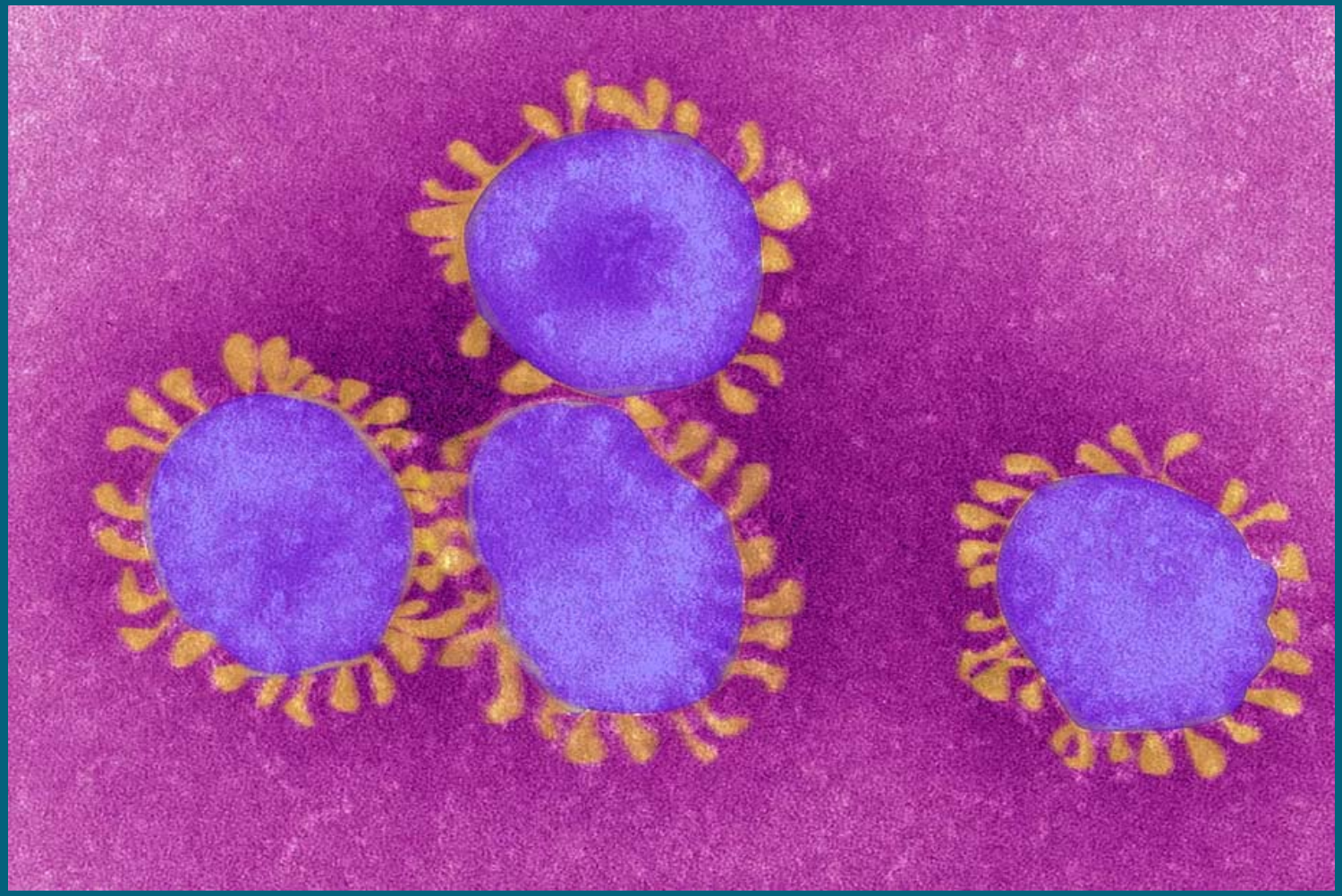


Clinical presentation

تعریف موارد بیماری

- **مورد مشکوک**
- الف (بیماری که دارای علائم بالینی و ملاک های اپیدمیولوژیک است:
- یافته های بالینی:
- شروع ناگهانی تب و سرفه
- یا
- شروع ناگهانی حداقل سه یا بیشتر از علائمی چون تب، سرفه، ضعف عمومی/خستگی مفرط، سردرد، درد عضلانی، گلو درد، آبریزش بینی، تنگی نفس، بی اشتهایی/تهوع/استفراغ، اسهال،
- کاهش سطح هوشیاری

تعریف موارد بیماری

- شواهد اپیدمیولوژیک:
- اقامت، اشتغال یا مسافرت به مناطقی که احتمال چرخش ویروس وجود دارد)
- نظیر مراکز اقامتی ،
- محل های پرازدحام،
- همایش ها و مراسم ها، مراکز بهداشتی-درمانی و ...(در طی ۱۴ روز گذشته
- ب(فرد با بیماری حاد تنفسی) SARIبا شروع علائم در طی ۱۰ روز گذشته که نیاز به بستری داشته باشد

تعریف موارد بیماری

- **مورد محتمل**
- الف(بیمار مشکوکی که در تماس با یک بیمار محتمل یا قطعی و یا خوشه ای ۲ از بیمارانی باشد که حداقل یک مورد
- قطعی در بین آنها گزارش شده باشد
- ب(بیمار مشکوکی که یافته های تصویر برداری به نفع کووید- ۱۹ داشته باشد
- نظیر انفیلتراسیون مولتی لوبولر یک یا دو طرفه خصوصاً انفیلتراسیون نواحی محیطی در CT scan ریه یا
- رادیوگرافی قفسه صدری و ground glass در CT scan ریه) Clinically confirmed)
- ج(بیماری که بطور حاد دچار از دست دادن حس بویایی یا چشایی شده باشد
- د(مرگ در بیمار مشکوک به کووید)ملاک های فوق(که با دلیل دیگری توجیه نشود

تعریف موارد بیماری

- **مورد قطعی**
- فرد با تایید آزمایشگاهی ویروس ناشی از کووید-۱۹ ، صرف نظر از وجود علائم و نشانه های بالینی

1 Public health surveillance for COVID-19 , WHO Interim guidance 7 August 2020

2 Cluster

تعریف تماس نزدیک

- **فردی که در شرایط زیر، در طی ۲ روز قبل تا ۱۴ روز بعد از شروع علائم بیمار محتمل یا قطعی، در تماس با او قرار گرفته باشد، شامل:**
- ۱ . *تماس چهره به چهره در فاصله کمتر از ۱ متر و برای حداقل ۱۵ دقیقه*
- ۲ . تماس مستقیم فیزیکی با فرد محتمل یا قطعی
- ۳ . مراقبت از بیمار محتمل یا قطعی بدون استفاده از تجهیزات مناسب حفاظت فردی
- یا
- ۴ . در شرایط دیگر بر اساس احتمال انتقال منطقه ای ، ارزیابی انجام می شود

تعریف مرگ ناشی از کووید- ۱۹

بروز مرگ در فرد محتمل یا قطعی که از نظر بالینی به دلیل بیماری کووید- ۱۹ باشد و دلیل مشخص دیگری، غیرمرتبط با کووید (نظیر تصادفات و..) نداشته باشد و

دوره بهبودی کامل بین **بیماری فعال** کووید- ۱۹ و مرگ نباید وجود داشته باشد.

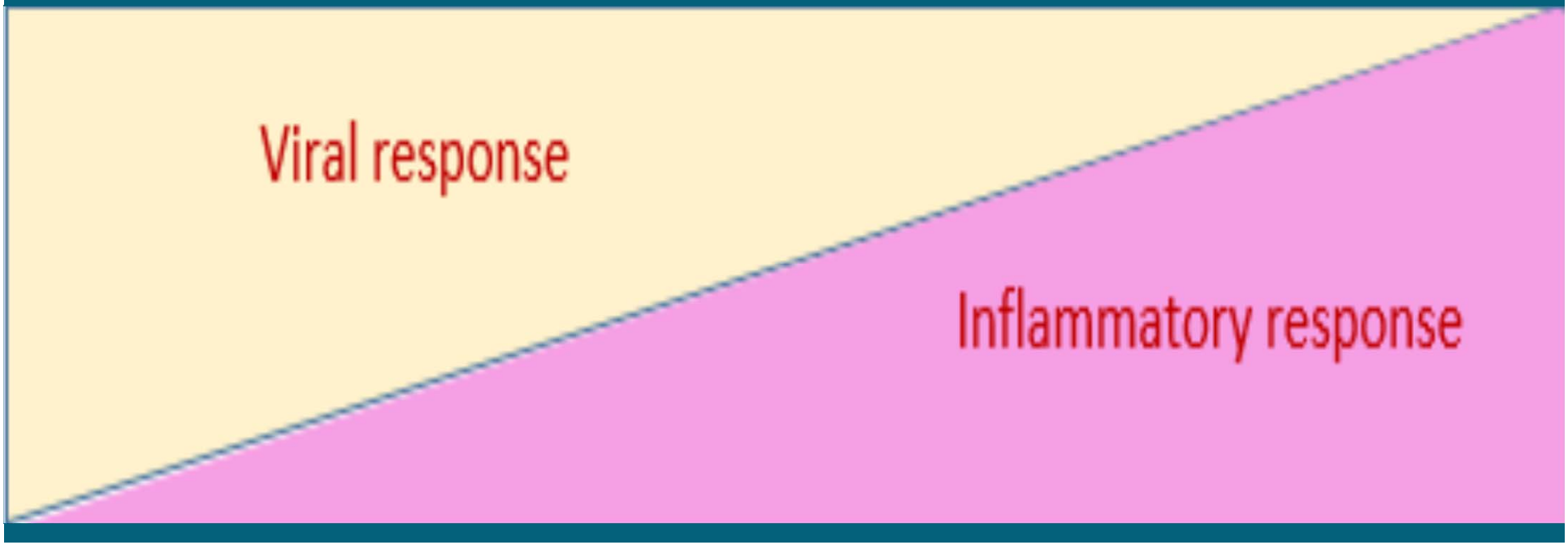
- بیماری کووید ۱۹ به صورت طیفی از علائم، از بی علامتی/قبل از بروز علائم (Asymptomatic/pre-symptomatic) تا موارد پنومونی شدید و سندروم دیسترس حاد تنفسی (ARDS) ظاهر می کند.
- خاطر نشان میشود که علائم ثابت نیست و در هر زمان ممکن است بیمار، وارد مرحله بعدی شود.

دوران کمون بیماری کووید- ۱۹

- حدود ۱۴ - ۳ روز می باشد و بطور متوسط در طی ۵ - ۴ روز پس از تماس، علائم آشکارمی شود.
- در حدود ۸۰ % موارد بیماران مبتلا به کووید- ۱۹ بصورت بی علامت بوده یا علائم خفیف تا متوسط دارند و
- در حدود ۱۵ % موارد مبتلایان با علائم شدید و نیازمند بستری مراجعه می کنند.
- در ۵ % موارد شرایط بیمار بحرانی شده و ممکن است نیازمند بستری در ICUو مراقبت های ویژه باشند

- از دست دادن حس بویایی و نیز حس چشایی
- از جمله علائمی هست که در بسیاری از مبتلایان گزارش شده است. از علائم دیگر می توان به علائم گوارشی نظیر بی
- اشتهایی، ضعف, بی حالی، خستگی زودرس، دل درد، تهوع، استفراغ و اسهال اشاره نمود

- به نظر میرسد که علائم بیماری در مراحل ابتدایی، عمدتا مربوط به واکنش های وایرال است و در مراحل پیشرفته بیماری، پاسخ های ایمنی بیشترین تأثیر را در بروز علائم دارند. البته واکنش های ویروسی تا انتهای بیماری کم وبیش ادامه دارد



سیر بیماری کووید-۱۹

- ۱ . مرحله صفر: بی علامت/قبل از بروز علائم
- ۲ . مرحله یک: مراحل ابتدایی عفونت (Early infection)
- ۳ . مرحله دو: فاز تنفسی
- ۴ . مرحله سه: فاز التهابی شدید (Hyper inflammation

- نمی توان مرز دقیقی بین مراحل مختلف بیماری تصور کرد و **هم پوشانی** ممکن است وجود داشته باشد. از سوی تغییر فاز به ترتیب مراحل نیست و ممکن است فرد از **مرحله یک به سرعت و ناگهانی به مرحله پیشرفته** برسد

- **مرحله صفر (بی علامت/قبل از بروز علائم)**
- تشخیص بیماری در این مرحله صرفا با تست آزمایشگاهی RT-PCR است
- که در حین بیماریابی در افراد بی علامت **در تماس نزدیک با افراد مبتلا به کووید- ۱۹** با تست RT-PCR مثبت و یا حین غربالگری از افراد بی علامت در مکانهای تجمعی) **نظیر زندان** و... (صورت می گیرد.
- **این افراد بعد از مدتی ممکن است علامت دار شوند لذا پایش علامتی آنها لازم است انجام شود**

