spectrum of disease (N = 44 415)
- Mild: 81% (36 160 cases)
- Severe: 14% (6168 cases)
- Critical: 5% (2087 cases)

Case-fatality rate
- 2.3% (1023 of 44 672 confirmed cases)
- 14.8% in patients aged ≥80 years (208 of 1408)
- 8.0% in patients aged 70-79 years (312 of 3918)
- 49.0% in critical cases (1023 of 2087)

Health care personnel infected
- 3.8% (1716 of 44 672)
- 63% in Wuhan (1080 of 1716)
- 14.8% cases classified as severe or critical (247 of 1668)
- 5 deaths

Wu et al. JAMA 2020;323:1239-1242

The proportion of severe or fatal infections may vary by location

- The adjusted case fatality rate in mainland China was 1.4 %
  - Most of the fatal cases occurred in patients with advanced age or underlying medical comorbidities
- In Italy, the estimated case fatality rate was 7.2 %
  - 12 % of all detected COVID-19 cases and 16 % of all hospitalized patients were admitted in ICU
- In contrast, the estimated case fatality rate in South Korea was 0.9 %
  - This may be related to distinct demographics of infection, in Italy, the median age of patients with infection was 64 years, whereas in Korea the median age was in the 40s

UpToDate 2020

Risk factors for severe illness

Established and possible epidemiologic risk factors for severe COVID-19[1-6]

- Age >65 years*
- Pre-existing pulmonary disease
- Chronic kidney disease
- Diabetes mellitus
- History of hypertension
- History of cardiovascular disease
- Obesity (BMI ≥30)
- Use of biologics (eg, TNF inhibitors, interleukin inhibitors, anti-B cell agents) (presumed)¶
- History of transplant or other immunosuppression (presumed)¶
- HIV, CD4 cell count <200 cells/microL or unknown CD4 count (presumed)¶

https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-epidemiology-virology-clinical-features-diagnosis-and-prevention

Laboratory features associated with severe COVID-19[1-6]

Abnormality	Possible threshold
Elevations in:	
▪ D-dimer	>1000 ng/mL (normal range: <500 ng/mL)
▪ CRP	>100 mg/L (normal range: <8.0 mg/L)
▪ LDH	>245 units/L (normal range: 110 to 210 units/L)
▪ Troponin	>2× the upper limit of normal (normal range for troponin T high sensitivity: females 0 to 9 ng/L; males 0 to 14 ng/L)
▪ Ferritin	>500 mcg/L (normal range: females 10 to 200 mcg/L; males 30 to 300 mcg/L)
▪ CPK	>2× the upper limit of normal (normal range: 40 to 150 units/L)
Decrease in:	
▪ Absolute lymphocyte count	<800/microL (normal range for age ≥21 years: 1800 to 7700/microL)

https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-epidemiology-virology-clinical-features-diagnosis-and-prevention

Asymptomatic disease

- SARS-CoV2 may be transmitted by the asymptomatic carrier
- True percentage is difficult to assess
- [1]Cruise ship Diamond Princess was 17.9%
- [2]Another study reported that the asymptomatic ratio was estimated at 30.8% among evacuees tested positive for SARS-CoV-2 using the information on Japanese nationals that were evacuated from Wuhan, China

