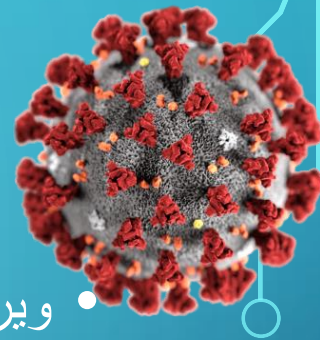


The background of the slide is a solid blue color. Scattered across this background are numerous red, spherical virus particles. Each particle is covered in small, white, conical spikes, giving them a textured, three-dimensional appearance. The particles vary in size and are positioned at various angles, creating a sense of depth and movement.

COVID-19

Dr. Narges Najafi

Associate professor of
Mazandaran University of Medical Sciences



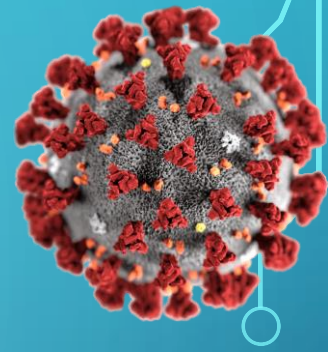
• ویروس **آبله** بزرگترین قاتل انسان بود با این حال اکنون یکی از معدود بیماری هایست که ریشه کن شده است

• **انفلوانزا** با ویرانگری های دوره ای همچنان بار سنگینی به دوش جهان است

• ویروس های جدیدی چون **HIV** همچنان بشر را با تهدیدها و چالش های جدیدی روبه رو می کنند

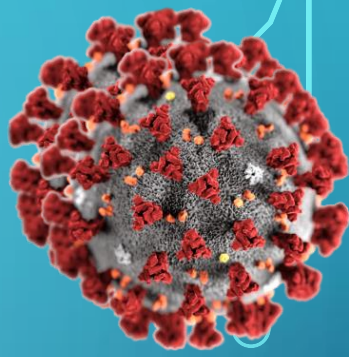
• و ویروس ها همچنان به غافلگیر کردن ما ادامه می دهند

UPPER RESPIRATORY INFECTIONS



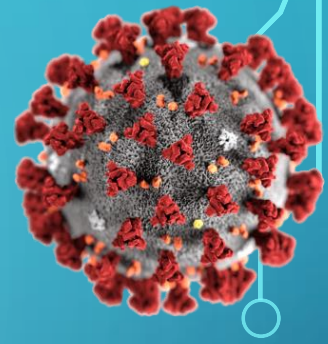
- Normal human coronaviruses cause **5-10%** of common cold/URIs,
- with outbreaks to **30%** of common cold
 - **229E** and **NL63** (alpha coronaviruses)
 - **OC43** and **HKU1** (beta coronaviruses)
- These four predominately attach to receptors in UPPER airway (receptors: aminopeptidase N, dipeptidyl peptidase 4)
- Seasonality unpredictable (generally winter, but persists year round), different pattern in tropics than temperate regions
- **URI symptoms, croupy or dry cough, rarely pneumonia** (except sometimes NL63, but usually just causes croup); Mild diarrhea in infants
 - Don't forget other URI viruses: Rhinovirus, Influenza A/B, Adenovirus, Parainfluenza, Respiratory syncytial virus, Human metapneumovirus

“NOVEL” CORONAVIRUSES



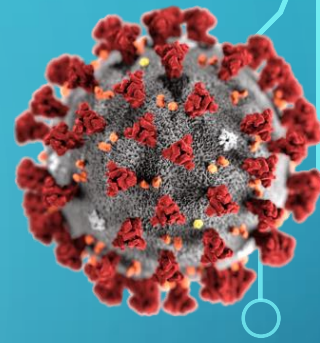
- Novel coronaviruses predominantly in **LOWER respiratory tract**
- **SARS, MERS, SARS-CoV-2**
- Don't forget other LRIs:
 - **Viral Pneumonia:** Influenza (A/B), Adenovirus, Parainfluenza (Type 1-4), Respiratory syncytial virus, Human metapneumovirus, **NL63**
 - **Typical bacteria CAP:** Lobar – *Streptococcus pneumoniae*, *Staphylococcus aureus*, *Haemophilus influenzae*, *Moraxella catarrhalis*; Gram neg, anaerobic if aspiration
 - **Bacterial bronchitis or atypical CAP:** *Bordetella pertussis*, *Mycoplasma pneumoniae*, and *Chlamydia pneumoniae*

INTRODUCTION



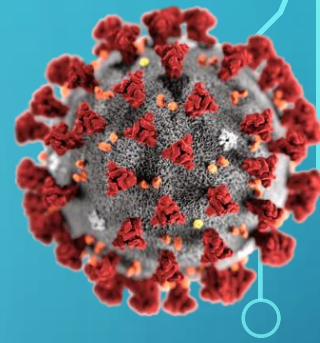
- The World Health Organization (WHO) was alerted on 31st December 2019 to a cluster of pneumonia cases of unknown etiology in patients in Wuhan City, China
- A week later it was known to be the novel coronavirus
- Also called Severe Acute Respiratory Syndrome coronavirus 2 (SARS-CoV-2)
- That is why the illness is called COVID-19 as of 11st February 2020

COVID-19



•Symptoms and Clinical Manifestations

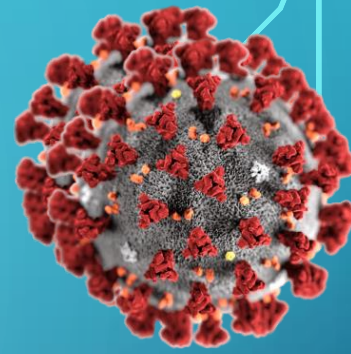
COVID-19 INCUBATION



Infection to Illness Onset

“Symptoms may appear ***2-14 days after exposure*** to the virus”

CLINICAL PRESENTATION

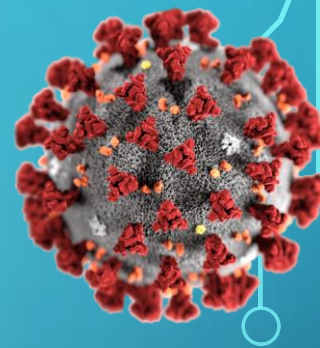


- Truly asymptomatic COVID-19 patients (as distinguished from pre-symptomatic patients) have been described, but their proportion is not well characterized yet.
- **Among symptomatic patients in China:**
 - a) 81 % developed mild disease
 - b) 14% developed severe disease with hypoxaemia, dyspnea and tachypnea and
 - c) 5% become critically ill (with respiratory failure, septic shock and/or multiorgan dysfunction).