- **مرحله یک (مراحل ابتدایی عفونت)**
- از نظر شدت بیماری این مرحله به عنوان **مرحله خفیف** در نظر گرفته می شود.
- علائم خفیف بصورت **تب کمتر از ۳۸درجه، گلودرد با یا بدون سرفه های خشک، لرز، سردرد، از دست دادن حس چشایی و بویایی، تهوع، استفراغ، بی اشتهایی، اسهال، بدن درد، ضعف و خستگی مفرط است.**
- این علائم می تواند در هر فرد متفاوت باشد و بیمار یک یا
- چندین مورد از علائم را داشته باشد.
- در این مرحله **علائم حیاتی (نبض، فشارخون و تعداد تنفس) پایدار** است و (SpO2≥93%سطح اشباع اکسیژن)می باشد .
- **عموما فرد نیاز به بستری ندارد.**

- **در مرحله اول** ممکن است علائم آزمایشگاهی بصورت **لنفوپنی** (کمتر از ۱۱۰۰)و/یا افزایش خفیف *ESR/CRP* وجود اشته باشد.
- **در اغلب موارد نشانه ای از درگیری ریوی در رادیوگرافی/ *CT scan* وجود ندارد.**
- در برخی موارد ممکن است یافته های مختصری بصورت
- درگیری حداکثر دو لوب ریوی به شکل تظاهرات *Ground glass (GGO)*، (تجامد *Consolidation* .)یا **ندول با وسعت کمتر از یک سوم حجم هر لوب دیده شود که خصوصاً در مناطق محیطی و در قواعد ریه ها می تواند باشد**

- **مرحله دو (فاز تنفسی)**
- این مرحله خود به دو **قسمت متوسط و شدید** تقسیم می شود
- **فاز تنفسی متوسط** (Moderate)
- در این مرحله علائم قبلی با شدت بیشتر ممکن است وجود داشته باشد.
- **ملاک های ورود به این مرحله عبارت است از:**
- ۱ . **وجود علائم تنفسی** (شامل تنگی نفس، احساس درد و فشار در قفسه سینه، ...) با یا بدون تب مساوی/بیشتراز ۳۸°C
- **SpO2 .بین ۹۰ % تا ۹۳ %**

- **در مرحله دوم** ممکن است علائم آزمایشگاهی بصورت **تشدید لنفوپنی** و/یا **افزایش خفیف** ***CRP/ESR*** ، ***PT/PTT*** و یا ***D-dimer*** و/یا ***LDH*** و/یا **فریتین** ممکن است دیده شود .
- خاطر نشان می شود که در **اسکور بندی یافته های سی تی اسکن تعداد لوب ها درگیر و نیز شدت درگیری هر لوب، تعیین کننده است**
- در مرحله دوم **درگیری حداکثر ۳ یا ۴ لوب ریوی** با **وسعت کمتر از یک سوم حجم هر لوب یا ابتلای یک یا دو لوب با وسعت بیشتر** ممکن است دیده شود.)**اسکور کمتر از ۸**)

- **فاز تنفسی شدید (Severe)**
- در این مرحله نیز عموما علائم بالینی با شدت بیشتری وجود دارد.
- ملاک های ورود به این مرحله عبارتند از :
- **۱ . پیشرفت سریع علائم تنفسی به ویژه تشدید تنگی نفس**
- ۲ . تاکی پنه . RR>30
- ۳، SpO2<90% . FiO2 ≤300 mmHg5PaO2/4
- ۴ . افزایش ۶ a gradient-A و نیز **افزایش درگیری بیش از ۵۰ % از ریه در سی تی اسکن**
- **لازم به ذکر است که بروز انواع شدید بیماری در هر زمانی از سیر بیماری ممکن است رخ دهد و بروز ان الزاما مستلزم طی همه مراحل قبلی نیست .**

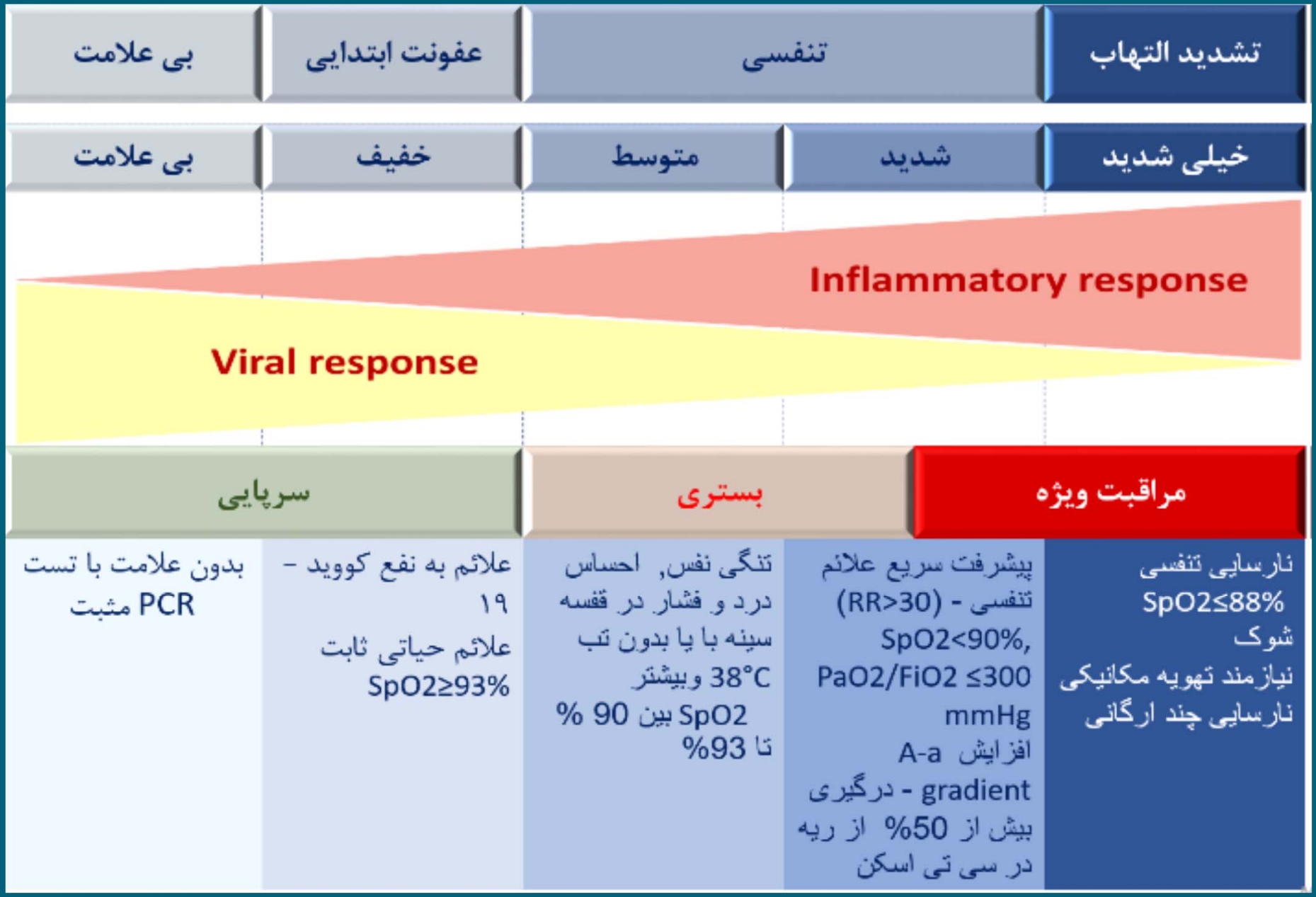
- در این مرحله ممکن است علائم آزمایشگاهی بصورت تشدید **لنفوپنی**، افزایش پیشرونده ***D-dimer*** و/یا فریتین)بیش از ۵۰۰ (*ng/dl*
- و/یا ***LDH>245 U/l*** و/یا **افزایش آنزیم های کبدی** و/یا تری گلیسیرید، **علائم بروز یا تشدید نارسائی ارگانی دیده شود**. نیز ممکن است
- **افزایش خفیف *NT-proBNP*** و **تروپونین و/یا افزایش *IL6* و/یا افزایش *CRP* بیش از ۱۰۰ و کاهش پلاکت ها ، کاهش شدید ائوزینوفیل ها نیز عارض شود**

- درگیری ۵ لوب ریوی با وسعت کمتر از یک سوم حجم هر لوب و یا ابتلای سه لوب با وسعت بیشتر می تواند دیده شود.
- معمولاً درگیری ریوی دوطرفه است . اسکور بیشتر/مساوی ۸.
  اغلب وسعت درگیری ریه در سی تی اسکن در موارد شدید بیماری بیش از موارد متوسط است
- و بر اساس چند مطالعه انجام شده در این زمینه بیش از ۵۰ درصد کل ریه درگیر است. انفیلتراسیون منتشر دو طرفه ممکن است
- در نهایت بصورت ***White lung*** دیده شود.

- لازم به ذکر است که در مواردی با وجود درگیری متوسط ریوی در سی تی اسکن بیمار علائم شدید بالینی نشان می دهد و در مواردی نیز با وجود درگیری وسیع ریوی بیمار علائم متوسطی دارد که البته این موارد نادر است.

- **مرحله سه (فاز تشدید التهاب(-بحرانی) (Critical**
- ملاک های ورود به این مرحله وجود حداقل یکی از موارد زیر است:
- **۱ . بروز علائم نارسایی تنفسی که علیرغم اکسیژن درمانی غیرتهاجمی SpO2≤88%باشد**
- **۲ . بروز نشانه های شوک**
- **۳ . بروز نارسایی چند ارگانی**
- **در این مرحله بیمار نیازمند مراقبت های ویژه است** .
- همانطور که اشاره شد، بروز انواع شدید بیماری در هر زمانی از
- سیر بیماری ممکن است رخ دهد و بروز آن الزاما مستلزم طی همه مراحل قبلی نیست

- در این مرحله ممکن است علائم آزمایشگاهی بصورت **تشدید لنفوپنی، افزایش شدید مارکرهای التهابی** (***IL6***، ***D-dimer>1000***،
- ***Ferritin>1000ngdl***، **تروپونین** ، (***NT-proBNP***، **سیتوپنی پیشرفته**، مارکرهای نارسایی/آسیب چند ارگانی)**افزایش شدید/بیش از ۵ برابر آنزیم های** کبدی، **ترمبوسیتوپنی**، **افزایش** ***BUN/Cr***، اختلالات انعقادی. عارض شود.
- **درگیری منتشر/دوطرفه ریه ها، درگیری منطبق با *ARDS* ممکن است دیده شود.**
- **یافته هایی نظیر پلورال افیوژن، لنفادنوپاتی، افزایش ضخامت جداری برونش و تغییرات ساختمانی ریه ها ممکن است در این مرحله دیده شود**


تشدید التهاب
تنفسی
عفونت ابتدایی
بی علامت
خیلی شدید
شدید
متوسط
خفیف
بی علامت
Inflammatory response
Viral response
مراقبت ویژه
بستری
سرپایی
نارسایی تنفسی
SpO2≤88%
شوک
نیازمند تهویه مکانیکی
نارسایی چند ارگانی
پیشرفت سریع علائم تنفسی - (RR>30)
SpO2<90%,
PaO2/FiO2 ≤300 mmHg
افزایش A-a gradient - درگیری بیش از 50% از ریه در سی تی اسکن
تنگی نفس, احساس درد و فشار در قفسه سینه با یا بدون تب 38°C وبیشتر
SpO2 بین 90 % تا 93%
علائم به نفع کووید – ۱۹
علائم حیاتی ثابت
SpO2≥93%
بدون علامت با تست PCR مثبت

گروه های در معرض خطر ابتلا نوع عارضه دار کووید- ۱۹

- بطور کلی در افراد بالای ۶۵ سال.