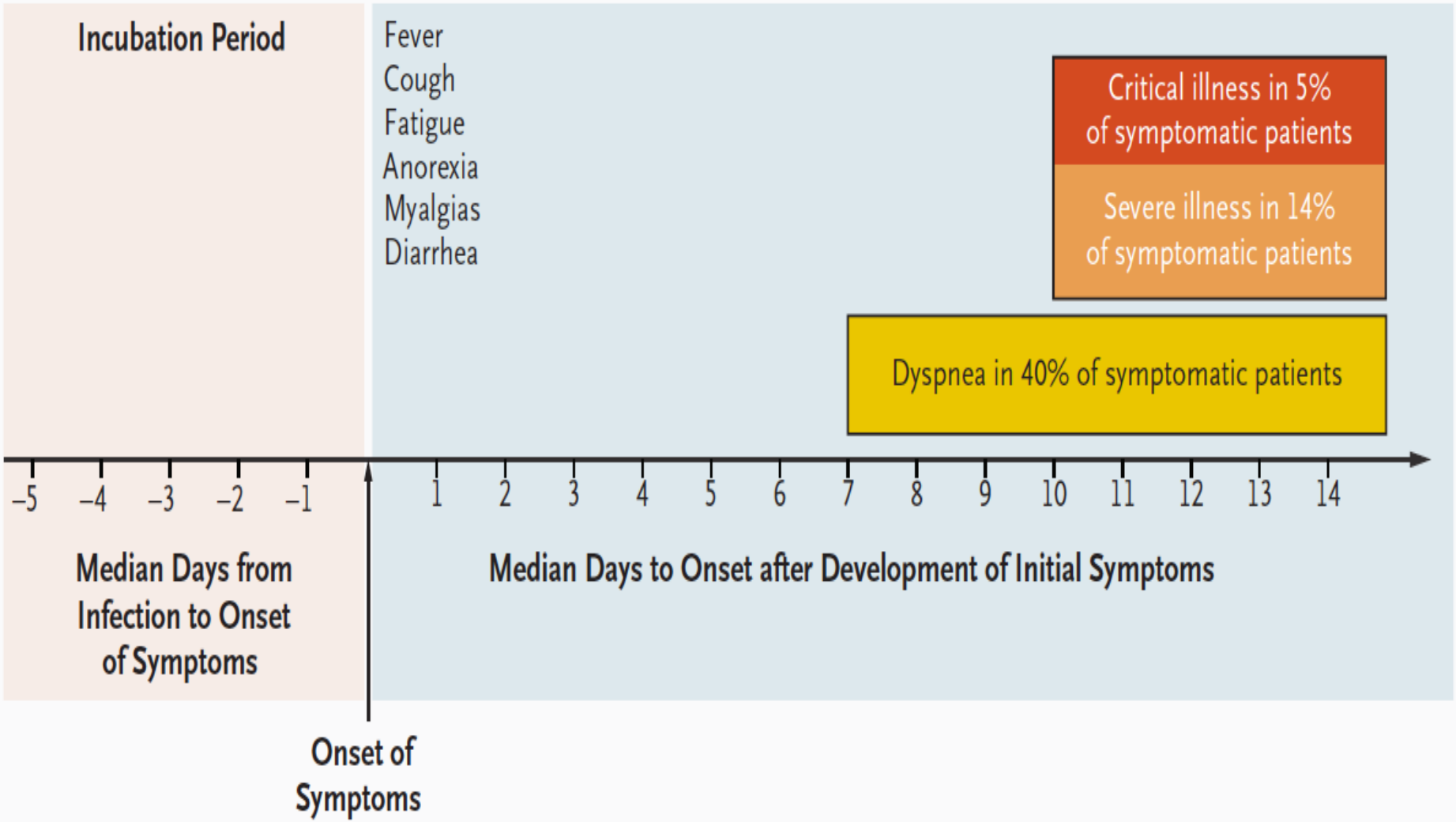
1.Mizumoto et al. Euro Surveill. 2020;25(10):pii=2000180, 2. Nishiura H, et al. Int J Infect Dis. 2020;94:154-155.
3. Wang et al. J Infect Dis 2020;221:1770–4

Incubation period

- The incubation period 14 days following exposure
- In a study of 1099 patients, the median incubation period was 4 days (interquartile range 2 to 7 days).[1]
- In a study of 181 cases from China[2]
  - Symptoms developed in
    - 2.5 % of infected individuals within 2.2 days
    - in 97.5 % of infected individuals within 11.5 days
    - The median incubation period in this study was 5.1 days.

1. Gouan et al. N Engl J Med. 2020;382:1708-1720, 2. Wu et al. JAMA 2020;323:1239-1242

Clinical manifestations



DOI: 10.1056/NEJMcp2009575

Initial presentation

- Pneumonia appears to be the most frequent serious manifestation of infection, characterized primarily by fever, cough, dyspnea, and bilateral infiltrates on chest imaging.

