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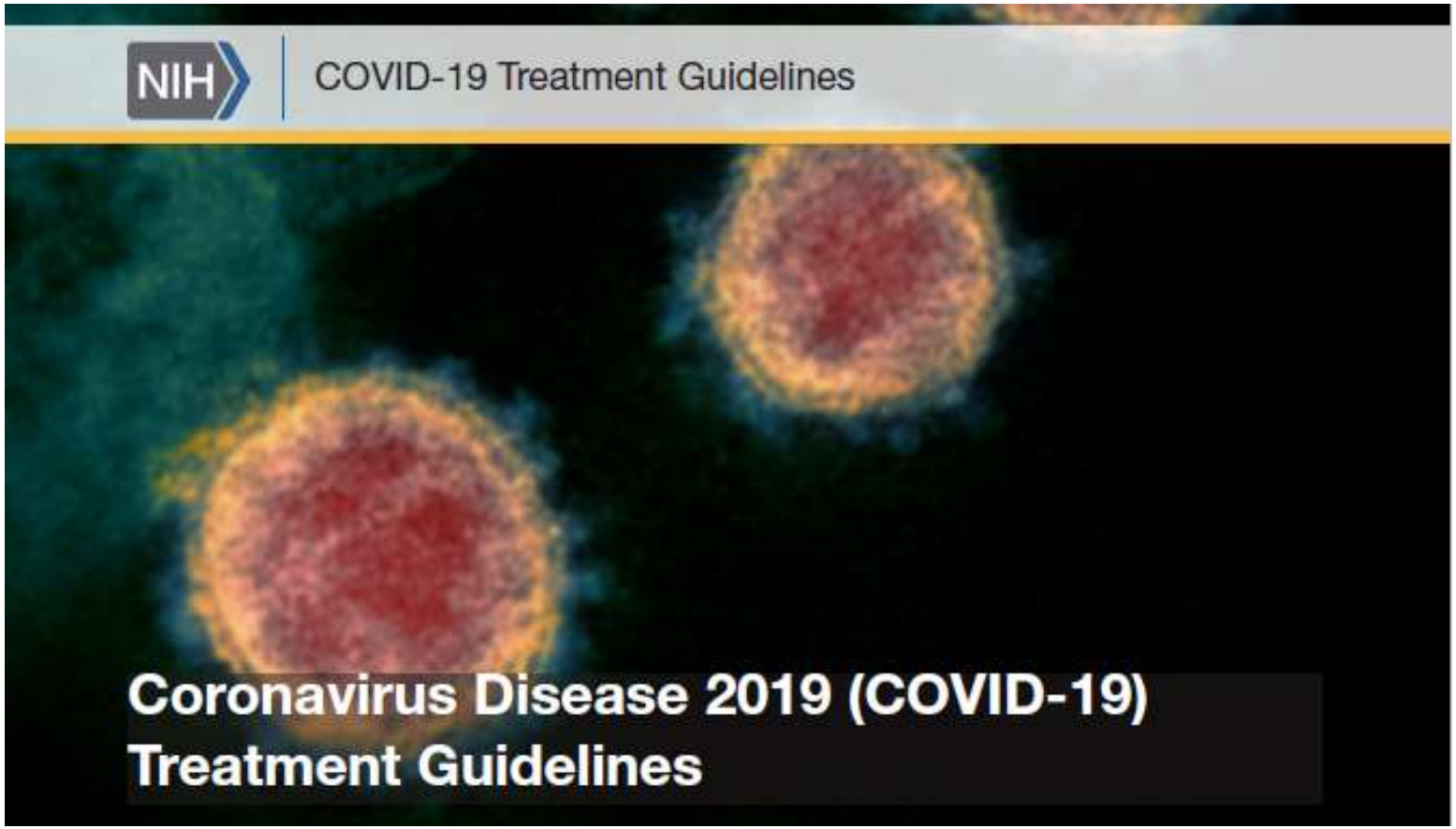
NIH
COVID-19 Treatment Guidelines
Coronavirus Disease 2019 (COVID-19)
Treatment Guidelines

چه دارویی در پیشگیری نقش دارد ؟

- هیدروکسی کلروکین
- رمدسیویر
- استروئید
- آزیترومایسین
- داکسی سایکلین
- فاویپراویر
- و .....