گروههایی که شواهد قوی وجود دارد که خطر بیماری شدید ناشی از کووید- ۱۹ را افزایش می دهند:

- بیماری های شدید قلبی- عروقی نظیر نارسایی قلب, بیماری های عروق کرونر , کاردیومیوپاتی
- بدخیمی ها
- نارسایی مزمن کلیوی
- چاقی (BMI≥30)
- آنمی سیکل سل
- پیوند Solid organ
- دیابت تیپ ۲

در مورد گروههای زیر شواهد متوسط وجود دارد که خطر بیماری شدید ناشی از کووید- ۱۹ را افزایش می دهند:

- oآسم (متوسط تا شدید)
- CVA
- oپرفشاری خون
- oبارداری
- oسیگار
- oمصرف کورتیکواستروئیدها و سایر داروهای ایمونوساپرسیو (بیش از ۲۰ mg/d پردنیزولون بیش از دو)
- هفته یا دوز تجمیعی بیش از ۶۰۰ میلی گرم معادل پردنیزولون

در مورد گروههای زیر شواهد بسیار محدودی وجود دارد که خطر بیماری شدید ناشی از کووید- ۱۹ را افزایش می دهند:

- oپیوند مغز استخوان
- o HIV
- oنقص ایمنی
- oبیماریهای متابولیک ارثی
- oبیماری های کبدی
- oاختلالات نورولوژیک
- oسایر بیماری های مزمن ریوی
- oکودکان
- oتالاسمی
- oدیابت تیپ

General Symptoms

Neurological Manifestation

via hematogenous,

synapse-connected

or retrograde neuronal routess

lymphatic,

central nervous system,

peripheral nervous system,

skeletal muscles

headache, languidness, malaise, cerebral hemorrhage, or cerebral infarction

CASES

encephalitis, necrotizing ⊡

hemorrhagic encephalopathy, ⊡

strokes, ⊡

epileptic seizures, or ⊡

polyneuritis cranialis ⊡

Guillain–Barré syndrome ⊡

rhabdomyolysis ⊡

Olfactory and Gustatory Dysfunctions

Dermatological Manifestations

Ophthalmic Manifestations

Cardiovascular Manifestations

Hepatic Manifestations Gastrointestinal

Rheumatology

Clinical Manifestations in Pediatric Patients

Incubation period

- — The incubation period for COVID-19 is **thought** to be within **14 days** following exposure,
- **Most cases** occurring approximately **four to five days after exposure**
- (interquartile range **two to seven days**)..

Spectrum of illness severity

- **The proportion of severe or fatal infections may vary by location**
- Chinese CDC
- Mild (no or mild pneumonia) 81 %.
- ●Severe disease (eg, with dyspnea, hypoxia, or >50 percent lung involvement on imaging within 24 to 48 hours) 14 %
- ●Critical disease (eg, with respiratory failure, shock, or multiorgan dysfunction) 5 %.
- ●The overall case fatality rate was 2.3 %;
- No deaths were reported among noncritical cases.

Spectrum of illness severity

- . In **Italy**, 12 % of all COVID-19 cases and **16 percent of all hospitalized patients were admitted to the ICU** (case fatality rate was **7.2 %**in mid-March) median age of patients with infection was **64 years**
- **In contrast**, case fatality rate in mid-March in **South Korea** was **0.9 %** (median age was in the **40s.**)

Risk factors for severe illness

- **Severe illness can occur in otherwise healthy individuals of any age**,
- **but** it predominantly occurs in a**dults with advanced age** or underlying medical comorbidities.

Comorbidities that have been associated with severity

- Cardiovascular disease
- ●Diabetes mellitus
- ●Hypertension
- ●Chronic lung disease
- ●Cancer
- ●Chronic kidney disease
- ●Obesity (body mass index ≥30)

Comorbidities that have been associated with severity

- **US CDC** also includes
- immunocompromising conditions,
- severe obesity (**body mass index ≥40**),
- and **liver disease**

More severe in

- **long-term care facilities**
- **Males**
- **black individuals** possibly related to underlying socioeconomic disparities
- higher viral RNA levels in respiratory specimens ?

Impact of age

Any age can can involved(SARS-CoV-2)

- **Older adults are more likely to have severe disease and mortality**
- **Median age ranged from 49 to 56 years**
- **87 % of patients were between 30 and 79 years old**
- **The hospitalization rate** for COVID-19 increased with age
  1 % (20 to 29 years old), 4 % (50 to 59 years old), and
  18 % (older than 80 years)
- **with 80 % of deaths occurring in those aged ≥65 years.**

Particular laboratory features have also been associated with worse outcomes

- Lymphopenia
- Elevated liver enzymes
- Elevated lactate dehydrogenase (LDH)
- Elevated inflammatory markers (eg, C-reactive protein [CRP], ferritin)
- Elevated D-dimer (>1 mcg/mL)
- Elevated prothrombin time (PT)
- Elevated troponin
- Elevated creatine phosphokinase (CPK)
- Acute kidney injury

Asymptomatic infections

- Asymptomatic infections have been well documented
- Several studies performed in various settings suggest that they **are common**
- About **half of the 619 confirmed** COVID-19 cases were **asymptomatic at the time of diagnosis**
- (18 percent were true asymptomatic cases)

Asymptomatic infections

- Even patients with **asymptomatic** infection may have **objective clinical abnormalities**
-

- As an example, in a study of **24 patients** with asymptomatic **50 % had typical GGO or patchy shadowing**, and another 20 percent had atypical imaging abnormalities
- **Five patients developed low-grade fever, with or without other typical symptoms, a few days after diagnosis.**
- In another study **of 55 patients** with asymptomatic infection, **67 percent had CT evidence of pneumonia on admission**;
- only two patients developed hypoxia, and all recovered

Clinical manifestations

- **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**
- ***There are no specific clinical features that can yet reliably distinguish COVID-19 from other viral respiratory infections.***

138 patients hospitalized with COVID-19 pneumonia in Wuhan

- Fever in 99 percent (37/3-39 c)
- ●Fatigue in 70 percent
- ●Dry cough in 59 percent
- ●Anorexia in 40 percent
- ●Myalgias in 35 percent
- ●Dyspnea in 31 percent
- ●Sputum production in 27 percent

Clinical manifestations

- However, fever might not be a universal finding.
- In another study of **1099 patients** from Wuhan
- fever (defined as an axillary temperature over 99.5°F/**37.5°C**) was present in **only 44 percent on admission**
- ***But was ultimately noted in 89 percent during the hospitalization***

Clinical manifestations

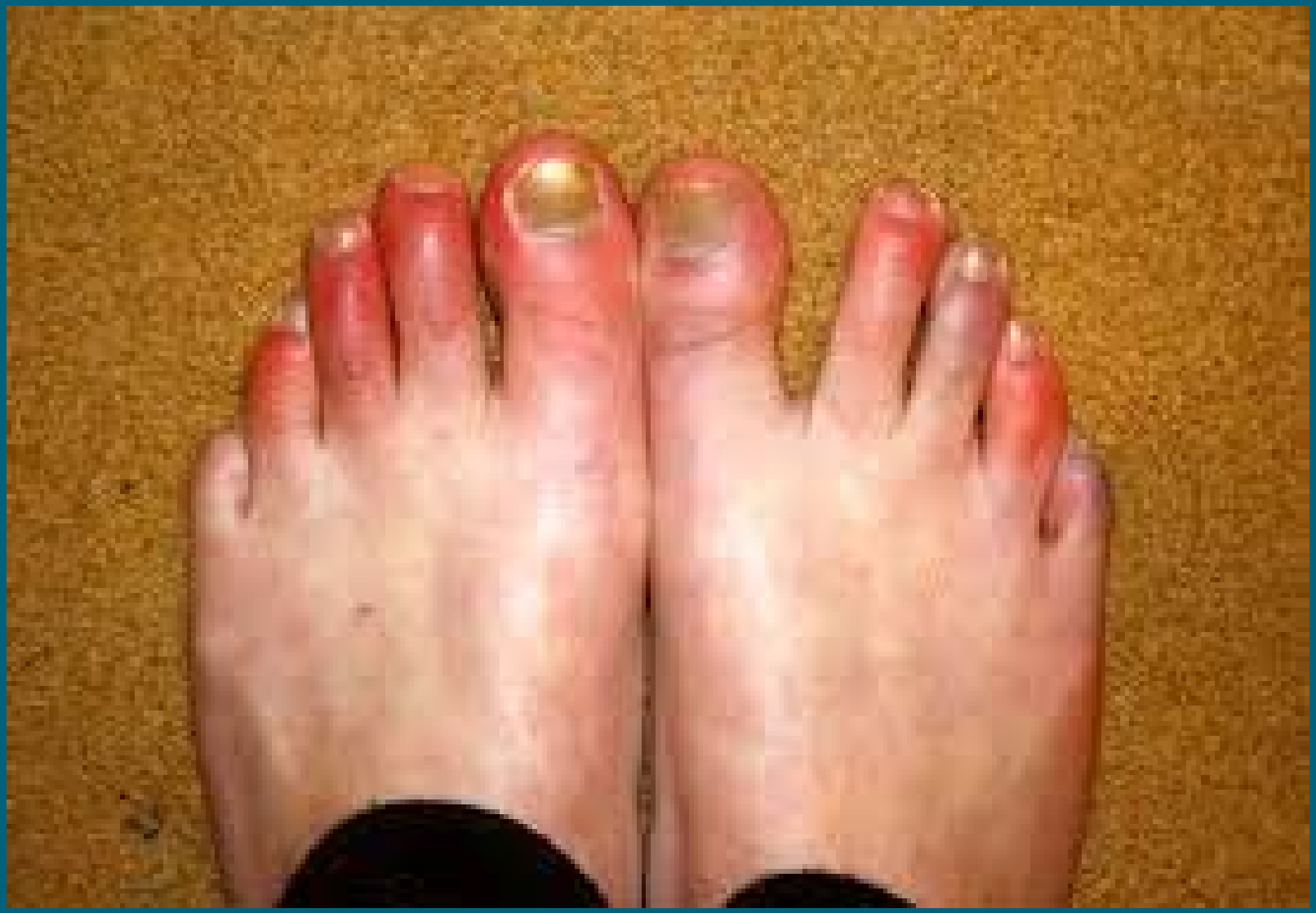
- **Anosmia and dysgeusia**
- In a survey of 59 patients in **Italy,** ***34 % self-reported either a smell or taste aberration and 19 percent reported both***

Other**, less common symptoms**

- **Headache**
- **Sore throat**
- **Rhinorrhea.**
- **GI symptoms 18 %** (diarrhea, nausea/vomiting, or abdominal pain reported in 13, 10, and 9 %)

Dermatologic findings

- **In patients with COVID-19 are not well characterized.**
- **Rare reports**
- Urticarial eruptions
- **Transient livedo reticularis**
- Reddish-purple nodules on the distal digits similar in appearance to pernio (chilblains) (in children and young adults with suspected COVID-19,) although an association has not been clearly established

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Neurological symptoms

Three categories:

- (CNS) symptoms or diseases
- (headache, dizziness, impaired consciousness, ataxia, **acute cerebrovascular disease**, and epilepsy),
- peripheral nervous system (PNS) symptoms (hypogeusia, hyposmia, hypopsia, and neuralgia)
- Skeletal muscular symptoms (skeletal muscle pain, CPK >200)

Course and complications

- — Some patients (Wuhan) with initially non severe symptoms may progress **over the course of a week**.
- **Pneumonia, dyspnea developed** after a median of **five days** since the onset of symptoms, hospital admission occurred after a median of **seven days** of symptoms
- In another study, the **median time to dyspnea was eight days**

Clinical Course

- Illness Severity
- The largest cohort of >44,000 persons with COVID-19 from China :
- **Mild to moderate (mild symptoms up to mild pneumonia): 81%**
- Severe (dyspnea, hypoxia, or >50% lung involvement on imaging): 14%
- Critical (respiratory failure, shock, or multiorgan system dysfunction): 5%

- In this study, all deaths occurred among patients with critical illness and the overall case fatality rate was 2.3%.[38] The case fatality rate among patients with critical disease was 49%.[38]

Clinical Progression

- Among patients who developed severe disease, the medium time to dyspnea ranged from 5 to 8 days, the median time to acute respiratory distress syndrome (ARDS) ranged from 8 to 12 days, and the median time to ICU admission ranged from 10 to 12 days.

- **INITIAL DIAGNOSTIC EVALUATION**The diagnostic evaluation is focused on identifying ARDS and its cause (table 1) and assessing for potential mimicking etiologies (algorithm 1). (See 'Differential diagnosis' below.)