- However, other features, including upper respiratory tract symptoms, myalgias, diarrhea, and smell or taste disorders, are also common

https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19-

Clinical presentation-Symptoms

Clinical symptoms	All	Severe Disease	Non-Severe
Fever,%	88.7	91.9	88.1
Cough,%	67.8	70.5	67.3
Fatigue,%	38.1	39.9	37.8
Sputum production,%	33.7	35.3	33.4
Shortness of breath,%	18.7	37.6	15.1
Myalgia or arthralgia,%	14.9	17.3	14.5
Sore throat,%	13.9	13.3	14.0
Headache,%	13.6	15.0	13.4
Chills,%	11.5	15.0	10.8
Nausea or vomiting,%	5.0	6.9	4.6
Nasal congestion,%	4.8	3.5	5.1
Diarrhea,%	3.8	5.8	3.5

Gouan et al. N Engl J Med. 2020;382:1708-1720

Cutaneous manifestations

- 88 patients with COVID-19 reported 20.4% of cutaneous manifestations
  - Erythematous maculopapular rash (14 patients)
  - Widespread urticaria (three patients)
  - Chickenpoxlike vesicles (one patient).
  - Trunk was the mainly involved region.
  - Itching was low or absent and usually lesions healed in few days.
- Apparently, there was not any correlation with disease's severity

Recalcati S. J Eur Acad Dermatol Venereol 2020

Course and complications

- Symptomatic infection can range from mild to critical.
- Some patients with initially non-severe symptoms may progress over the course of a week.
- In one study of 138 patients hospitalized in Wuhan for pneumonia due to SARS-CoV-2
  - dyspnea developed after a median of 5 days since the onset of symptoms
  - hospital admission occurred after a median of 7 days of symptoms.
- In another study, the median time to dyspnea was eight days

https://www.uptodate.com/contents/coronavirus-disease-2019-covid-19

Complications

- Acute respiratory distress syndrome (ARDS)
- Other complications have included arrhythmias, acute cardiac injury, and shock
- Thromboembolic complications
- Exuberant inflammatory response, similar to cytokine release syndrome
- Guillain-Barré syndrome
- Kawasaki disease and toxic shock syndrome

- According to the WHO, recovery time appears to be around 2 weeks for mild infections and 3-6 weeks for severe disease

Cardiovascular Sequelae of COVID-19

- Patients with pre-existing CVD appear to have worse outcomes with COVID-19.
- CV complications include biomarker elevations, myocarditis, heart failure, arrythmia, cardiogenic shock and venous thromboembolism.
- Therapies under investigation for COVID-19 may have significant drug-drug interactions with CV medications.

Driggin et al. JACC 2020;75: 2352

- In a series of 21 severely ill patients admitted to the ICU in the United States, one-third developed cardiomyopathy

Arentz M et al. JAMA. 2020

Association of Cardiac Injury With Mortality in Hospitalized Patients With COVID-19 in Wuhan, China

Table 2. Treatment, Complications, and Clinical Outcome of 416 Patients With COVID-19

Characteristic	Patients, No. (%)			
		Cardiac injury		
	All (n = 416)	With (n = 82)	Without (n = 334)	*P* value
Complications				
ARDS	97 (23.3)	48 (58.5)	49 (14.7)	<.001
Acute kidney injury	8 (1.9)	7 (8.5)	1 (0.3)	<.001
Electrolyte disturbance	30 (7.2)	13 (15.9)	17 (5.1)	.003
Hypoproteinemia	27 (6.5)	11 (13.4)	16 (4.8)	.01
Anemia	13 (3.1)	4 (4.9)	9 (2.7)	.30
Coagulation disorders	12 (2.9)	6 (7.3)	6 (1.8)	.02
Clinical outcome				
Remained in hospital	319 (76.7)	38 (46.3)	281 (72.2)	<.001
Discharged	40 (9.6)	2 (2.4)	38 (23.4)	
Died	57 (13.7)	42 (51.2)	15 (4.5)	<.001

Shi et al. JAMA Cardiol. doi:10.1001/jamacardio.2020.0950

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Regular Article

THROMBOSIS AND HEMOSTASIS

COVID-19 and coagulation: bleeding and thrombotic manifestations of SARS-CoV-2 infection

Hanny Al-Samkari,[1,2] Rebecca S. Karp Leaf,[1,2] Walter H. Dzik,[1,2] Jonathan C. T. Carlson,[1,2] Annemarie E. Fogerty,[1,2] Anem Waheed,[1,2] Katayoon Goodarzi,[1,2] Pavan K. Bendapudi,[1,2] Larissa Bornikova,[1,2] Shruti Gupta,[2,3] David E. Leaf,[2,3] David J. Kuter,[1,2] and Rachel P. Rosovsky[1,2]

[1]Division of Hematology Oncology, Massachusetts General Hospital, Boston, MA; [2]Harvard Medical School, Boston, MA; and [3]Division of Renal Medicine, Brigham

Overall thrombotic complication rate and management

- The overall thrombotic complication rate was 9.5% (95% CI, 6.8-12.8; 45 events in 38 patients).
- This included a rate of 4.7% (95% CI, 2.4-8.0), in non-critically ill patients and a rate of 18.1% (95% CI, 12.1-25.3), in critically ill patients.
- Four patients with thrombotic complications also developed bleeding complications.