Table I Simple clinical classification

Grade	Type	Clinical findings
0	asymptomatic patients	individuals without clinical signs
I	mild	outpatients and patients with mild clinical symptoms or lower or upper respiratory tract infections.
II	moderate	patients requiring hospitalization, with lobar or multilobar pneumonia with/without the need for supplemental oxygen, or refractory to initial treatment.
III	severe	patients who need ICU treatment, noninvasive or invasive mechanical ventilatory support, or with acute respiratory distress syndrome and/or non-pulmonary involvement.
IV	very severe or critical	patients who need immunomodulatory therapy or with multiorgan failure and/or cytokine storm.
ICU, intensive care unit		

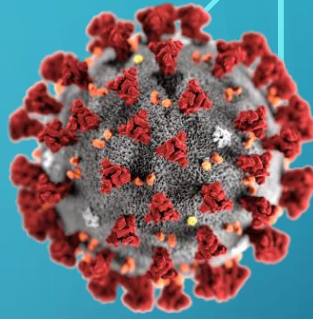
It first emerged as relatively common, early, and moderately specific symptoms.



CORMORBIDITIES AND RISK CONDITIONS

- **Age**
- **HTN**
- **Diabetes**
- **Coronary Heart Disease**
- **Cerebrovascular Disease**
- **COPD**
- **Cancer**
- **Children and pregnant women seem to do okay**

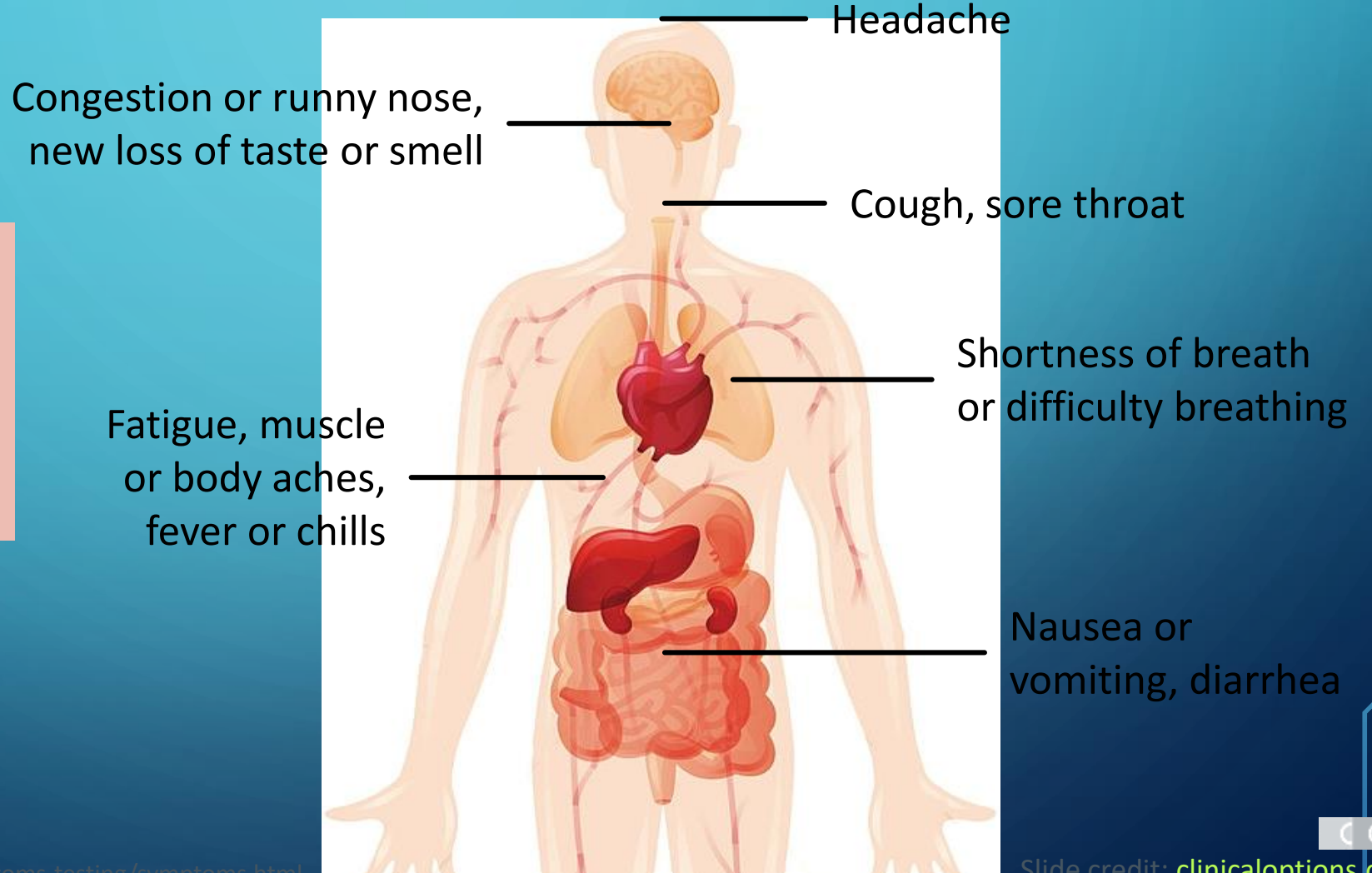
CLINICAL PRESENTATION :SYMPTOMATOLOGY



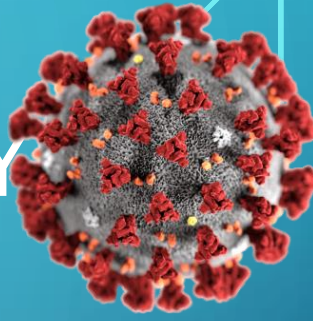
- **Fever is the most common**
- **Cough is also very common**
- **Fatigue**
- **Sputum production**
- **Shortness of breath**
- **Myalgia or arthralgia**
- **Sore throat**
- **Headache**
- **Chills**
- **Gastrointestinal symptoms such as nausea, vomiting or diarrhea are uncommon**
- **Anosmia (loss of sense of smell) and dysgeusia (alteration of the sense of taste) have also emerged as relatively common, early, and moderately specific symptoms.**