Last Updated: April 21, 2021

Summary Recommendations
• The COVID-19 Treatment Guidelines Panel (the Panel) **recommends against** the use of any drugs for SARS-CoV-2 pre-exposure prophylaxis (PrEP), except in a clinical trial **(AIII)**. • The Panel **recommends against** the use of **hydroxychloroquine** for SARS-CoV-2 post-exposure prophylaxis (PEP) **(AI)**. • The Panel **recommends against** the use of other drugs for SARS-CoV-2 PEP, except in a clinical trial **(AIII)**. • The Panel recommends that health care providers follow recommendations from the Advisory Committee on Immunization Practices when using SARS-CoV-2 vaccines **(AI)**.
Rating of Recommendations: A = Strong; B = Moderate; C = Optional **Rating of Evidence:** I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

خفیف یا شدید ؟

- دکتر ، دارم میمیرم یا برم خونه ؟

Clinical Spectrum of SARS-CoV-2 Infection

- **Asymptomatic or Presymptomatic Infection**: Individuals who test positive for SARS-CoV-2 using a virologic test (i.e., a nucleic acid amplification test [NAAT] or an antigen test) but who have no symptoms that are consistent with COVID-19.

Clinical Spectrum of SARS-CoV-2 Infection

- **Mild Illness**: Individuals who have any of the various signs and symptoms of COVID-19 (e.g., fever, cough, sore throat, malaise, headache, muscle pain, nausea, vomiting, diarrhea, loss of taste and smell) but who do not have shortness of breath, dyspnea, or abnormal chest imaging.

Clinical Spectrum of SARS-CoV-2 Infection

- **Moderate Illness:** Individuals who show **evidence of lower respiratory disease during clinical assessment or imaging** and who have an oxygen saturation (SpO2) .94% on room air at sea level.

Clinical Spectrum of SARS-CoV-2 Infection

- **Severe Illness:** Individuals who have SpO2 <94% on room air at sea level, a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (PaO2/FiO2) <300 mm Hg, respiratory frequency >30 breaths/min, or lung infiltrates >50%.

Clinical Spectrum of SARS-CoV-2 Infection

- **Critical Illness:** Individuals who have respiratory failure, septic shock, and/or multiple organ dysfunction.

نسخه سرپایی چی بنویسم؟

- چرک خشک کن ؟
- استروئید؟
- ویتامین؟
- سرم ؟

Outpatient Management of Acute COVID-19

Last Updated: April 21, 2021

Summary Recommendations

Managing Outpatients With COVID-19

- Outpatient management of acute COVID-19 should include providing supportive care, taking steps to reduce the risk of SARS-CoV-2 transmission (including isolating the patient), and advising patients on when to contact a health care provider and seek an in-person evaluation **(AIII)**.
- Patients with symptoms of COVID-19 should be triaged, when possible, via telehealth visits before receiving in-person care. Patients with dyspnea should be referred for an in-person evaluation by a health care provider and should be followed closely during the initial days after the onset of dyspnea to assess for worsening respiratory status **(AIII)**.
- Management plans should be based on a patient's vital signs, physical exam findings, risk factors for progression to severe illness, and the availability of health care resources **(AIII)**.

Specific Therapy for Outpatients With Mild to Moderate COVID-19

- The COVID-19 Treatment Guidelines Panel (the Panel) recommends using one of the following combination anti-SARS-CoV-2 monoclonal antibodies to treat outpatients with mild to moderate COVID-19 who are at high risk of clinical progression, as defined by the Emergency Use Authorization criteria (treatments are listed in alphabetical order):
  - **Bamlanivimab 700 mg plus etesevimab 1,400 mg (AIIa)**; *or*
  - **Casirivimab 1,200 mg plus imdevimab 1,200 mg (AIIa)**.

- The Panel **recommends against** the use of **chloroquine** or **hydroxychloroquine** with or without **azithromycin (AI)**. There are insufficient data for the Panel to recommend either for or against the use of other agents for the treatment of outpatients with COVID-19.
- The Panel **recommends against** the use of **dexamethasone** or **other systemic glucocorticoids** in outpatients in the absence of another indication **(AIII)**. There is currently a lack of safety and efficacy data on the use of these agents in outpatients with COVID-19, and systemic glucocorticoids may cause harm in these patients.
- The Panel **recommends against** the use of **antibacterial therapy** (e.g., **azithromycin**, **doxycycline**) in the absence of another indication **(AIII)**.
- Health care providers should provide information about ongoing clinical trials of investigational therapies to eligible outpatients with COVID-19 so they can make informed decisions about participating in clinical trials **(AIII)**.