  - **General evaluation and testing** — For most patients with suspected ARDS, initial testing typically involves the following:

- Clinicians should be aware of the potential for some patients to rapidly deteriorate one week after illness onset. Among all hospitalized patients, a range of 26% to 32% of patients were admitted to the ICU.[6,8,11] Among all patients, a range of 3% to 17% developed ARDS compared to a range of 20% to 42% for hospitalized patients and 67% to 85% for patients admitted to the ICU.[1,4-6,8,11] Mortality among patients admitted to the ICU ranges from 39% to 72% depending on the study.[5,8,10,11] The median length of hospitalization among survivors was 10 to 13 days.[1,6,8]

- Risk Factors for Severe Illness
- Age is a strong risk factor for severe illness, complications, and death.[1,6,8,10,11,38-41] Among more than 44,000 confirmed cases of COVID-19 in China, the case fatality rate was highest among older persons: ≥80 years: 14.8%, 70–79 years: 8.0%, 60–69 years: 3.6%, 50–59 years: 1.3%, 40–49 years: 0.4%, <40 years: 0.2%.[38,42] Early U.S. epidemiologic data suggests that the case fatality was highest in persons aged ≥85 years (range 10%–27%), followed by 3%–11% for ages 65–84 years, 1%–3% for ages 55–64 years, and <1% for ages 0–54 years

- Patients in China with no reported underlying medical conditions had an overall case fatality of 0.9%, but case fatality was higher for patients with comorbidities: 10.5% for those with cardiovascular disease, 7.3% for diabetes, and approximately 6% each for chronic respiratory disease, hypertension, and cancer.[42] Heart disease, hypertension, prior stroke, diabetes, chronic lung disease, and chronic kidney disease have all been associated with increased illness severity and adverse outcomes.[1,6,10,11,38,42,43] Accounting for differences in age and prevalence of underlying condition, mortality associated with COVID-19 in the United States was similar to China.[39]

- **A thorough history and clinical examination** – Clinicians should inquire about fever, productive cough, pleuritic chest pain, and witnessed aspiration (may suggest infectious or aspiration pneumonia), orthopnea (may suggest cardiogenic pulmonary edema), and hemoptysis (may suggest cancer, vasculitis, or alveolar hemorrhage). They should also inquire about history of asthma (may suggest vasculitis), cardiac dysfunction, cancer, stem cell transplant, or pulmonary fibrosis (may suggest cardiogenic pulmonary edema, lymphangitic tumor spread, immune reaction, or interstitial pneumonitis, respectively), and about abdominal symptoms (pain, vomiting, or diarrhea may suggest pancreatitis, colitis, or viscus rupture). Clinicians should seek evidence of recent trauma, surgery, smoke or other toxin inhalation, sick contacts, environmental or occupational exposures (eg, animal exposure and fire eating), travel, pregnancy, transplant, transfusions, fetal delivery, illicit drug use (inhaled, intravenous, and oral), and recent changes in prescribed medications (eg, antibiotics, amiodarone, chemotherapy).

- On examination, the clinician should assess for signs of acute cardiogenic pulmonary edema (eg, raised jugular venous pressure, crackles, murmurs, S3/S4 gallops, and lower extremity edema) and pneumonia (eg, dullness on percussion, rales, egophony, or bronchial breath sounds). The abdomen should be examined for tenderness and distension and/or absent bowel sounds to suggest subdiaphragmatic etiologies for ARDS. The skin should be examined for burns, rashes, wounds, track marks, and systemic manifestations of septic emboli; lymph nodes should be examined for size and tenderness (eg, possible infections or cancer); and dentition examined for possible source of sepsis. Volume status (eg, mucus membrane assessment and skin turgor) should also be assessed and fluid balance calculated, if feasible.

- **Laboratory studies** – Laboratory studies should include complete blood count, chemistries, liver function tests, coagulation studies, and arterial blood gas (ABG) analysis. Some clinicians also measure D-dimer, troponin, and lactate levels to investigate common etiologies that can cause or mimic ARDS. Brain natriuretic peptide (BNP) levels are often ordered when assessing cardiogenic pulmonary edema (see 'Excluding acute cardiogenic pulmonary edema' below). Lipase should be checked in patients with abdominal symptoms, particularly if the patient has no other obvious risk factors for ARDS.

- **Imaging** – All patients with suspected ARDS should have a chest radiograph since abnormal imaging is essential for the diagnosis of ARDS. Chest radiography is also critical to evaluate for etiologies of ARDS (eg, lobar consolidation and air bronchograms consistent with pneumonia) as well as for conditions that mimic ARDS, particularly acute cardiogenic pulmonary edema (eg, pulmonary venous congestion, pleural effusions, Kerley B lines, and cardiomegaly).
- While computed tomography (CT) of the chest is not necessary for the diagnosis, it may be helpful when there is a need for a more detailed pulmonary evaluation (eg, seeking evidence for cavitation or pleural effusions or chronic interstitial lung disease that may be missed on chest radiograph).
- Additional imaging may be performed when specific etiologies for ARDS are suspected. For example, CT or magnetic resonance imaging of the brain (eg, for trauma patients), or CT of the abdomen (eg, for patients with suspected pancreatitis, abscess, colitis, peritonitis, appendicitis), or pelvis (for patients with suspected retained fetal products) may be useful to search for evidence of associated pathologies.

Electrocardiography – Electrocardiography should also be obtained to look for evidence of cardiac dysfunction, including arrhythmias, obvious changes consistent with right or left ventricular strain, or ST segment changes to suggest ischemia.

- **Microbiologic studies** – When feasible, respiratory tract sampling (eg, sputum or endotracheal aspirates) for gram stain and culture of the sputum and/or endotracheal aspirates should be obtained. Urinary legionella and streptococcal antigen should also be sent when pneumonia is suspected, along with cultures of other body fluids such as blood and urine as the patient's presentation dictates. Interpretation of sputum culture should be performed in the context of gram stain.

- **Excluding acute cardiogenic pulmonary edema** — The most important condition to exclude is acute cardiogenic pulmonary edema, which can be difficult to distinguish from ARDS. In practice, most clinicians use clinical evaluation and BNP or N-terminal proBNP (NT-proBNP), with or without transthoracic echocardiography to confirm or exclude pulmonary edema:

- **Clinical assessment** – Cardiogenic pulmonary edema is usually due to left ventricular systolic or diastolic dysfunction, but may also be due to fluid overload, severe hypertension, or severe renal disease. It may be distinguished from ARDS by evidence of cardiac dysfunction (eg, an S3 or S4 gallop, new or changed murmur), elevated right-sided filling pressures (eg, elevated jugular venous pressure, leg edema), or related radiographic abnormalities (eg, pulmonary venous congestion, Kerley B lines, cardiomegaly, and pleural effusions). A response to diuresis can also confirm the diagnosis retrospectively.

- **BNP or NT-proBNP** – In patients with suspected ARDS, BNP alone in general is not a reliable indicator for distinguishing ARDS from edema. Rather, it should be used in conjunction with clinical assessment to make this distinction. One observational study found that a plasma BNP level less than 100 pg/mL identified ARDS with a sensitivity and specificity of 27 and 95 percent, respectively [7]. Thus, a plasma BNP level below 100 pg/mL may favor ARDS, but higher levels neither confirm heart failure nor exclude ARDS [7,8]. (See "Evaluation of the patient with suspected heart failure", section on 'BNP and NT-proBNP'.)

- **Transthoracic echocardiography (TTE)** – In patients with suspected ARDS, TTE may be performed to seek evidence of cardiac dysfunction when cardiogenic pulmonary edema cannot be excluded by clinical evaluation, laboratory findings, or imaging. TTE is not routinely needed if clinical suspicion for cardiogenic pulmonary edema is low and the workup clearly points to noncardiogenic causes of pulmonary infiltrates.

- A normal ejection fraction may favor ARDS while severe aortic or mitral valve dysfunction, severe diastolic dysfunction, or a severely reduced left ventricular ejection fraction may favor cardiogenic pulmonary edema. However, these findings are not specific. For example, some precipitants of ARDS (eg, septic shock) can cause an acute cardiomyopathy that develops concomitantly with ARDS [9,10]. Conversely, if left heart function appears normal, pulmonary edema may occur due to volume overload (eg, pulmonary edema from blood product transfusions, fluid overload from aggressive fluid resuscitation). In addition, ARDS can coexist with cardiogenic pulmonary edema; while the diagnosis of ARDS requires that hydrostatic edema be excluded, it is clear that patients with volume overload can develop acute lung injury, supported by the observation of elevated pulmonary artery wedge pressures when pulmonary artery catheters are placed in patients with ARDS

- For those in whom the diagnosis of acute cardiogenic pulmonary edema remains uncertain (which is rare), additional testing may be indicated.

ADDITIONAL TESTING

Diagnosis and etiology is apparent — In most patients a preliminary diagnosis of ARDS and its etiology can be confirmed with initial evaluation while patients receive supportive therapy (eg, oxygen, low tidal volume mechanical ventilation, and conservative fluid management (algorithm 1)). In such individuals, no further investigations are necessary, particularly if they show signs of stabilization and/or improvement. (See "Acute respiratory distress syndrome: Supportive care and oxygenation in adults" and "Ventilator management strategies for adults with acute respiratory distress syndrome".)

Diagnosis and etiology is unclear — In a small proportion of patients, additional testing may be required in the following circumstances:

- When initial evaluation does not sufficiently exclude acute cardiogenic pulmonary edema or suggest a specific cause for ARDS (eg, no obvious risk factors)
- When an unusual etiology (eg, fungal pneumonia) or an alternate condition that mimics ARDS (eg, diffuse alveolar hemorrhage, pneumocystis pneumonia) are suspected

Suspicion for any of these potential situations may be raised during the initial evaluation or when patients develop progressive hypoxemia despite adequate supportive care.

Further testing may involve reevaluation of fluid status, additional laboratory tests, right heart catheterization, bronchoscopy with bronchoalveolar lavage (BAL), and rarely, lung biopsy. Choosing among these tests is individualized and is dependent upon the suspected condition that needs to be confirmed or excluded as well as the safety of testing and the therapeutic and prognostic value of the test.

Ensuring normal fluid status — Patients should be clinically **re**-evaluated for fluid status. For patients whose fluid status is assessed as normal and cardiogenic pulmonary edema has been sufficiently excluded, no additional testing for fluid status is required. For those in whom fluid status remains uncertain, we suggest the following.

Formal echocardiography – A transthoracic echocardiogram (TTE; if not already performed) with or without shunt testing can assess left ventricular function and valvular pathology. Rarely TTE is valuable if endocarditis or complex valvular etiology is suspected. (See "Transthoracic echocardiography: Normal cardiac anatomy and tomographic views" and "Transesophageal echocardiography: Indications, complications, and normal views".)

- **Right heart catheterization (RHC)** – While there is no value to routine RHC for either the diagnosis or management of ARDS [12,13], it may occasionally be useful if fluid status remains uncertain despite other means of testing. (See "Approach to diagnosis and evaluation of acute decompensated heart failure in adults", section on 'Swan-Ganz catheter'.)

- **Bedside hemodynamic monitoring tools** – If rapid assessment is required, bedside lung ultrasonography may be helpful in distinguishing B lines with a smooth pleural morphology (which may indicate cardiogenic pulmonary edema) from B lines with irregular pleural morphology (which may suggest ARDS). Bedside cardiac ultrasonography is being increasingly used for rapid assessment of left and right ventricular wall morphology and function in patients with shock, but it should not supplant formal echocardiography as the gold standard. Additional bedside tools such as passive leg raising and pulse contour analysis in response to a fluid challenge are novel tools that may assist in determining volume status in patients with shock, but their role in the evaluation of volume status in patients with ARDS is also unclear. Further details are provided separately.

Bronchoscopy (bronchoalveolar lavage, brush) — Bronchoscopy is most useful when the cause of ARDS is uncertain and concern is raised that the etiology may require specific treatment. For example, bronchoscopy may help clinicians identify infectious etiologies for ARDS, typically pneumonia, by providing specimens for culture when sputum is unavailable or unrevealing (eg, invasive mycotic infections, tuberculosis [TB], or pneumocystis). Bronchoscopy may also help clinicians diagnose specific noninfectious causes of ARDS (eg, acute eosinophilic pneumonia [AEP]) or conditions that mimic ARDS (eg, diffuse alveolar hemorrhage, lymphangitis carcinomatosis) by providing specimens for cytologic or biochemical analysis.

Bronchoscopy is generally considered valuable when the following is suspected:

- **Occult infection/pneumonia** – Bilateral pneumonia is both a cause and mimicker of ARDS. In many cases, it is difficult to decide what is actually bilateral pneumonia and what is ARDS. Thus, many patients with ARDS end up being treated empirically with antibiotics. This was illustrated by an autopsy study that found pneumonia in 58 percent of patients with ARDS, although pneumonia was suspected antemortem in only 20 percent [14]. In addition, 20 percent of patients thought to have pneumonia did not have histologic evidence of pneumonia. Bronchoscopy may be useful when specific organisms need to be ruled out or are suspected. Examples include patients with a history of TB exposure, immunosuppression, risk factors for fungus (travel history, neutropenia), select viruses (eg, cytomegalovirus [CMV] in transplant patients, varicella in pregnant women) or parasites (eg, travel), suspected *nocardia* species (eg, coexistent brain lesion), *actinomyces* species (eg, trauma), or resistant organisms in patients with bronchiectasis. Specific testing includes:
  - Serology and site-specific cultures – This includes fungal, blood, and site-specific cultures (including cerebrospinal fluid), influenza antigen, viral titers (eg, CMV, Epstein Barr virus), cryptococcal antigen, and beta-D glucan and galactomannan levels.
  - BAL – BAL is important in identifying culprit organisms if sputum or endotracheal aspirates are unrevealing (eg, fungal, *pneumocystis jirovecii, actinomyces,* and *nocardia* species).
- **Select inflammatory conditions or occult cancer** – Conditions including diffuse alveolar hemorrhage (DAH) or AEP can be readily identified on BAL. Elevated eosinophils on BAL may also be useful for the diagnosis of Churg-Strauss syndrome or chronic eosinophilic pneumonia (CEP). Less commonly, invasive malignancy may be identified on BAL cytology. (See 'Acute eosinophilic pneumonia' below and 'Pulmonary vasculitis' below and 'Disseminated malignancy' below.)
- **Others** – Recovery of recognizable food particles or lipid-laden macrophages on BAL may suggest aspiration pneumonitis or lipoid pneumonia, although definitive diagnosis of lipoid pneumonia usually requires biopsy. Recovery of cancer cells supports lymphangitis or pulmonary embolism. (See "Aspiration pneumonia in adults".)