PRIMARY SYMPTOMS OF COVID-19

“Symptoms may appear **2-14 days** after exposure to the virus”



. COVID-19 CLINICAL PRESENTATION MAY VARY BY AGE, SEX



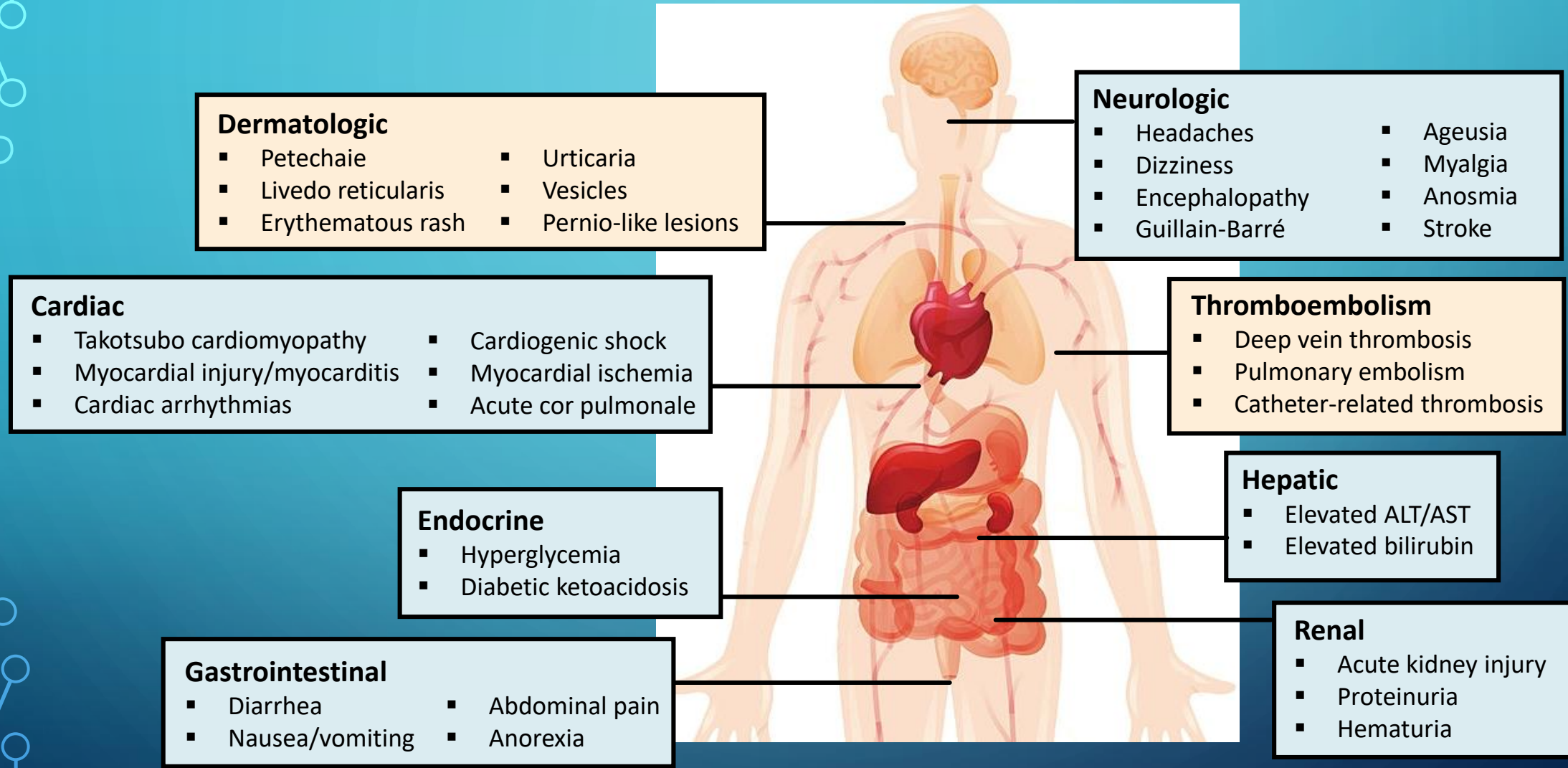
J Intern Med. 2020;288:335. 2. Wang. J Med Virol. 2020;92:441

Clinical and Epidemiological Characteristics of 1,420 European Patients with mild-to-moderate Coronavirus Disease 2019.

Ear, nose, throat complaints more common in **young patients**;
fever, fatigue, loss of appetite, diarrhea in **elderly patients**
($P < .01$)

Loss of smell, headache, nasal obstruction, throat pain, fatigue more common in **women**;
cough, fever in **men** ($P < .001$)

EXTRAPULMONARY MANIFESTATIONS OF COVID-19



Me Which of These Return or Last?

COVID TOES: PERNIO-LIKE LESIONS



COVID toes: One or more toes may swell and turn pink, red, or a purplish color



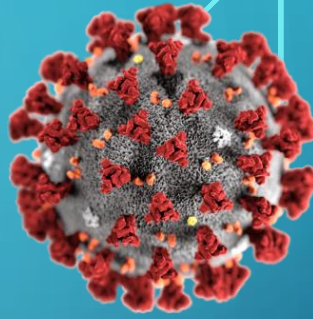
Fig. 1 Erythematous to purpuric macules and thin papules on distal aspect of the dorsal toes.