Rating of Recommendations: A = Strong; B = Moderate; C = Optional

Rating of Evidence: I = One or more randomized trials without major limitations; IIa = Other randomized trials or subgroup analyses of randomized trials; IIb = Nonrandomized trials or observational cohort studies; III = Expert opinion

Care of Critically Ill Adult Patients With COVID-19

- For health care workers who are performing aerosol-generating procedures on patients with COVID-19, the COVID-19 Treatment Guidelines Panel (the Panel) recommends using an N95 respirator (or equivalent or higher-level respirator) rather than surgical masks, in addition to other personal protective equipment (PPE) (i.e., gloves, gown, and eye protection such as a face shield or safety goggles) (AIII).
- For health care workers who are providing usual care for nonventilated patients with COVID-19, the Panel recommends using an N95 respirator (or equivalent or higher-level respirator) or a surgical mask in addition to other PPE (i.e., gloves, gown, and eye protection such as a face shield or safety goggles) (AIIa).

Care of Critically Ill Adult Patients With COVID-19

- For the acute resuscitation of adults with COVID-19 and shock, the Panel recommends against the initial use of albumin for resuscitation (BIIa).
- The Panel recommends against using hydroxyethyl starches for intravascular volume replacement in patients with sepsis or septic shock (AIIa).

Care of Critically Ill Adult Patients With COVID-19

- The Panel recommends norepinephrine as the first-choice vasopressor (AIIa)
- • The Panel recommends against using low-dose dopamine for renal protection (BIIa).
- When norepinephrine is available, the Panel recommends against using dopamine for patients with COVID-19 and shock (AIIa).

Care of Critically Ill Adult Patients With COVID-19

- For adults with COVID-19 and acute hypoxemic respiratory failure despite conventional oxygen therapy, the Panel recommends high-flow nasal cannula (HFNC) oxygen over noninvasive positive pressure ventilation (NIPPV) (BIIa).
- The Panel recommends against using awake prone positioning as a rescue therapy for refractory hypoxemia to avoid intubation in patients who otherwise meet the indications for intubation and mechanical ventilation (AIII).

Interferons (Alfa, Beta)

- The COVID-19 Treatment Guidelines Panel recommends against the use of interferons for the treatment of patients with severe or critical COVID-19, except in a clinical trial (AIII).
- There are insufficient data to recommend either for or against the use of interferon beta for the treatment of early (i.e., <7 days from symptom onset) mild and moderate COVID-19.

Empiric Broad-Spectrum Antimicrobial Therapy

- In patients with COVID-19 and severe or critical illness, there are insufficient data to recommend empiric broad-spectrum antimicrobial therapy in the absence of another indication

- If antimicrobials are initiated, the Panel recommends that their use should be reassessed daily in order to minimize the adverse consequences of unnecessary antimicrobial therapy (AIII).

Empiric Broad-Spectrum Antimicrobial Therapy

- Some experts routinely administer broad-spectrum antibiotics as empiric therapy for bacterial pneumonia to all patients with COVID-19 and moderate or severe hypoxemia

- Other experts administer antibiotics only for specific situations, such as the presence of a lobar infiltrate on a chest X-ray, leukocytosis, an elevated serum lactate level, microbiologic data, or shock.

- There are no clinical trials that have evaluated the use of empiric antimicrobial agents in patients withCOVID-19 or other severe coronavirus infections.

Remdesivir

- Remdesivir is an intravenous nucleotide prodrug of an adenosine analog
- Remdesivir binds to the viral RNA-dependent RNA polymerase and inhibits viral replication through premature termination of RNA transcription
- Remdesivir is approved by the Food and Drug Administration (FDA) for the treatment of COVID-19 in hospitalized adult and pediatric patients (aged .12 years and weighing .40 kg).

Monitoring and Adverse Effects

- Remdesivir can cause gastrointestinal symptoms (e.g., nausea), elevated transaminase levels, an increase in prothrombin time (without a change in the international normalized ratio), and hypersensitivity reactions.
- Remdesivir may need to be discontinued if alanine transaminase (ALT) levels increase to >10 times the upper limit of normal and should be discontinued if an increase in ALT level and signs or symptoms of liver inflammation are observed

Monitoring and Adverse Effects

- Each 100 mg vial of remdesivir lyophilized powder contains 3 g of sulfobutylether beta-cyclodextrin sodium (SBECD), whereas each 100 mg/20 mL vial of remdesivir solution contains 6 g of SBECD
- SBECD is a vehicle that is primarily eliminated through the kidneys
- Accumulation of SBECD in patients with renal impairment may result in liver and renal toxicities.
- Remdesivir is not recommended for patients with an eGFR <30 mL/min

Not Hospitalized,
Mild to Moderate COVID-19

For patients who are not at high risk for disease progression, provide supportive care and symptomatic management **(AIII)**.