Thrombotic events and event rates

- The rate of radiographically confirmed VTE was 4.8% (95% confidence interval [CI], 2.9-7.3, including 19 events in 19 patients)
  - All but 1 of the patients were receiving anticoagulation with standard prophylactic doses (supplemental Table 1) of UFH or LMWH at the time of the event
- The arterial thrombosis rate was 2.8% (95% CI, 1.4-4.9);
  - including 11 events in 11 patients patients with non-ST elevation myocardial infarction, 1 patient with unstable angina, and 1 patient with bilateral line–associated radial artery thromboses.
  - All patients were receiving anticoagulation with prophylactic doses of UFH or LMWH at the time of the event.

JAMA Neurology | Original Investigation

Neurologic Manifestations of Hospitalized Patients With Coronavirus Disease 2019 in Wuhan, China

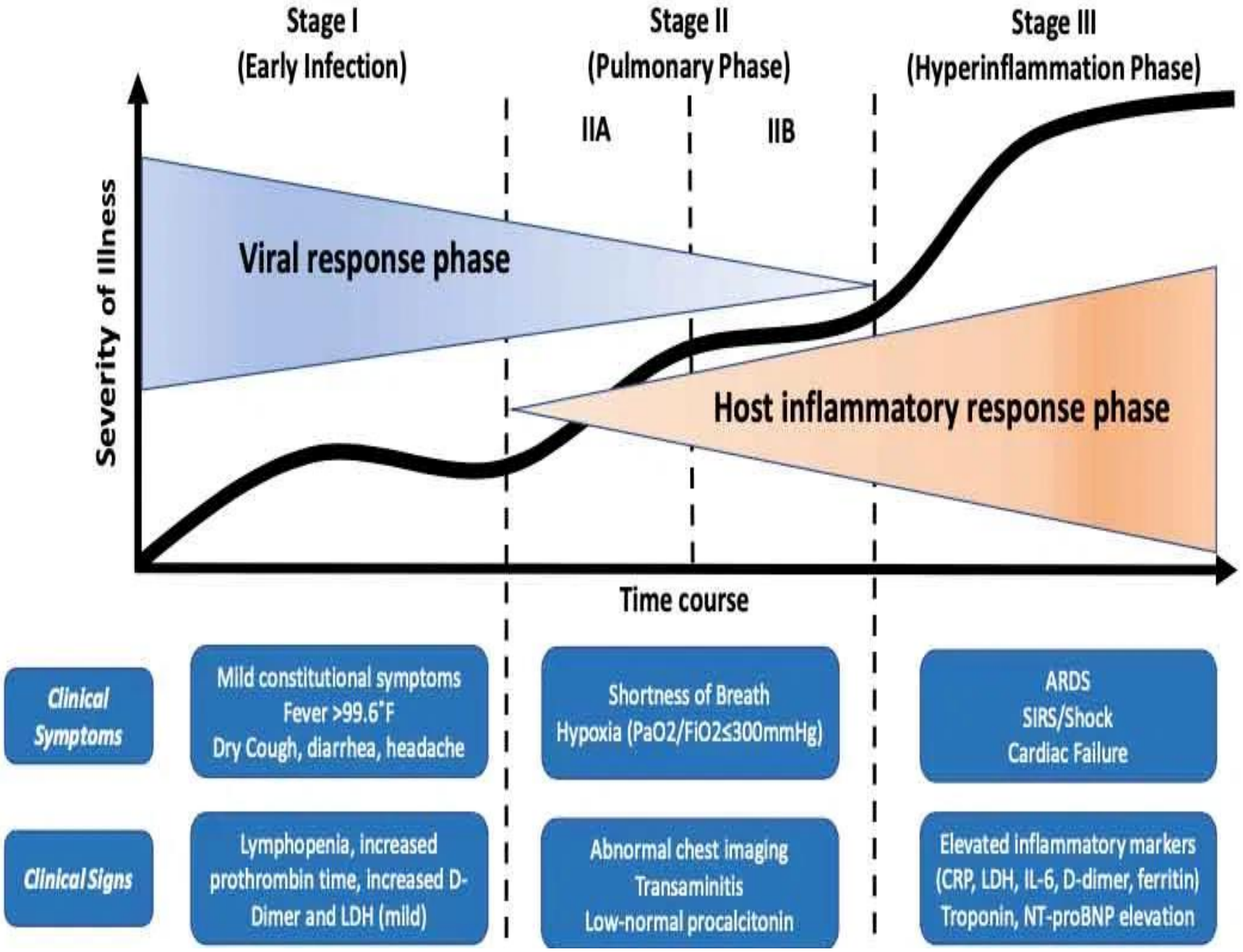
- 214 patients (41% severe)
- 36,4% neurological symptoms: 45,5% of severe patients Vs 30,2% of non-severe