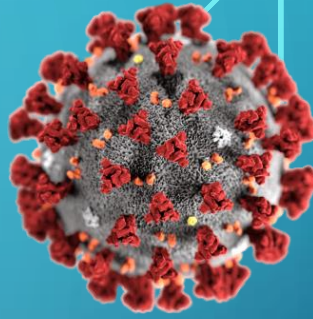
Fig. 2 Dusky papules and incipient vesicles on the dorsal toes.

ORAL MANIFESTATIONS

**ulcerative lesions,
vesiculobullous/
macular lesions,
and acute sialadenitis of the parotid gland
(parotitis).**



ORAL MANIFESTATIONS



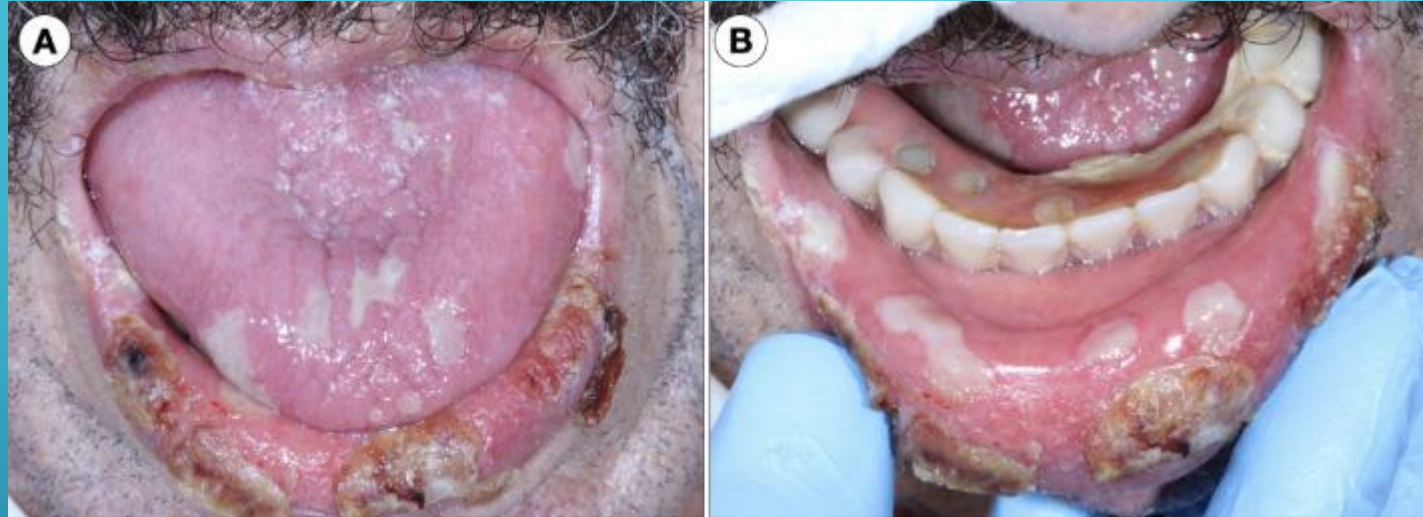
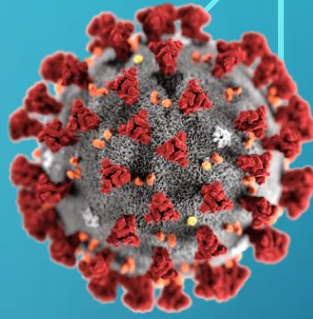
The etiology of oral lesions in patients with COVID-19 is still uncertain and seems to be multi-factorial.

The appearance of such lesions may be related to the direct or indirect action of SARS-CoV-2 on the oral mucosa cells,

hypersensitivity of drugs used in the treatment of COVID-19

,downgrading of the general state of health of the patient due to the disease and long period of hospitalization

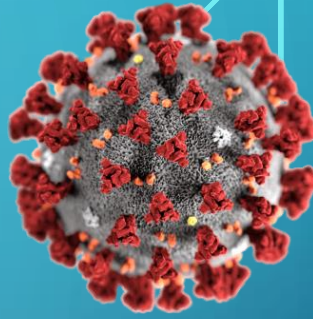
ORAL MANIFESTATIONS



A, Clustered ulcers 1 to 1.5 cm in diameter covered with crusts occurring on the lower lip (vermilion). Ulcerative painful lesions with superficial necrosis affecting the anterior dorsal tongue.

B, Lower lip mucosal ulcers covered with a mucopurulent membrane and the so-called aphthous-like pattern.

ORAL MANIFESTATIONS

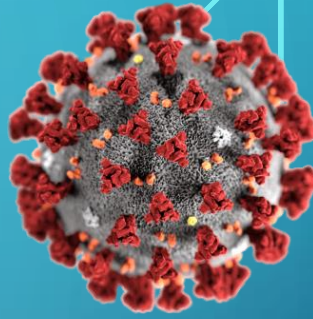


A, Painful ulcer on the right lateral border of the tongue.

B, Focal erythema/petechia and a shallow necrotic area on the anterior hard palate.

[Go to:](#)

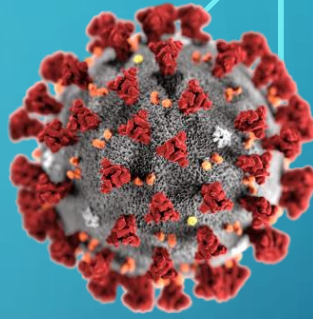
ORAL MANIFESTATIONS



A, Hemorrhagic ulcerations affecting the upper and lower lip vermilions.

B, Painful “aphthous-like” necrotic ulceration affecting the right lower lip mucosa

COVID-19



1%-3% of people with COVID-19 will get conjunctivitis, also called **pinkeye**.