Once the decision is made to proceed with bronchoscopy and consent is obtained, the airways should be visually inspected for edema, infections, secretions, foreign bodies, lipid or food particles, and endobronchial masses. Lavage fluid, with or without bronchial brushings, should be taken from the most affected regions of the lung. Samples should be analyzed for cell count (including eosinophils), microbiologic analysis (routine, fungal, viral), galactomannan level, and cytologic analysis for organisms (eg, fungus, CMV, *mycobacterium*, *actinomyces*, and *nocardia* species) and for malignancy. (

DIFFERENTIAL DIAGNOSISA variety of conditions may present as acute hypoxemic respiratory failure with bilateral alveolar opacities and, therefore, should be considered whenever ARDS is suspected [23]. It is important to note that an almost limitless number of pulmonary conditions can present with bilateral infiltrates and hypoxemia. It is therefore imperative that previous diagnostic studies done prior to admission, particularly chest radiographs and computed tomography (CT) scans, be reviewed to document that the abnormalities identified are new.

- **Acute cardiogenic pulmonary edema** — Distinguishing acute cardiogenic pulmonary edema from ARDS is essential for the diagnosis of ARDS and is discussed above. (See 'Excluding acute cardiogenic pulmonary edema' above and 'Ensuring normal fluid status' above.)
- **Bilateral pneumonia** — Bilateral pneumonia may mimic ARDS but may also be an etiology of ARDS and in many cases it is hard to distinguish pneumonia from ARDS. (See 'Bronchoscopy (bronchoalveolar lavage, brush)' above.)
- **Diffuse alveolar hemorrhage** — Several conditions are associated with diffuse alveolar hemorrhage (DAH), a condition that mimics ARDS (table 2). Up to two-thirds will present with hemoptysis, and some patients present with sudden-onset respiratory distress, symptoms that are unusual for patients with ARDS. Bronchoscopy and bronchoalveolar lavage (BAL) are also helpful in distinguishing DAH from ARDS. In DAH, the clinician may appreciate frothy bloody secretions throughout the airways, increasing red blood cells in serial BAL specimens, and hemosiderin-laden macrophages in the BAL fluid. However, these findings are not specific and more subtle forms of hemorrhage may not be evident on BAL. (See "The diffuse alveolar hemorrhage syndromes" and 'Bronchoscopy (bronchoalveolar lavage, brush)' above.)
- **Inflammatory or autoimmune conditions** — Several specific acute inflammatory conditions may mimic ARDS but can be distinguished by a more indolent time of onset (eg, longer than one week) and by specific pathological findings on biopsy. Some conditions may present in a manner that is indistinguishable from ARDS with the acute onset of bilateral lung infiltrates and hypoxemia. Whether the term ARDS should be used to describe these conditions is a matter of uncertainty; nonetheless, it is important to consider these diagnoses, some of which are reversible with specific treatments. With the exception of acute eosinophilic pneumonia (AEP), which can be diagnosed bronchoscopically, most can only be definitively distinguished from ARDS on lung biopsy.

Acute eosinophilic pneumonia — AEP occurs in previously healthy individuals and is characterized by cough, fever, dyspnea, and sometimes chest pain. It can be distinguished from ARDS on BAL specimens by the identification of a large number of eosinophils, typically 35 to 55 percent of all recovered cells [24,25]. Peripheral eosinophilia may or may not be present [26].

Pulmonary vasculitis — Pulmonary vasculitis (eg, systemic lupus erythematosus, granulomatosis with polyangiitis [formerly Wegner's granulomatosis], Goodpasture's syndrome, eosinophilic granulomatosis with polyangiitis [Churg-Strauss syndrome]) is a rare phenomenon that may be suspected in patients with a known rheumatologic diagnosis or underlying asthma (Churg-Strauss), or in those that present with hemoptysis. These conditions may be distinguished from ARDS by serology including a rheumatologic panel (eg, antinuclear antibody [ANA], antidouble stranded DNA) or vasculitis panel (eg, c- and p-antineutrophil cytoplasmic autoantibody [ANCA], anti-glomerular basement membrane antibody [anti-GBMA]). Although Churg-Strauss syndrome may be suspected on the basis of elevated eosinophils on BAL, BAL is not typically diagnostic and lung biopsy is often needed. (See "Anti-GBM (Goodpasture) disease: Pathogenesis, clinical manifestations, and diagnosis" and "Granulomatosis with polyangiitis and microscopic polyangiitis: Respiratory tract involvement" and "Clinical features and diagnosis of eosinophilic granulomatosis with polyangiitis (Churg-Strauss)" and 'Lung biopsy' above and "Clinical manifestations and diagnosis of systemic lupus erythematosus in adults", section on 'Clinical manifestations'.)

Cryptogenic organizing pneumonia (COP) — COP may be suspected in patients who present with the symptoms of nonresolving pneumonia heralded by a flu-like illness. BAL usually contains a smaller proportion of macrophages and higher proportions of lymphocytes, neutrophils, and eosinophils than healthy patients. The diagnosis is made by ruling out infectious causes of pneumonia and documenting typical pathologic changes on lung biopsy. (See "Cryptogenic organizing pneumonia" and 'Lung biopsy' above.)

Acute interstitial pneumonitis (AIP; Hamman-Rich syndrome) — AIP is a rare and fulminant form of diffuse lung injury that has a presentation similar to ARDS. Many people consider AIP a subset of idiopathic ARDS since its clinical manifestations are similar and both demonstrate diffuse alveolar damage (DAD) on histopathology. The distinguishing characteristic is that ARDS is typically associated with an identifiable risk factor, whereas AIP is not. When AIP is suspected, lung biopsy is usually required since bronchoscopic BAL is not diagnostic. (See "Acute interstitial pneumonia (Hamman-Rich syndrome)" and 'Lung biopsy' above.)

Acute exacerbation of idiopathic pulmonary fibrosis (AEIPF) — Like ARDS, the pathological findings of AEIPF are dominated by DAD/AIP, but the prognosis is substantially worse. This diagnostic possibility is easily overlooked in patients with previously undiagnosed interstitial lung disease. The diagnosis is suggested by careful review of previous and current chest radiographic and CT images that may reveal changes consistent with underlying IPF. When AEIPF is suspected, lung biopsy is usually required since bronchoscopic BAL is not diagnostic. (See "Treatment of idiopathic pulmonary fibrosis", section on 'Acute exacerbations' and 'Lung biopsy' above.)

Acute fibrinous organizing pneumonia (AFOP) — AFOP is a rare alveolar filling disease that can be idiopathic or follow organ transplantation. It can only be distinguished from ARDS pathologically on lung biopsy

- **Disseminated malignancy** — Cancer can disseminate through the lungs (invasive cancer) or lymphatics (lymphangitic spread) so rapidly that the ensuing respiratory failure may be mistaken for ARDS. It should be suspected in patients with malignancy (lymphoma, acute leukemia, or solid tumors) (table 3) who have progressive unexplained dyspnea and hypoxemia not responding to supportive therapy such as antibiotics. Cytological preparation of bronchoscopic specimens (eg, brushings, lavage) sometimes reveals malignant cells. Rarely, bronchoscopy may reveal an endobronchial lesion not detected on imaging and pulmonary artery catheter sampling may detect malignant cells. Lung biopsy is typically diagnostic. (See "Pulmonary tumor embolism and lymphangitic carcinomatosis in adults: Diagnostic evaluation and management" and 'Lung biopsy' above.)

- **Others** — Embolic syndromes may present with hypoxemia and bilateral opacities. They usually have an abrupt onset in an appropriate clinical setting such as in patients with orthopedic fractures (fat embolism syndrome [FES]) or peripartum patients (amniotic fluid embolism syndrome [AFES]). Occasionally, fat or amniotic fluid debris may be identified on BAL to support a clinical diagnosis of fat embolism or amniotic fluid embolism, although this is not diagnostic. Pulmonary embolism (PE) is also typically abrupt in onset but bilateral opacities are unusual unless complicated by infarction and pneumonitis. PE can be easily distinguished on computed tomographic pulmonary angiography. Air embolism should always be suspected when patients experience sudden-onset respiratory distress in the setting of a known risk factor, intravenous catheter insertion, or trauma. A transthoracic echocardiogram may identify air in the intravascular space. (See "Fat embolism syndrome" and "Amniotic fluid embolism" and "Air embolism" and

Acute respiratory distress syndrome (ARDS) is a major complication in patients with severe disease and can manifest shortly after the onset of dyspnea. In the study of 138 patients described above, ARDS developed in 20 percent a median of eight days after the onset of symptoms; mechanical ventilation was implemented in 12.3 percent [35]. In another study of 201 hospitalized patients with COVID-19 in Wuhan, 41 percent developed ARDS; age greater than 65 years, diabetes mellitus, and hypertension were each associated with ARDS [75].

- Other complications have included arrhythmias, acute cardiac injury, and shock [35,70,100,101]. In one study, these were reported in 17, 7, and 9 percent, respectively [35]. In a series of 21 severely ill patients admitted to the ICU in the United States, one-third developed cardiomyopathy [100]. Thromboembolic complications, including pulmonary embolism and acute stroke, have also been reported

- Some patients with severe COVID-19 have laboratory evidence of an exuberant inflammatory response, similar to cytokine release syndrome, with persistent fevers, elevated inflammatory markers (eg, D-dimer, ferritin), and elevated proinflammatory cytokines; these laboratory abnormalities have been associated with critical and fatal illnesses [56,107]. (See 'Risk factors for severe illness' above.)

- According to the WHO, recovery time appears to be around two weeks for mild infections and three to six weeks for severe disease [10].

Laboratory findings

- In patients with COVID-19, the white blood cell count can vary. Leukopenia, leukocytosis, and lymphopenia have been reported, although lymphopenia appears most common [14,35,56,57]. Elevated lactate dehydrogenase and ferritin levels are common, and elevated aminotransferase levels have also been described. On admission, many patients with pneumonia have normal serum procalcitonin levels; however, in those requiring ICU care, they are more likely to be elevated

- High D-dimer levels and more severe lymphopenia have been associated with mortality

Imaging findings

- — Chest radiographs may be normal in early or mild disease. In a retrospective study of 64 patients in Hong Kong with documented COVID-19, 20 percent did not have any abnormalities on chest radiograph at any point during the illness [108]. Common abnormal radiograph findings were consolidation and ground glass opacities, with bilateral, peripheral, and lower lung zone distributions; lung involvement increased over the course of illness, with a peak in severity at 10 to 12 days after symptom onset.

- Although chest CT may be more sensitive than chest radiograph and some chest CT findings may be characteristic of COVID-19, no finding can completely rule in or rule out the possibility of COVID-19. In the United States, the American College of Radiology (ACR) recommends not using chest CT for screening or diagnosis of COVID-19 and recommends reserving it for hospitalized patients when needed for management [109]. If CT is performed, the Radiological Society of North America has categorized features as typical, indeterminate, or atypical for COVID-19, and has suggested corresponding language for the interpretation report

- Chest CT in patients with COVID-19 most commonly demonstrates ground-glass opacification with or without consolidative abnormalities, consistent with viral pneumonia [91,111]. Case series have suggested that chest CT abnormalities are more likely to be bilateral, have a peripheral distribution, and involve the lower lobes. Less common findings include pleural thickening, pleural effusion, and lymphadenopathy.

- In a study of 1014 patients in Wuhan who underwent both reverse-transcription polymerase chain reaction (RT-PCR) testing and chest CT for evaluation of COVID-19, a "positive" chest CT for COVID-19 (as determined by a consensus of two radiologists) had a sensitivity of 97 percent, using the PCR tests as a reference; however, specificity was only 25 percent [112]. The low specificity may be related to other etiologies causing similar CT findings. In another study comparing chest CTs from 219 patients with COVID-19 in China and 205 patients with other causes of viral pneumonia in the United States, COVID-19 cases were more likely to have a peripheral distribution (80 versus 57 percent), ground-glass opacities (91 versus 68 percent), fine reticular opacities (56 versus 22 percent), vascular thickening (59 versus 22 percent), and reverse halo sign (11 versus 1 percent), but less likely to have a central and peripheral distribution (14 versus 35 percent), air bronchogram (14 versus 23 percent), pleural thickening (15 versus 33 percent), pleural effusion (4 versus 39 percent), and lymphadenopathy (2.7 versus 10 percent) [113]. A group of radiologists in that study was able to distinguish COVID-19 with high specificity but moderate sensitivity.