- CNS 24,8% Dizziness, Headache, impaired consciousness
- PNS 8,9% Hypogeusia, Hyposmia
- Skeletal muscle injury 10,7%

- Acute cerebrovascular disease: 5 patients
- Ischemic Stroke: 4 patients
- Intracranial hemorrhage: 1 patient (died form respiratory failure after 22 days)

Mao et al. JAMA Neurol 2020 Apr 10;e201127.

Course and complications



COVID-19: consider cytokine storm syndromes and immunosuppression

- Tissue damage in COVID-19 is mediated by the host innate immunity.
- Is characterised by a cytokine storm resembling that of MAS seen in viral-induced haemophagocytic lymphohistiocytosis
- It is associated with COVID-19 disease severity, characterised by increased
  - Interleukin (IL)-2, IL-7
  - Granulocyte colonystimulating factor
  - Interferon-γ inducible protein 10
  - Monocyte chemoattractant protein 1
  - Macrophage inflammatory protein 1-α
  - TNF-α.

1. Huang Cet al. Lancet 2020; 395: 497–506. 2. https://doi.org/10.1016/ S0140-6736(20)30628-0

Diagnosis

Reverse transcription polymerase chain reaction

- Positive PCR from respiratory samples (eg, nasopharynx) is the standard for diagnosis.
- **The sensitivity of testing varies with**

1. **Timing of testing relative to exposure**
   - 33% 4 days after exposure
   - 62% on the day of symptom onset, and
   - 80% 3 days after symptom onset.
2. **Sample type**
   - BAL 93%
   - Sputum 72%
   - Nasal swabs 63%
   - Pharyngeal swabs 32%

Serology

- The presence of antibodies may not confer immunity because not all antibodies produced in response to infection are neutralizing.
- IgM antibodies are detectable within 5 days of infection, with higher IgM levels during weeks 2 to 3 of illness,
- IgG response is first seen approximately 14 days after symptom onset.
- Higher antibody titers occur with more severe disease.

Treatment

Treatment

Supportive Care and Respiratory Support

- > 75% of patients hospitalized require supplemental oxygen therapy.
- Approximately 8% of hospitalized patients with COVID-19 experience a bacterial or fungal co-infection, but up to 72% are treated with broad-spectrum antibiotics.

Targeting the Virus and the Host Response

- The following classes of drugs are being evaluated or developed for the management of COVID-19:
  - Antivirals (eg, remdesivir, favipiravir)
  - Antibodies (eg, convalescent plasma, hyperimmune immunoglobulins),
  - Anti-inflammatory agents (dexamethasone, statins)
  - Targeted immunomodulatory therapies (eg, tocilizumab, sarilumab, anakinra, ruxolitinib),
  - Anticoagulants (eg, heparin)
  - Antifibrotics (eg, tyrosine kinase inhibitors)

Antiviral drugs
Remdesivir

- The first preliminary results of a double-blind, randomized, placebo-controlled trial of 1063 adults hospitalized with COVID- 19 and evidence of lower respiratory tract involvement patients randomized to receive remdesivir had a
- shorter time to recovery than patients in the placebo group (11 vs. 15 days).