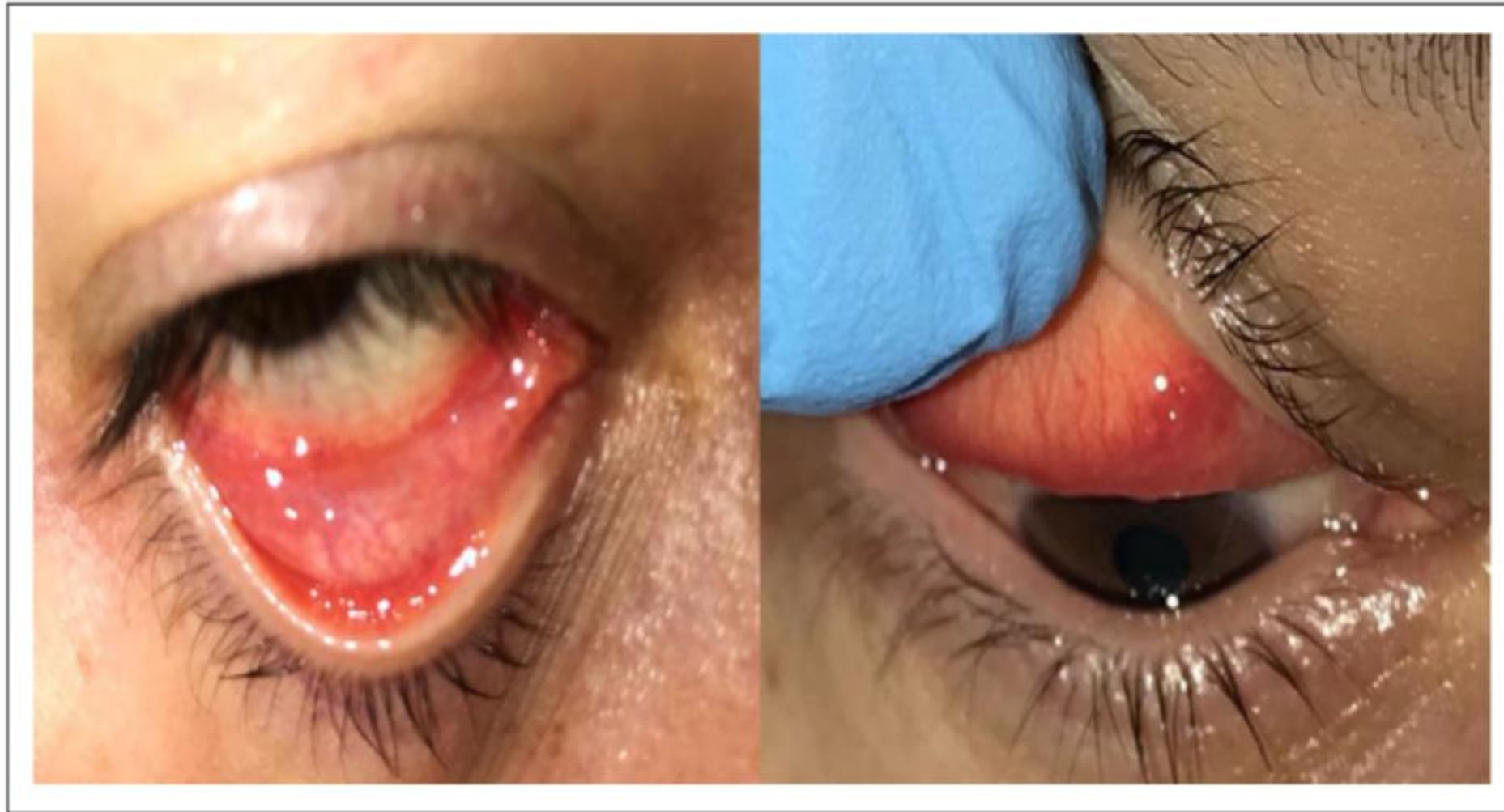
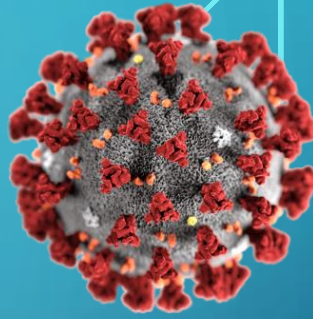


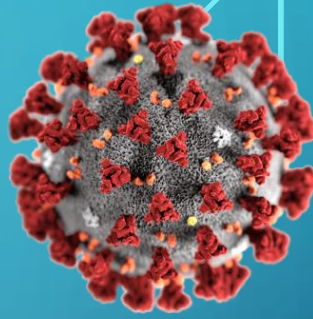
Figure 1. Follicular conjunctival reaction in the upper and lower fornices, serous secretion, and mild chemosis in the right eye of the patient 2 days before the diagnosis of COVID-19.

ATYPICAL MANIFESTATIONS



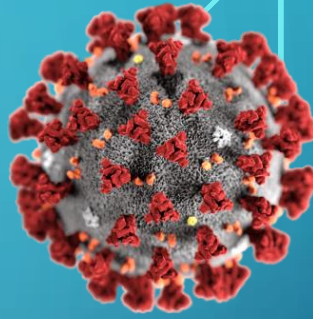
Atypical manifestations are increasingly being recognized, including large vessel strokes in young patients, unexplained abdominal pain, various dermatological manifestations, and a multisystem inflammatory syndrome in children

DIFFERENTIAL DIAGNOSIS INCLUDE



- Influenza
- Both conventional and atypical bacterial pneumonias
- Pneumocystis jiroveci pneumonia (PJP)
($CD4 < 200$)
- Malaria (in patients with history of travel)
- Non-infectious cases of dyspnoea and/or fever should be considered, such as pulmonary emboli, myocardial infarction, and heart failure

PREGNANT WOMEN



Pregnancy and childbirth have not been shown to substantially alter susceptibility to or the clinical course of infection with SARS-CoV-2

. Preliminary data indicate that rates of ICU admission for pregnant women are similar to those of the nonpregnant population.