- In one report of 21 patients with laboratory-confirmed COVID-19 who did not develop severe respiratory distress, lung abnormalities on chest imaging were most severe approximately 10 days after symptom onset [90]. However, chest CT abnormalities have also been identified in patients prior to the development of symptoms and even prior to the detection of viral RNA from upper respiratory specimens

- Among patients who clinically improve, resolution of radiographic abnormalities may lag behind improvements in fever and hypoxia

- **DIAGNOSIS**
- **Clinical suspicion and criteria for testing** — The possibility of COVID-19 should be considered primarily in patients with new onset fever and/or respiratory tract symptoms (eg, cough, dyspnea). It should also be considered in patients with severe lower respiratory tract illness without any clear cause. Although these syndromes can occur with other viral respiratory illnesses, the likelihood of COVID-19 is increased if the patient:

- Resides in or has traveled within the prior 14 days to a location where there is community transmission of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2; ie, large numbers of cases that cannot be linked to specific transmission chains) (see 'Geographic distribution' above); or
- ●Has had close contact with a confirmed or suspected case of COVID-19 in the prior 14 days, including through work in health care settings. Close contact includes being within approximately six feet (about two meters) of a patient for a prolonged period of time while not wearing personal protective equipment (PPE) or having direct contact with infectious secretions while not wearing PPE.

- Patients with suspected COVID-19 who do not need emergency care should be encouraged to call prior to presenting to a health care facility for evaluation. Many patients can be evaluated regarding the need for testing over the phone. For patients in a health care facility, infection control measures should be implemented as soon as the possibility of COVID-19 is suspected.

- The diagnosis cannot be definitively made without microbiologic testing, but limited capacity may preclude testing all patients with suspected COVID-19. Local health departments may have specific criteria for testing. In the United States, the Centers for Disease Control and Prevention (CDC) and the Infectious Diseases Society of America have suggested priorities for testing (table 2); high-priority individuals include hospitalized patients (especially critically ill patients with unexplained respiratory illness), symptomatic health care workers, and symptomatic individuals who have risk factors for severe disease

- Testing criteria suggested by the World Health Organization (WHO) can be found in its technical guidance online. These are the same criteria used by the European Centre for Disease Prevention and Control.
- An approach to suspected cases when testing is not available is discussed elsewhere.

- **Microbiologic diagnosis**
- **RT-PCR** — The diagnosis of COVID-19 is made by detection of SARS-CoV-2 RNA by reverse-transcription polymerase chain reaction (RT-PCR) [118]. In the United States, testing is performed by the CDC, local public health departments, hospitals that have developed and validated their own tests, and certain commercial reference laboratories.

- **Specimen collection** — In the United States, the CDC recommends collection of a nasopharyngeal swab specimen to test for SARS-CoV-2 [119]. An oropharyngeal swab can be collected but is not essential; if collected, it should be placed in the same container as the nasopharyngeal specimen. Oropharyngeal, nasal mid-turbinate, or nasal swabs (of both nares) are acceptable alternatives for symptomatic patients if nasopharyngeal swabs are unavailable.
- Expectorated sputum should be collected from patients with productive cough; induction of sputum is not recommended. A lower respiratory tract aspirate or bronchoalveolar lavage should be collected from patients who are intubated. Additional information on testing and handling of clinical specimens can be found on the CDC website. Infection control practices during specimen collection are discussed elsewhere.

- **Interpretation** — A positive test for SARS-CoV-2 generally confirms the diagnosis of COVID-19. However, false-negative tests from upper respiratory specimens have been well documented. If initial testing is negative but the suspicion for COVID-19 remains and determining the presence of infection is important for management or infection control, we suggest repeating the test. In such cases, the WHO also recommends testing lower respiratory tract specimens, if possible [120]. Infection control precautions for COVID-19 should continue while repeat evaluation is being performed. (See 'Infection control for suspected or confirmed cases' below.)
- In many cases, because of the limited availability of testing and concern for false-negative results, the diagnosis of COVID-19 is made presumptively based on a compatible clinical presentation in the setting of an exposure risk (residence in or travel to an area with widespread community transmission or known contact).

- The accuracy and predictive values of SARS-CoV-2 testing have not been systematically evaluated, and the sensitivity of testing likely depends on the precise RT-PCR assay, the type of specimen obtained, the quality of the specimen, and duration of illness at the time of testing. In a study of 51 patients who were hospitalized in China with fever or acute respiratory symptoms and ultimately had a positive SARS-CoV-2 RT-PCR test (mainly on throat swabs), 15 patients (29 percent) had a negative initial test and only were diagnosed by serial testing [121]. The likelihood of a positive upper respiratory RT-PCR may be higher early in the course of illness. One study using a combination of RT-PCR and an IgM serologic test to make the diagnosis of COVID-19 suggested that RT-PCR positivity rates were >90 percent on days 1 to 3 of illness, <80 percent at day 6, and <50 percent after day 14; however, these results should be interpreted with caution, since the serologic test used was not validated for detection of acute infection and IgM tests are generally prone to false positivity [122].

- Lower respiratory tract specimens may have higher viral loads and be more likely to yield positive tests than upper respiratory tract specimens [17,123]. In a study of 205 patients with COVID-19 who were sampled at various sites, the highest rates of positive viral RNA tests were reported from bronchoalveolar lavage (95 percent, 14 of 15 specimens) and sputum (72 percent, 72 of 104 specimens), compared with oropharyngeal swab (32 percent, 126 of 398 specimens) [17]. Data from this study suggested that viral RNA levels are higher and more frequently detected in nasal compared with oral specimens, although only eight nasal swabs were tested.

- **Other tests** — Serologic tests, as soon as generally available and adequately evaluated, should be able to identify patients who have either current or previous infection but a negative PCR test [122,124]. In one study that included 58 patients with clinical, radiographic, and epidemiologic features suspicious for COVID-19 but with negative SARS-CoV-2 PCR testing, an IgM enzyme-linked immunosorbent assay (ELISA) was positive in 93 percent (and was negative when tested separately on plasma specimens that predated the COVID-19 outbreak) [122]. In the United States, several serologic tests have been granted emergency use authorization by the Food and Drug Administration for use by laboratories certified to perform moderate- and high-complexity tests [34]. Although several manufacturers are selling rapid, point-of-care tests based on antigen testing or antibody detection, the WHO does not recommend these tests because of accuracy concerns in the absence of validation studies

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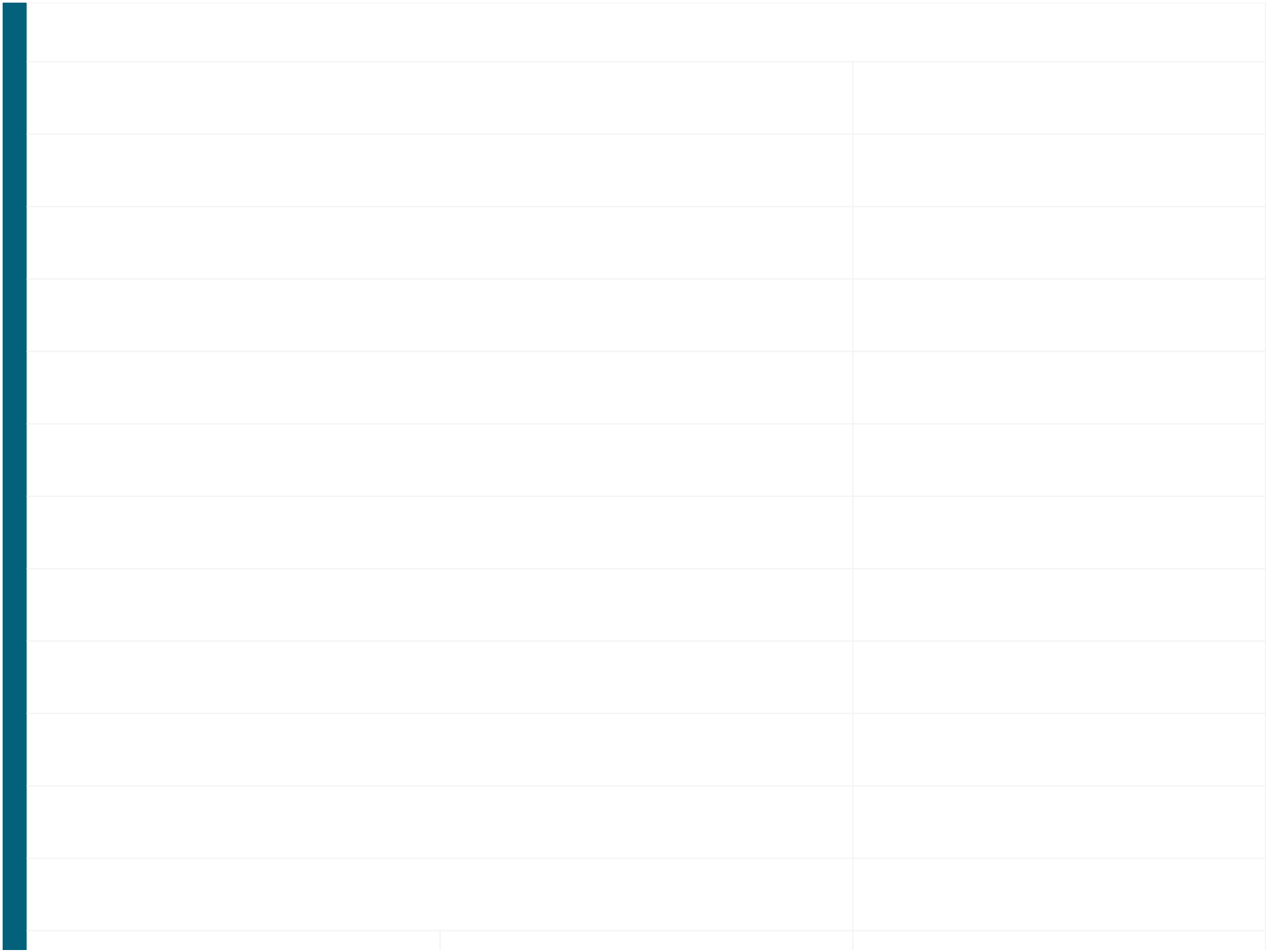
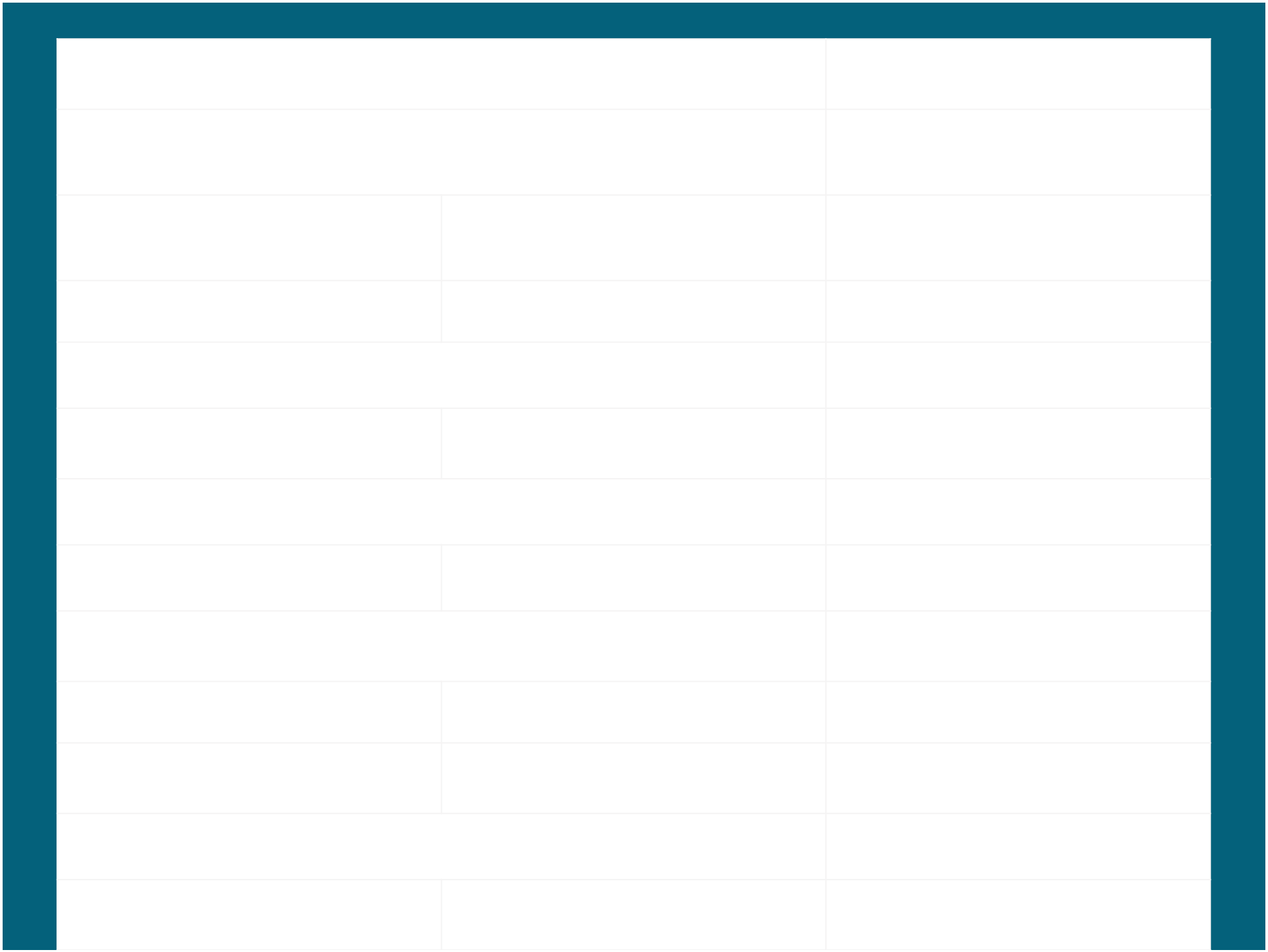
- For safety reasons, specimens from a patient with suspected or documented COVID-19 should **not** be submitted for viral culture.
- **Testing for other pathogens** — If influenza is circulating in the community, it is reasonable to also test for influenza when testing for SARS-CoV-2, as this could have management implications.
- However, detection of another viral (or bacterial) pathogen does not necessarily rule out SARS-CoV-2 in locations where there is widespread transmission. Coinfection with SARS-CoV-2 and other respiratory viruses, including influenza, has been reported