For patients who are at high risk of disease progression (as defined by the FDA EUA criteria for treatment with anti-SARS-CoV-2 monoclonal antibodies), use one of the following combinations:

- **Bamlanivimab plus etesevimab (AIIa)**
- **Casirivimab plus imdevimab (AIIa)**

Hospitalized but Does Not Require Supplemental Oxygen

There are insufficient data to recommend either for or against the routine use of remdesivir. For patients at high risk of disease progression, the use of remdesivir may be appropriate.

Hospitalized and Requires Supplemental Oxygen

Use one of the following options:

- **Remdesivir**[a,b] (e.g., for patients who require minimal supplemental oxygen) **(BIIa)**
- **Dexamethasone**[c] **plus remdesivir**[a,b] (e.g., for patients who require increasing amounts of supplemental oxygen) **(BIII)**[d,e]
- **Dexamethasone**[c] (e.g., when combination therapy with remdesivir cannot be used or is not available) **(BI)**

Hospitalized and Requires Oxygen Delivery Through a High-Flow Device or Noninvasive Ventilation

Use one of the following options:

- **Dexamethasone[c] (AI)[e]**
- **Dexamethasone[c] plus remdesivir[a,b] (BIII)[d,e]**

For patients who were recently hospitalized[f] with rapidly increasing oxygen needs and systemic inflammation:

- Add **tocilizumab[g]** to one of the two options above **(BIIa)**

Hospitalized and Requires Invasive Mechanical Ventilation or ECMO

- **Dexamethasone[c] (AI)[h]**

For patients who are within 24 hours of admission to the ICU:

- **Dexamethasone[c] plus tocilizumab[g] (BIIa)**

- If dexamethasone is not available, alternative glucocorticoids such as prednisone, methylprednisolone, or hydrocortisone can be used.
- For these drugs, the total daily dose equivalencies to dexamethasone 6 mg (oral or intravenous [IV]) are:
- Prednisone 40 mg
- Methylprednisolone 32 mg
- Hydrocortisone 160 mg

Ivermectin

- Ivermectin is not approved by the FDA for the treatment of any viral infection.

- There are insufficient data for the COVID-19 Treatment Guidelines Panel (the Panel) to recommend either for or against the use of ivermectin for the treatment of COVID-19.

Convalescent Plasma

- The COVID-19 Treatment Guidelines Panel recommends against the use of low-titer COVID-19 convalescent plasma for the treatment of COVID-19 (AIIb).
- The Panel recommends against the use of COVID-19 convalescent plasma for the treatment of COVID-19 in mechanically ventilated patients (AI).
- The Panel recommends against the use of high-titer COVID-19 convalescent plasma for the treatment of COVID-19 in hospitalized patients who do not require mechanical ventilation, except in a clinical trial (AI).

Convalescent Plasma

- Observational data including data from case reports, case series, and a retrospective case control study suggest a benefit of COVID-19 convalescent plasma in patients with various primary and secondary humoral immunodeficiencies
- Several case reports indicate that patients with impaired humoral immunity may experience persistent SARS-CoV-2 viral replication and therefore, may be at risk for developing viral resistance to SARS-CoV-2 antibodies after treatment with COVID-19 convalescent plasma

Fluvoxamine ?

- Anti-Inflammatory Effect of Fluvoxamine
- There are insufficient data for the COVID-19 Treatment Guidelines Panel to recommend either for or against the use of fluvoxamine for the treatment of COVID-19.
- Results from adequately powered, well-designed, and well-conducted clinical trials are needed to provide more specific, evidence-based guidance on the role of fluvoxamine for the treatment of COVID-19.

- ↓ severity

Colchicine

- There are insufficient data for the COVID-19 Treatment Guidelines Panel to recommend either for or against the use of colchicine for the treatment of nonhospitalized patients with COVID-19.
- A large, randomized trial in outpatients, the Colchicine Coronavirus SARS-CoV-2 Trial (COLCORONA), did not reach its primary efficacy endpoint of reducing hospitalizations and death
- a slight reduction in hospitalizations was observed in the subset of patients whose diagnosis was confirmed by a positive nasopharyngeal swab on a SARS-CoV-2 polymerase chain reaction (PCR) test.

Colchicine

- The Panel recommends against the use of colchicine in hospitalized patients for the treatment of COVID-19, except in a clinical trial (AIII).