Pregnant women with COVID-19 have not been reported to have severe maternal complications but were noted to be at increased risk of **preterm** and **cesarean** delivery in a few studies

Learning from the Past

Influenza 1918

- Respiratory viral infections predispose patients to co-infections and these lead to increased disease severity and mortality. Most fatalities in the 1918 influenza outbreak were due to **subsequent bacterial infection**, particularly with ***Streptococcus pneumoniae***.



Viral Infections associated with secondary Bacterial Infections



- Poor outcomes in the 2009 H1N1 influenza pandemic were also associated with bacterial co-infections, although few studies captured these data.

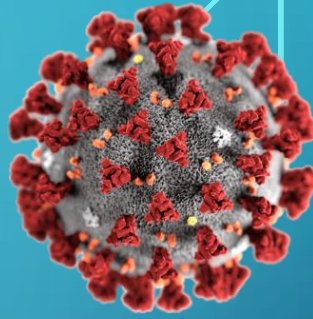
COINFECTIONS AND COVID-19

Co-infections, secondary infections, and antimicrobial use in patients hospitalised with COVID-19 during the first pandemic wave from the ISARIC WHO CCP-UK study: a multicentre, prospective cohort study

Clark D Russell, Cameron J Fairfield*, Thomas M Drake, Lance Turtle, R Andrew Seaton, Dan G Wootton, Louise Sigfrid, Ewen M Harrison, Annemarie B Docherty, Thushan I de Silva, Conor Egan, Riinu Pius, Hayley E Hardwick, Laura Merson, Michelle Girvan, Jake Dunning, Jonathan S Nguyen-Van-Tam, Peter J M Openshaw†, J Kenneth Baillie†, Malcolm G Semple†, Antonia Ho†, on behalf of the ISARIC4C investigators‡*



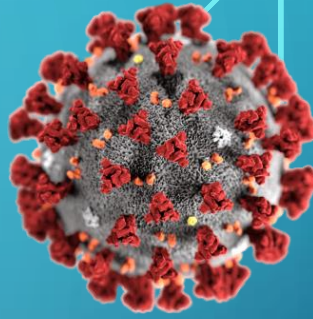
COINFECTIONS AND COVID-19



260 hospitals in England, Scotland, and Wales

In this multicentre, prospective cohort of 48 902 patients admitted to hospital with COVID-19,

COINFECTIONS AND COVID-19



microbiologically confirmed infections were infrequent
(1107 patients).

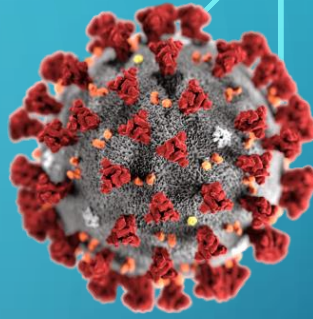
and when infections were identified, most were secondary.

Gram-negative organisms and **S aureus**

were the most frequently recovered pathogens from respiratory and blood cultures.

These findings have implications for empirical therapy until culture results are available.

COINFECTIONS AND COVID-19

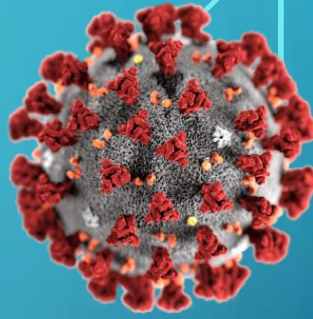


Despite little evidence of bacterial infections in our cohort, a high proportion of patients received antimicrobials. **around 75%**

Elevated **C-reactive protein** and radiological **pulmonary infiltrates** are often used to differentiate bacterial from viral causes in community-acquired pneumonia.

However, both of these findings are commonly present in patients with COVID-19

COINFECTIONS AND COVID-19



Nevertheless, the infrequency of confirmed co-infection supports restrictive empirical antimicrobial usage.

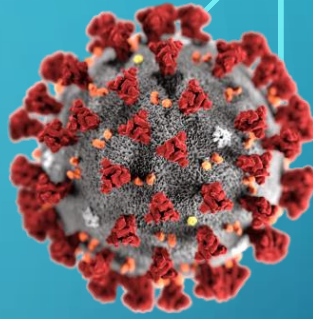
Antimicrobials should be restricted to individuals with atypical features of COVID-19, such as

purulent sputum

or lobar pneumonia

, or evidence of distinct non-respiratory co-infection

COINFECTIONS AND COVID-19



UK guidelines advise against empirical therapy when lower respiratory tract infection is thought to be due to COVID-19, without specific evidence of bacterial infection

systematic reviews and meta-analyses have reported **a low prevalence of confirmed**

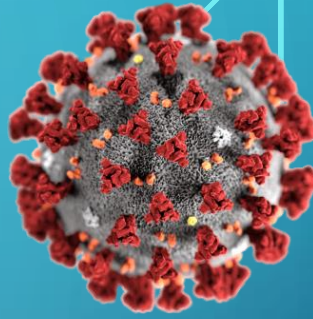
bacterial co-infection (8%), but a high proportion of patients with COVID-19 received antimicrobials (pooled prevalence 75%).

ORIGINAL ARTICLE

Occurrence of Invasive Pulmonary Fungal Infections in Patients with Severe COVID-19 Admitted to the ICU

✉ Arnaud Fekkar^{1,2}, Alexandre Lampros¹, Julien Mayaux³, Corentin Poignon¹, Sophie Demeret⁴, Jean-Michel Constantin⁵, Anne-Geneviève Marcelin⁶, Antoine Monsel^{7,8,9}, Charles-Edouard Luyt^{10,11}, and Marion Blaize¹

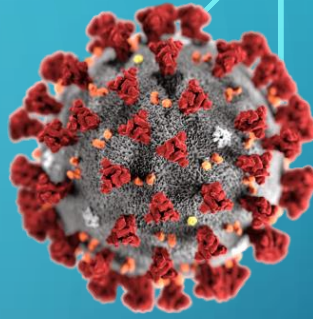
FUNGAL CO-INFECTION



Unlike influenza, SARS-CoV-2 does not seem to promote invasive fungal infection in critically ill patients.