- **MANAGEMENT**Home management is appropriate for patients with mild infection (eg, fever, cough, and/or myalgias without dyspnea) or asymptomatic infection who can be adequately isolated in the outpatient setting. Management of such patients should focus on prevention of transmission to others and monitoring for clinical deterioration, which should prompt hospitalization. Management of patients who warrant hospitalization consists of ensuring appropriate infection control and supportive care (including oxygenation and potentially ventilatory support for acute respiratory distress syndrome). Investigational approaches are also being evaluated, and should be used in the setting of a clinical trial, whenever available. Management of COVID-19 is discussed in detail elsewhere:



		۴۰ (%۴۰)

- **Unilateral pneumonia 25 (25%)**
- **Bilateral pneumonia 74 (75%)**
- **Multiple mottling and ground-glass opacity 14 (14%)**
- (1%) patient had pneumothorax



- Of the remaining nine patients who died, eight patients had lymphopenia,
- seven had bilateral pneumonia,
- five were older than 60 years,
- three had hypertension,
- and one was a heavy smoker.

- Comorbid conditions Any 33 (33%)
- ARDS 17 (17%)
- Acute renal injury 3 (3%)
- Acute respiratory injury 8 (8%)
- Septic shock 4 (4%)
- Ventilator-associated pneumonia 1 (1%)

- Oxygen therapy 75 (76%)
- Mechanical ventilation Non-invasive (ie, face mask) 13 (13%)
- Invasive 4 (4%)
- CRRT 9 (9%)
- ECMO 3 (3%)
- Antibiotic treatment 70 (71%) Antifungal treatment 15 (15%) Antiviral treatment 75 (76%) Glucocorticoids 19 (19%)
- Intravenous immunoglobulin therapy 27 (27%)

به چه کسانی مشکوک شویم

Clinical Features	&	Epidemiologic Risk
[1]		[2] [3,4]
[1]		
[1] [4]		

- Notes

  [1]Close contact is defined as:

  a) being within approximately 6 feet (2 meters), or within the room or care area, of a 2019-nCoV case for a prolonged period of time while not wearing recommended personal protective equipment or PPE (e.g., gowns, gloves, NIOSH-certified disposable N95 respirator, eye protection); close contact can include caring for, living with, visiting, or sharing a health care waiting area or room with a 2019-nCoV case

  – or –

  b) having direct contact with infectious secretions of a 2019-nCoV case (e.g., being coughed on) while not wearing recommended personal protective equipment.

  [2]Fever may be subjective or confirmed

Flowchart to Identify and Assess 2019 Novel Coronavirus

For the evaluation of patients who may be ill with or who may have been exposed to 2019 Novel Coronavirus (2019-nCoV)

A. Identify

if in the ***past 14 days since first onset of symptoms*** a history of ***either***

Travel to China	← OR →	**Close contact with** a person known to have 2019-nCoV illness*

B. AND the person has

Fever or symptoms of lower respiratory illness
(e.g., cough or shortness of breath)

if both exposure and illness are present

↓

1. Isolate

- Place facemask on patient
- Isolate the patient in a private room or a separate area
- Wear appropriate personal protective equipment (PPE)

2. Assess clinical status

EXAM	**Is fever present?**	**Is respiratory illness present?**
	☐ Subjective?	☐ Cough?
	☐ Measured? _____°C/F	☐ Shortness of breath?

3. Inform

- Contact health department to report at-risk patients and their clinical status
- Assess need to collect specimens to test for 2019-nCoV
- Decide disposition

If discharged to home

↓

Instruct patient

As needed depending on severity of illness and health department consultation

- Home care guidance
- Home isolation guidance

Advise patient

If the patient develops new or worsening fever or respiratory illness

- Call clinic to determine if reevaluation is needed
- If reevaluation is needed call ahead and wear facemask

* Documentation of laboratory-confirmation of 2019-nCoV may not be possible for travelers or persons caring for patients in other countries. For more clarification on the definition for close contact see CDC's Interim Guidance for Healthcare Professionals: www.cdc.gov/coronavirus/2019-nCoV/hcp/clinical-criteria.html

If a patient meets these criteria:

- should be asked to wear a surgical mask as soon as they are identified and directed to a separate area, if possible, with at least 6 feet (2 meters) separation from other persons.
- Patients should be evaluated in a private room with the door closed, ideally an airborne infection isolation room (AIIR), if available.
- Healthcare personnel entering the room should use standard precautions, contact precautions, airborne precautions, and use eye protection (e.g., goggles or a face shield).

Prevention

- **No vaccine** to prevent 2019-nCoV infection.
- **Wash your hands often with soap and water for at least 20 seconds**.
- **Use an alcohol-based hand sanitizer that contains at least 70% alcohol if soap and water are not available.**
- **Avoid touching your eyes, nose, and mouth with unwashed hands.**
- **Avoid close contact with people who are sick.**
- **Stay home when you are sick.**
- **Cover your cough or sneeze with a tissue, then throw the tissue in the trash.**
- **Clean and disinfect frequently touched objects and surfaces.**

- . **Adherence to Standard, Contact and Airborne Precautions, Including the Use of Eye Protection**
- **All HCP (see section 3 for measures for non-HCP visitors) who enter the room of a patient with suspected or confirmed 2019-nCoV should adhere to Standard, Contact, and Airborne Precautions, including the following:**
- **Patient Placement(negative pressure Room)**
- **Hand Hygiene (20** seconds)
- **Personal Protective Equipment**

- **Gloves** (clean, non-sterile gloves)
- **Gowns**
- **Respiratory Protection**
- **disposable N95 filtering facepiece respirator**
- **Eye Protection**
- **goggles**

.

- AIIRs are single patient rooms at negative pressure relative to the surrounding areas12 air changes per hour are recommended for new construction or renovation)
- . Air from these rooms should be exhausted directly to the outside or be filtered through a high-efficiency particulate air (HEPA) filter before recirculation.
- Room doors should be kept closed except when entering or leaving the room, and entry and exit should be minimized. Facilities should monitor and document the proper negative-pressure function of these rooms.
- If an AIIR is not available, the patient should be transferred as soon as is feasible to a facility where an AIIR is available or discharged to home (in consultation with state or local public health authorities) if deemed medically appropriate. Pending transfer, place a facemask on the patient and isolate him/her in an examination room with the door closed.
- The patient should not be placed in any room where room exhaust is recirculated within the building without HEPA filtration.

- Once in an AIIR, the patient's facemask may be removed. Limit transport and movement of the patient outside of the AIIR to medically-essential purposes. When not in an AIIR (e.g., during transport or if an AIIR is not available), patients should wear a facemask to contain secretions.
- Personnel entering the room should use PPE, including respiratory protection, as described below.
- Only essential personnel should enter the AIIR. Implement staffing policies to minimize the number of HCP who enter the room.
  - Facilities should consider caring for these patients with dedicated HCP to minimize risk of transmission and exposure to other patients and other HCP.
- Facilities should keep a log of all persons who care for or enter the rooms or care area of these patients.

- **Use dedicated or disposable noncritical patient-care equipment (e.g., blood pressure cuffs). If equipment will be used for more than one patient, clean and disinfect such equipment before use on another patient according to manufacturer's instructions.**
  - **HCP entering the AIIR soon after a patient vacates the room should use respiratory protection. (See personal protective equipment section below) Standard practice for pathogens spread by the airborne route (e.g., measles, tuberculosis) is to restrict unprotected individuals, including HCP, from entering a vacated room until sufficient time has elapsed for enough air changes to remove potentially infectious particles (more information on clearance rates under differing ventilation conditions is available). We do not yet know how long 2019-nCoV remains infectious in the air. In the interim, it is reasonable to apply a similar time period before entering the room without respiratory protection as used for pathogens spread by the airborne route (e.g., measles, tuberculosis). In addition, the room should undergo appropriate cleaning and surface disinfection before it is returned to routine use.**

- HCP should perform hand hygiene using ABHR before and after all patient contact, contact with potentially infectious material, and before putting on and upon removal of PPE, including gloves. Hand hygiene in healthcare settings also can be performed by washing with soap and water for at least 20 seconds. If hands are visibly soiled, use soap and water before returning to ABHR.
- Healthcare facilities should ensure that hand hygiene supplies are readily available to all personnel in every care location.

Employers should select appropriate PPE and provide it to HCP in accordance with OSHA's PPE standards (29 CFR 1910 Subpart I)external icon. HCP must receive training on and demonstrate an understanding of when to use PPE; what PPE is necessary; how to properly don, use, and doff PPE in a manner to prevent self-contamination; how to properly dispose of or disinfect and maintain PPE; and the limitations of PPE. Any reusable PPE must be properly cleaned, decontaminated, and maintained after and between uses. Facilities should have policies and procedures describing a recommended sequence for safely donning and doffing PPE:

- **Gloves**
  - Perform hand hygiene, then put on clean, non-sterile gloves upon entry into the patient room or care area. Change gloves if they become torn or heavily contaminated.
  - Remove and discard gloves when leaving the patient room or care area, and immediately perform hand hygiene.

Gowns

- Put on a clean disposable gown upon entry into the patient room or area. Change the gown if it becomes soiled. Remove and discard the gown before leaving the patient room or care area.

Respiratory Protection

- Use respiratory protection (i.e., a respirator) that is at least as protective as a fit-tested NIOSH-certified disposable N95 filtering facepiece respirator before entry into the patient room or care area. See appendix for respirator definition.
- Disposable respirators should be removed and discarded after exiting the patient's room or care area and closing the door. Perform hand hygiene after discarding the respirator.
- If reusable respirators (e.g., powered air purifying respirator/PAPR) are used, they must be cleaned and disinfected according to manufacturer's reprocessing instructions prior to re-use.
- Respirator use must be in the context of a complete respiratory protection program in accordance with Occupational Safety and Health Administration (OSHA) Respiratory Protection standard (29 CFR 1910.134external icon). Staff should be medically cleared and fit-tested if using respirators with tight-fitting facepieces (e.g., a NIOSH-certified disposable N95) and trained in the proper use of respirators, safe removal and disposal, and medical contraindications to respirator use.

Eye Protection

- Put on eye protection (e.g., goggles, a disposable face shield that covers the front and sides of the face) upon entry to the patient room or care area. Remove eye protection before leaving the patient room or care area. Reusable eye protection (e.g., goggles) must be cleaned and disinfected according to manufacturer's reprocessing instructions prior to re-use. Disposable eye protection should be discarded after use.

- **Use Caution When Performing Aerosol-Generating Procedures**Some procedures performed on 2019-nCoV patients could generate infectious aerosols. In particular, procedures that are likely to induce coughing; e.g., nasopharyngeal specimen collection, sputum induction, and open suctioning of airways should be performed cautiously and avoided if possible.
- If performed, these procedures should take place in an AIIR, and personnel should use respiratory protection as described above. In addition:
  - Limit the number of HCP present during the procedure to only those essential for patient care and procedural support.
  - Clean and disinfect procedure room surfaces promptly as described in the section on environmental infection control below.