Plasma

- Results of studies of treatment with plasma obtained from patients who have recovered from viral infections are still controversial

Modulating inflammatory response - Corticosteroids

- The RECOVERY trial, which randomized 2104 patients with COVID-19 to receive 6mg daily of dexamethasone for up to 10 days and 4321 to receive usual care, found that
- dexamethasone reduced 28-day all-cause mortality (21.6% vs 24.6%; age adjusted rate ratio,0.83 [95%CI,0.74-0.92]; P < .001).
- The benefit was greatest in patients with symptoms for more than 7 days and patients who required mechanical ventilation.

Thromboembolic prophylaxis

- Thromboembolic prophylaxis with subcutaneous low molecular weight heparin is recommended for all hospitalized patients with COVID-19.
- Studies are ongoing to assess whether certain patients (ie, those with elevated D-dimer) benefit from therapeutic anticoagulation.

Prognosis

- Overall hospital mortality is approximately 15% to 20%
- > 40% among patients requiring ICU admission.
- Hospital mortality ranges from
- > 5% among patients younger than 40 years
- ~ 35% for patients aged 70 - 79 years
- > 60% for patients aged 80 to 89 years.

Genomic evidence for reinfection with SARS-CoV-2: a case study

Richard L Tillett, Joel R Sevinsky, Paul D Hartley, Heather Kerwin, Natalie Crawford, Andrew Gorzalski, Chris Laverdure, Subhash C Verma, Cyprian C Rossetto, David Jackson, Megan J Farrell, Stephanie Van Hooser, Mark Pandori

- The first case of likely COVID-19 reinfection in the U.S.
- The Nevada patient, a 25-year-old man, tested positive on April 18 and June 5. In between, he had two negative tests.
- During his second infection, he experienced worse symptoms and required oxygen.
- The two viruses causing the infections were genetically distinct.
- Previous exposure to SARS-CoV-2 might not guarantee total immunity in all cases. All individuals, whether previously diagnosed with COVID-19 or not, should take identical precautions to avoid infection with SARS-CoV-2

***Lancet Infect Dis* 2020**

Prevention

- Interventions can be divided into
- **Personal actions** (eg, physical distancing, personal hygiene, and use of
- protective equipment)
- **Case and contact identification** (eg, test trace- track-isolate, reactive school or workplace closure),
- **Regulatory actions** (eg, governmental limits on sizes of gatherings or business capacity; stay-at-home orders; proactive school, workplace, and public transport closure or restriction; cordon sanitaire or internal border closures)
- **International border measures** (eg, border closure or enforced quarantine).
- Risk of resurgence follows when these interventions are lifted.

JAMA | Original Investigation

Association Between Statewide School Closure and COVID-19 Incidence and Mortality in the US

Katherine A. Auger, MD, MSc; Samir S. Shah, MD, MSCE; Troy Richardson, PhD; David Hartley, PhD, MPH; Matthew Hall, PhD; Amanda Warniment, MD; Kristen Timmons, MS; Dianna Bosse, BA; Sarah A. Ferris, BA; Patrick W. Brady, MD, MSc; Amanda C. Schondelmeyer, MD, MSc; Joanna E. Thomson, MD, MPH

- The authors estimate that school closure may have been associated with
- 1.37 million fewer cases of COVID-19 over a 26-day period
- 40600 fewer deaths over a 16-day period during the spring of 2020.

JAMA. Published online July 29, 2020. doi:10.1001/jama.2020.14348

Vaccine

- A human vaccine is currently not available for SARS-CoV-2, but approximately 120 candidates are under development.
- More than a dozen candidate SARS CoV- 2 vaccines are currently being tested in phase 1-3 trials.

Conclusions

- Most of the patients have a mild RTI
- Severe illness usually begins approximately 1 week after the onset of symptoms.
- Dyspnea is the most common symptom of severe disease and is often accompanied by hypoxemia
- A striking feature of Covid-19 is the rapid progression of respiratory failure soon after the onset of dyspnea and hypoxemia.
- Patients with severe Covid-19 commonly meet the criteria for ARDS.
- Severe Covid-19 may also lead to acute cardiac, kidney, and liver injury, in addition to coagulopathy, and shock. These organ failures may be associated with a cytokine release syndrome characterized by high fevers, thrombocytopenia, hyperferritinemia, and other inflammatory markers.