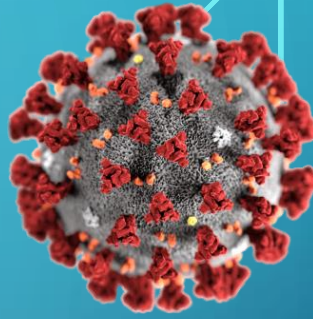
In this new disease, the precise pathophysiology of the lung damage remains unclear but seems to rely primarily on collateral cytokine-induced inflammatory injury rather than on direct viral replication in the low respiratory tract. This may partially explain the differences observed with influenza

FUNGAL CO-INFECTION



. Among secondary infections, only fungal co-infection (ie, pulmonary aspergillosis) was significantly associated with mortality, with patients with CAPA showing a significantly higher mortality (61·8% [95% CI 50·0–72·8]) than those without CAPA (32·1% [27·7–36·7]; $p < 0·0001$).

FUNGAL CO-INFECTION



The 15% CAPA incidence and high mortality might justify antifungal prophylaxis, but no antifungal drugs are currently licensed for prophylaxis in the ICU.

Compared with IAPA, CAPA develops **later** in the course of ICU admission

This delay in onset might provide a period to allow patients with COVID-19 to benefit from antifungal prophylaxis.

Long Term Complications of Covid-19

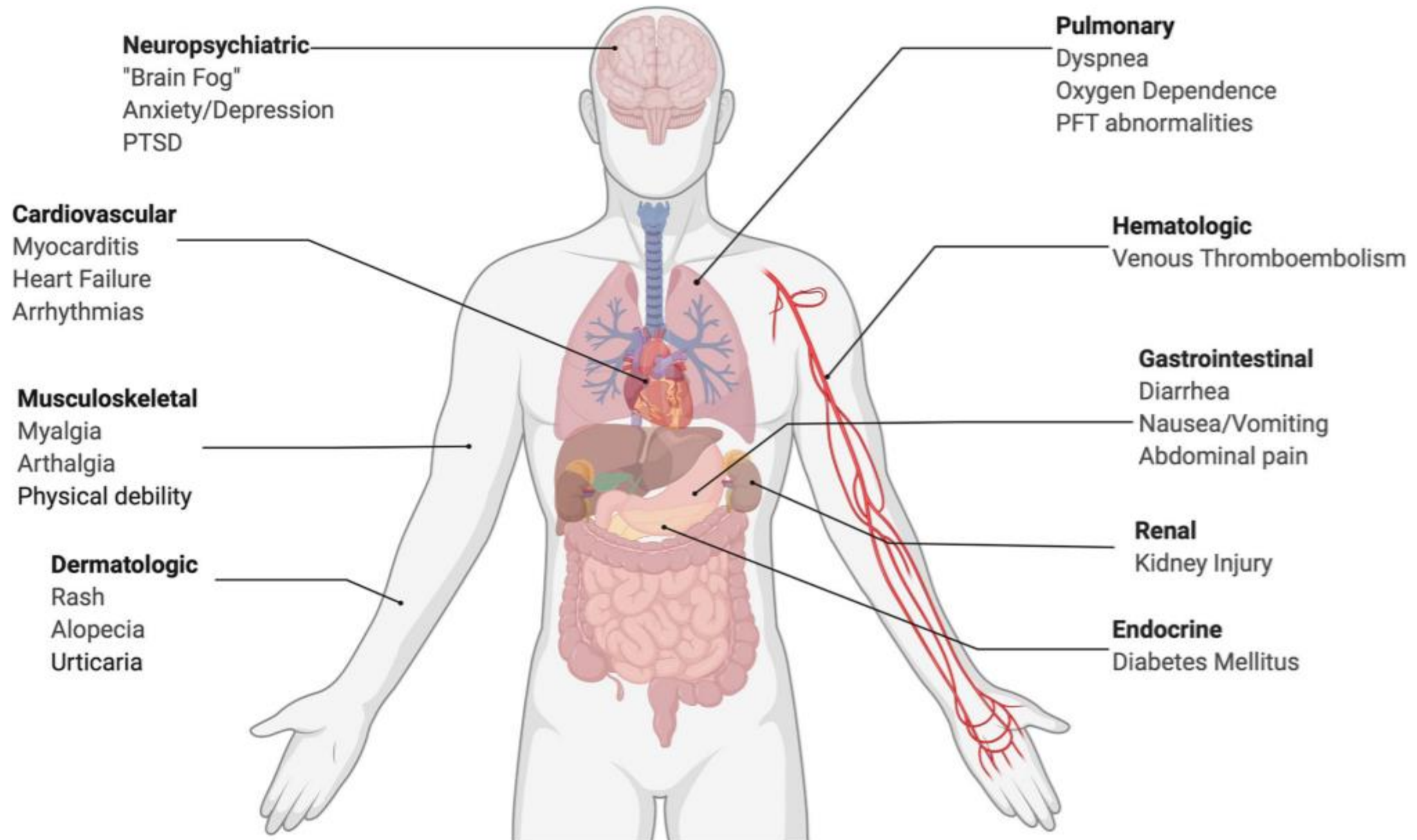
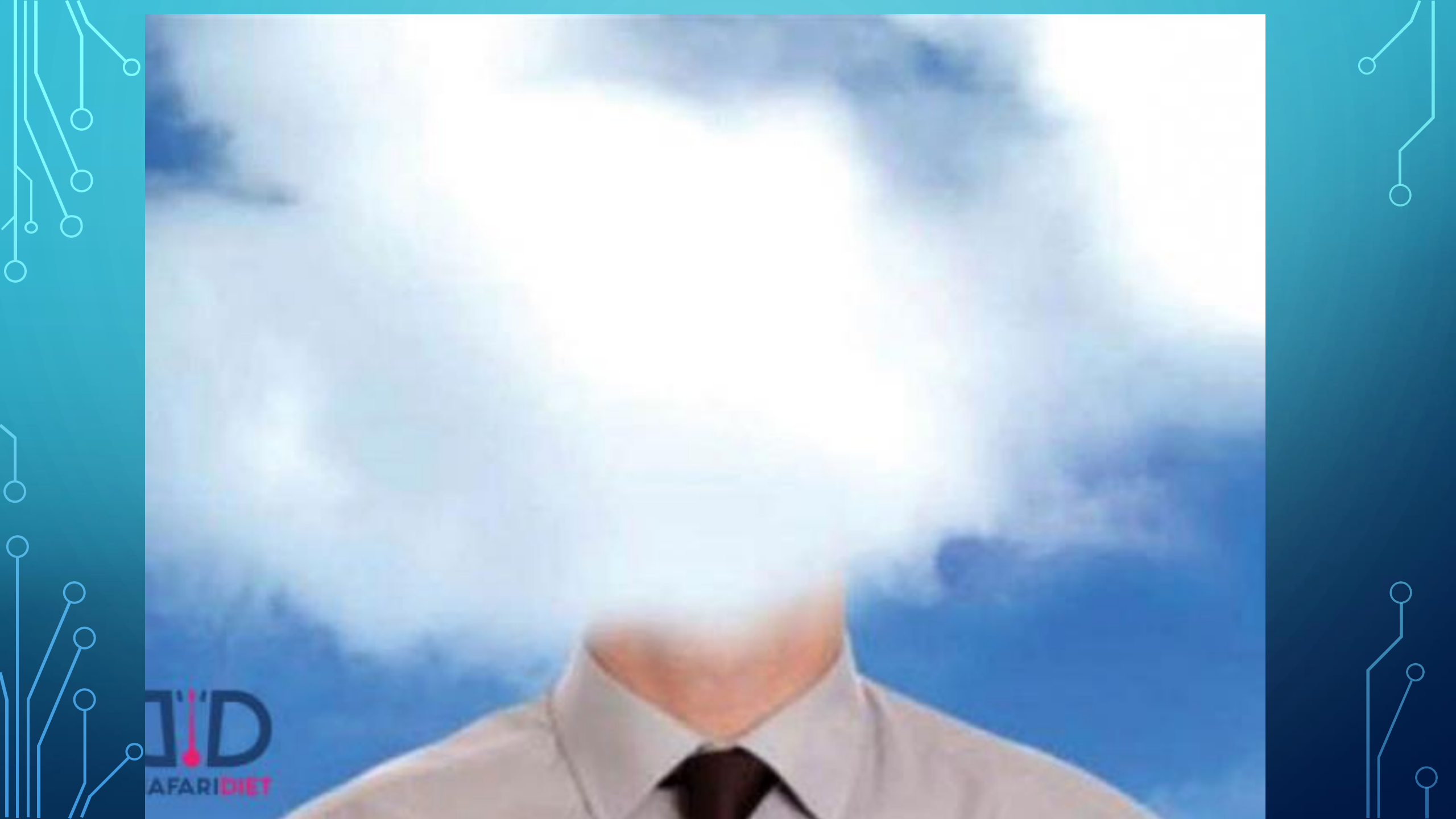