- **Duration of Isolation Precautions**Until information is available regarding viral shedding after clinical improvement, discontinuation of isolation precautions should be determined on a case-by-case basis, in conjunction with local, state, and federal health authorities.
- Factors that should be considered include: presence of symptoms related to 2019-nCoV, date symptoms resolved, other conditions that would require specific precautions (e.g., tuberculosis, *Clostridioides difficile),* other laboratory information reflecting clinical status, alternatives to inpatient isolation, such as the possibility of safe recovery at home.

- Manage Visitor Access and Movement Within the Facility
- Establish procedures for monitoring, managing and training visitors.
- Restrict visitors from entering the room of known or suspected 2019-nCoV patients (i.e., PUI). Alternative mechanisms for patient and visitor interactions, such as video-call applications on cell phones or tablets should be explored. Facilities can consider exceptions based on end-of-life situations or when a visitor is essential for the patient's emotional well-being and care.
- Visitors to known or suspected 2019-nCoV (i.e., PUI) patients should be scheduled and controlled to allow for:
  - Screening visitors for symptoms of acute respiratory illness before entering the healthcare facility.
  - Facilities should evaluate risk to the health of the visitor (e.g., visitor might have underlying illness putting them at higher risk for 2019-nCoV) and ability to comply with precautions.
  - Facilities should provide instruction, before visitors enter patients' rooms, on hand hygiene, limiting surfaces touched, and use of PPE according to current facility policy while in the patient's room.
  - Facilities should maintain a record (e.g., log book) of all visitors who enter patient rooms.
  - Visitors should not be present during aerosol-generating procedures.
  - Visitors should be instructed to limit their movement within the facility.
  - Exposed visitors (e.g., contact with symptomatic 2019-nCoV patient prior to admission) should be advised to report any signs and symptoms of acute illness to their health care provider for a period of at least 14 days after the last known exposure to the sick patient.
- All visitors should follow respiratory hygiene and cough etiquette precautions while in the common areas of the facility.

. Implement Engineering Controls

Consider designing and installing engineering controls to reduce or eliminate exposures by shielding HCP and other patients from infected individuals. Examples of engineering controls include physical barriers or partitions to guide patients through triage areas, curtains between patients in shared areas, closed suctioning systems for airway suctioning for intubated patients, as well as appropriate air-handling systems (with appropriate directionality, filtration, exchange rate, etc.) that are installed and properly maintained.

5. Monitor and Manage Ill and Exposed Healthcare Personnel

Movement and monitoring decisions for HCP with exposure to 2019-nCoV should be made in consultation with public health authorities.

Facilities and organizations providing healthcare should implement sick leave policies for HCP that are non-punitive, flexible, and consistent with public health guidance.

- Train and Educate Healthcare Personnel
- Provide HCP with job- or task-specific education and training on preventing transmission of infectious agents, including refresher training.
- HCP must be medically cleared, trained, and fit tested for respiratory protection device use (e.g., N95 filtering facepiece respirators), or medically cleared and trained in the use of an alternative respiratory protection device (e.g., Powered Air-Purifying Respirator, PAPR) whenever respirators are required. OSHA has a number of respiratory training videosexternal icon.
- Ensure that HCP are educated, trained, and have practiced the appropriate use of PPE prior to caring for a patient, including attention to correct use of PPE and prevention of contamination of clothing, skin, and environment during the process of removing such equipment.

- Implement Environmental Infection Control
- Dedicated medical equipment should be used for patient care.
- All non-dedicated, non-disposable medical equipment used for patient care should be cleaned and disinfected according to manufacturer's instructions and facility policies.
- Ensure that environmental cleaning and disinfection procedures are followed consistently and correctly.
- Routine cleaning and disinfection procedures (e.g., using cleaners and water to pre-clean surfaces prior to applying an EPA-registered, hospital-grade disinfectant to frequently touched surfaces or objects for appropriate contact times as indicated on the product's label) are appropriate for 2019-nCoV in healthcare settings, including those patient-care areas in which aerosol-generating procedures are performed. Products with EPA-approved emerging viral pathogens claims are recommended for use against 2019-nCoV. These products can be identified by the following claim:
  - "[Product name] has demonstrated effectiveness against viruses similar to 2019-nCoV on hard non-porous surfaces. Therefore, this product can be used against 2019-nCoV when used in accordance with the directions for use against [name of supporting virus] on hard, non-porous surfaces."
  - This claim or a similar claim, will be made only through the following communications outlets: technical literature distributed exclusively to health care facilities, physicians, nurses and public health officials, "1-800" consumer information services, social media sites and company websites (non-label related). Specific claims for "2019-nCoV" will not appear on the product or master label.
  - Additional information about EPA-approved emerging viral pathogens claims can be found here: https://www.epa.gov/pesticide-registration/guidance-registrants-process-making-claims-against-emerging-viral-pathogensexternal icon
  - If there are no available EPA-registered products that have an approved emerging viral pathogen claim for 2019-nCoV, products with label claims against human coronaviruses should be used according to label instructions.
- Management of laundry, food service utensils, and medical waste should also be performed in accordance with routine procedures.
- Detailed information on environmental infection control in healthcare settings can be found in CDC's Guidelines for Environmental Infection Control in Health-Care Facilities and Guideline for Isolation Precautions: Preventing Transmission of Infectious Agents in Healthcare Settings [section IV.F. Care of the environment].

Appendix: Additional Information about Respirators and Facemasks

Information about Respirators:

A respirator is a personal protective device that is worn on the face, covers at least the nose and mouth, and is used to reduce the wearer's risk of inhaling hazardous airborne particles (including dust particles and infectious agents), gases, or vapors. Respirators are certified by the CDC/NIOSH, including those intended for use in healthcare.

Respirator use must be in the context of a complete respiratory protection program in accordance with OSHA Respiratory Protection standard (29 CFR 1910.134external icon). HCP should be medically cleared and fit-tested if using respirators with tight-fitting facepieces (e.g., a NIOSH-approved N95 respirator) and trained in the proper use of respirators, safe removal and disposal, and medical contraindications to respirator use.

NIOSH information about respirators

OSHA Respiratory Protection eToolexternal icon

Filtering Facepiece Respirators (FFR) including N95 Respirators

A commonly used respirator is a filtering facepiece respirator (commonly referred to as an N95). Filtering facepiece respirators are disposable half facepiece respirators that filter out particles.

To work properly, FFRs must be worn throughout the period of exposure and be specially fitted for each person who wears one (this is called "fit-testing" and is usually done in a workplace where respirators are used).

Three key factors for an N95 respirator to be effective: (https://www.cdc.gov/niosh/npptl/pdfs/KeyFactorsRequiedResp01042018-508.pdfpdf icon)

FFR users should also perform a user seal check to ensure proper fit each time an FFR is used.

For more information on how to perform a user seal check: https://www.cdc.gov/niosh/docs/2018-130/pdfs/2018-130.pdf?id=10.26616/NIOSHPUB2018130pdf icon

A list of NIOSH-approved N95 respirators is located here: https://www.cdc.gov/niosh/npptl/topics/respirators/disp_part/n95list1.html

Powered Air-Purifying Respirators (PAPRs)

Powered air-purifying respirators (PAPRs) have a battery-powered blower that pulls air through attached filters, canisters, or cartridges. They provide protection against gases, vapors, or particles, when equipped with the appropriate cartridge, canister, or filter.

Loose-fitting PAPRs do not require fit testing and can be used with facial hair.

A list of NIOSH-approved PAPRs is located on the NIOSH Certified Equipment List: https://www.cdc.gov/niosh/npptl/topics/respirators/cel/

Information about Facemasks:

If worn properly, a facemask helps block respiratory secretions produced by the wearer from contaminating other persons and surfaces (often called source control).

Facemasks are cleared by the U.S. Food and Drug Administration (FDA) for use as medical devices. Facemasks should be used once and then thrown away in the trash.

Clinical Presentation

There are a limited number of reports that describe the clinical presentation of patients with confirmed 2019-nCoV infection, and most are limited to hospitalized patients with pneumonia. The incubation period is estimated at ~5 days (95% confidence interval, 4 to 7 days). Frequently reported signs and symptoms include fever (83–98%), cough (76%–82%), and myalgia or fatigue (11–44%) at illness onset. Sore throat has also been reported in some patients early in the clinical course. Less commonly reported symptoms include sputum production, headache, hemoptysis, and diarrhea. The fever course among patients with 2019-nCoV infection is not fully understood; it may be prolonged and intermittent. Asymptomatic infection has been described in one child with confirmed 2019-nCoV infection and chest computed tomography (CT) abnormalities.

- Risk factors for severe illness are not yet clear, although older patients and those with chronic medical conditions may be at higher risk for severe illness. Nearly all reported cases have occurred in adults (median age 59 years). In one study of 425 patients with pneumonia and confirmed 2019-nCoV infection, 57% were male. Approximately one-third to one-half of reported patients had underlying medical comorbidities, including diabetes, hypertension, and cardiovascular disease.

Clinical Course

- Clinical presentation among reported cases of 2019-nCoV infection varies in severity from asymptomatic infection or mild illness to severe or fatal illness. Some reports suggest the potential for clinical deterioration during the second week of illness. In one report, among patients with confirmed 2019-nCoV infection and pneumonia, just over half of patients developed dyspnea a median of 8 days after illness onset (range: 5–13 days).
- Acute respiratory distress syndrome (ARDS) developed in 17–29% of hospitalized patients, and secondary infection developed in 10%. Between 23–32% of hospitalized patients with 2019-nCoV infection required intensive care for respiratory support. Some hospitalized patients have required advanced organ support with invasive mechanical ventilation (4–10%), and a small proportion have also required extracorporeal membrane oxygenation (ECMO, 3–5%). Other reported complications include acute cardiac injury (12%) and acute kidney injury (4–7%). Among hospitalized patients with pneumonia, the case fatality proportion has been reported as high as 11–15%. However, as this estimate includes only-hospitalized patients, and therefore is biased upward.

- **Diagnostic Testing**
- Currently, confirmation of 2019-nCoV infection is performed at CDC using the CDC real-time RT-PCR assay for 2019-nCoV on respiratory specimens (which can include nasopharyngeal or oropharyngeal aspirates or washes, nasopharyngeal or oropharyngeal swabs, broncheoalveolar lavage, tracheal aspirates, or sputum) and serum. Information on specimen collection, handling, and storage is available at: Real-Time RT-PCR Panel for Detection 2019-Novel Coronavirus. After initial confirmation of 2019-nCoV infection, additional testing of clinical specimens can help inform clinical management, including discharge planning.

Laboratory and Radiographic Findings

- The most common laboratory abnormalities reported among hospitalized patients with pneumonia on admission included leukopenia (9–25%), leukocytosis (24–30%), lymphopenia (63%), and elevated alanine aminotransferase and aspartate aminotransferase levels (37%). Most patients had normal serum levels of procalcitonin on admission. Chest CT images have shown bilateral involvement in most patients. Multiple areas of consolidation and ground glass opacities are typical findings reported to date.
- 2019-nCoV RNA has been detected from upper and lower respiratory tract specimens, and the virus has been isolated from bronchoalveolar lavage fluid. The duration of shedding of 2019-nCoV RNA in the upper and lower respiratory tracts is not yet known but may be several weeks or longer, which has been observed in cases of MERS-CoV or SARS-CoV infection.

- **Clinical Management and Treatment**
- No specific treatment for 2019-nCoV infection is currently available. Clinical management includes prompt implementation of recommended infection prevention and control measures and supportive management of complications, including advanced organ support if indicated. Corticosteroids should be avoided unless indicated for other reasons (for example, chronic obstructive pulmonary disease exacerbation or septic shock per Surviving Sepsis guidelinesexternal icon), because of the potential for prolonging viral replication as observed in MERS-CoV patients.

- atients with a mild clinical presentation may not initially require hospitalization. However, clinical signs and symptoms may worsen with progression to lower respiratory tract disease in the second week of illness; all patients should be monitored closely. Possible risk factors for progressing to severe illness may include, but are not limited to, older age, and underlying chronic medical conditions such as lung disease, cancer, heart failure, cerebrovascular disease, renal disease, liver disease, diabetes, immunocompromising conditions, and pregnancy.

- 13 patients used non-invasive ventilator mechanical ventilation for 4–22 days (median 9 days [IQR 7–19]). Four patients used an invasive ventilator to assist ventilation for 3–20 days (median 17 [12–19]). The ventilator adopted P-SIMV mode, the inhaled oxygen concentration was 35–100%, and the positive end-expiratory pressure was 6–12 cm H_2O. All four patients were still using ventilators at data cutoff. Moreover, nine (9%) patients received continuous blood purification due to renal failure and three (3%) patients were treated with extracorporeal membrane oxygenation (ECMO; table 2)