Individualized treatment for COVID-19 patients should be based on three disease phases

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A new review details three distinct phases of COVID-19, the disease caused by the novel coronavirus SARS-CoV-2, and urges medical

professionals to consider an individualized treatment approach based on the disease phases and each patient's symptoms. The review is published ahead of print in *Physiological Reviews*.

SARS-CoV-2, the novel coronavirus that causes COVID-19, is transmitted through droplets expelled from an infected person's nose or mouth when they cough, sneeze or, in some cases, talk. Three distinct phases of COVID-19 infection have been observed in some people who test positive for the disease and have variable degrees of symptoms. Each phase is characterized by a different type of pathophysiological interaction with the virus.

During the early infection phase (Phase 1), the virus multiplies inside the body and is likely to cause mild symptoms that may be confused with a common cold or flu. The second phase is the pulmonary phase (Phase 2), when the immune system becomes strongly affected by infection and leads to primarily respiratory symptoms such as persistent cough, shortness of breath and low oxygen levels. Problems with blood clotting—especially with the formation of blood clots—may be predominant in Phase 2. The third, hyperinflammatory phase (Phase 3), occurs when a hyperactivated immune system may cause injury to the heart, kidneys and other organs. A "cytokine storm"—where the body attacks its own tissues—may occur in this phase. While there may be overlap among the three stages of disease, the review authors stress that it is crucial to recognize each stage in order to tailor treatment to the patient.

Many of the drugs used to treat people with COVID-19 are still being investigated for safety and effectiveness. The reviewers encourage researchers to evaluate these experimental treatments based on the specific disease phase they are being prescribed for, along with what is happening in the body as COVID-19 progresses. Drawing on experience treating patients in Italy, one of the hardest-hit countries during the

earliest days of the pandemic, the researchers suggest medical professionals choose a personalized treatment plan with the following medications and treatments:

- Plasma containing antibodies from recovered COVID-19 patients (i.e., hyperimmune plasma), which has been found to reduce the amount of live virus (viral load) in the early infection phase.
- Antiviral drugs, including remdesivir, which have helped interrupt viral replication in Phase 1 and may continue to be beneficial in Phase 2.
- Tissue plasminogen activator (tPA). A drug used to treat stroke, tPA breaks up blood clots that may occur during Phase 2.
- Inflammation-fighting medications, including corticosteroids, tocilizumab and sarilumab. These may help reduce system-wide inflammation in Phases 2 and 3.
- The anticoagulant (anti-clotting drug) heparin is important during any stage of the disease to prevent blood clots in blood vessels and capillaries (micro- and macro-vascular thrombosis).

Although to date, there are no drugs proven to treat COVID-19, research is progressing rapidly. "We are now entering a new era of the pandemic, with many ongoing [randomized controlled trials] aimed at identifying patient-tailored drugs, and drugs better suited to the specific phase of the disease with improved precision," the authors wrote. The scientific community is "making a tremendous effort to support an unprecedented number of pathophysiological studies and clinical trials to face this highly unexpected pandemic."

"SARS-CoV-2 and COVID-19: between pathophysiology complexity and therapeutic uncertainty" is published ahead of print in *Physiological Reviews*.

More information: Stefano Romagnoli et al. SARS-CoV-2 and

COVID-19: between pathophysiology complexity and therapeutic uncertainty, *Physiological Reviews* (2020). DOI: 10.1152/physrev.00020.2020