Figure 1. Schematic representation of long-term sequelae observed following COVID-19 infection. Created with BioRender.com.



A'D
AFARI DIET

Article

High-dimensional characterization of post-acute sequelae of COVID-19

<https://doi.org/10.1038/s41586-021-03553-9>

Received: 18 January 2021

Accepted: 14 April 2021

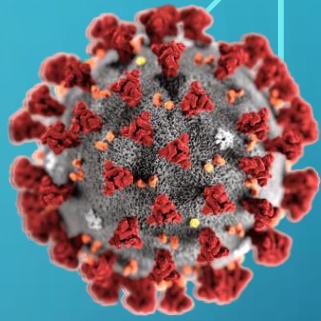
Published online: 22 April 2021

 Check for updates

Ziyad Al-Aly^{1,2,3,4,5}✉, Yan Xie^{1,2,6} & Benjamin Bowe^{1,2,6}

The acute clinical manifestations of COVID-19 have been well characterized^{1,2}, but the post-acute sequelae of this disease have not been comprehensively described. Here we use the national healthcare databases of the US Department of Veterans Affairs to

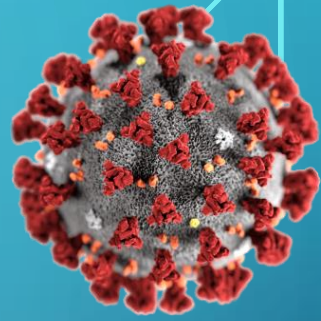
POST-ACUTE SEQUELAE OF COVID-19



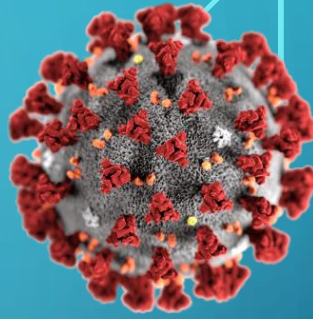
To our knowledge, this is the largest study of the post-acute sequelae of COVID-19; it involves **73,435 non-hospitalized patients** with COVID-19, and 4,990,835 control individuals (corresponding to 2,070,615.52 person years of follow-up), as well as **13,654 hospitalized patients** with COVID-19 and 13,997 patients hospitalized with seasonal influenza

POST-ACUTE SEQUELAE OF COVID-19

beyond the first 30 days of illness,
people with COVID-19 exhibit a higher risk
of death and use of health resources.



POST-ACUTE SEQUELAE OF COVID-19



Our high-dimensional approach identifies incident sequelae in the ***respiratory system***, as well as several other sequelae that include **nervous system** and neurocognitive disorders, mental health disorders, **metabolic disorders**, **cardiovascular disorders**, **gastrointestinal disorders**, **malaise, fatigue**, **musculoskeletal pain** and **anaemia**

THANKS FOR YOUR ATTENTION

THANKS FOR YOUR ATTENTION

