Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.
SARS-CoV-2 virus may cause COVID-19 disease, which causes mild-to-moderate disease in 80% of laboratory-confirmed cases which may be community-managed. A considerable age-dependent mortality is seen among elderly and other at-risk populations but among young and healthy individuals it is < 0.5%. Long-term health issues have been reported following severe COVID-19 requiring hospitalization as well as after cases of mild COVID-19 without hospitalization. Upon receiving COVID-19 suspected patients at hospitals, patients should be isolated and PPE should be worn by all health staff when in contact with the patients. Additionally, patients are tested for the presence of SARS-CoV-2 RNA by PCR, and blood samples are drawn. Imaging is not pivotal for the diagnosis, but chest X-ray is a relevant examination for all and is used to determine severity and treatment need Abnormal findings on CT scans are found in most patients, most frequently peripheral ground-glass opacity and bilateral patchy shadowing are present. Patients are, according to their needs and risks, treated with oxygen therapy, anticoagulation therapy, steroids, antivirals, or immunosuppressive drugs on special indications. Convalescent plasma therapy and monoclonal antibodies have a limited role in the treatment, mostly in severely immunocompromised patients. Patients with long-term sequelae should be evaluated in a post-COVID outpatient clinic. The most frequent reported symptoms include cognitive impairment, dyspnea, loss of smell and taste, and mental and physical fatigue although a wide spectrum of symptoms from other organ systems are also reported. The current treatment is based on symptom relief and rehabilitation as there is no documented specific medical treatment.
some studies up to 80%, present with no symptoms when tested but most develop symptoms during the course of the infection, yet up to 30% remain asymptomatic throughout the infection. Long term health issues has been reported following severe COVID-19 requiring hospitalization as well as mild COVID-19 without hospitalization. Long-term symptoms is estimated to occur in 2,5-14 % of people with a positive SARS-CoV-2 result.\(^\text{10,11}\)

### Receiving COVID-19 Suspected or Confirmed Patients

Patients with suspected COVID-19 include many groups of patients as COVID-19 may present with upper and lower respiratory symptoms but also with general symptoms. Distinct clusters of symptoms have been described: (1) respiratory (cough, sputum, sore throat, runny nose, ear pain, wheeze, and chest pain); (2) systemic (myalgia, joint pain and fatigue); (3) enteric (abdominal pain, vomiting and diarrhea).\(^\text{12}\) However, neither absence nor presence of any sign or symptom have been found accurate enough to rule in or rule out disease.\(^\text{13}\)

All COVID-19 suspected patients who are hospitalised should be isolated, and personal protective equipment should always be used by health care staff when in contact with the patients.\(^\text{14}\) In order to take into account, the heterogenic nature of clinical presentations, patients with only general symptoms of infection are handled similarly to patients who are admitted with respiratory symptoms.

### Diagnosis

Testing for the presence of SARS-CoV-2 RNA is required to confirm the preliminary diagnosis.\(^\text{15}\) Test samples are taken from upper or lower airways depending on if a patient shows symptoms involving upper airways, lower airways, or both. From the upper airways, an oro- or nasopharynx swap is made, and from the lower airways, tracheal suction or bronchoalveolar lavage (BAL) is performed. Sampling from the upper respiratory tract requires use of type 2 surgical mask as well as gloves, overcoat and eye protection. Lower airway sampling requires use of FFP2 / FFP3 mask. The diagnosis only requires one positive PCR result for SARS-CoV-2. A negative test result will terminate the isolation unless suspicion remains based on the patient’s history, the clinical presentation, blood tests or imaging results. This will lead to new PCR tests as well as broader diagnostic examinations such as sputum for culture, atypical pneumonia and influenza testing. A positive SARS-CoV-2 IgG antibody test is consistent with a previous COVID-19 infection. However, a negative antibody test does not exclude a previous infection, nor does it give any information to whether a patient is protected against a new infection or is infectious.\(^\text{15}\) SARS-CoV-2 serology is not therefore used in the acute COVID-19 diagnostics.

Biochemistry should involve hematology including a differential count, inflammation markers such as CRP, procalcitonin and suPAR, renal markers creatinine and eGFR as well as hepatic enzymes with lactate dehydrogenase (LDH) and alanine aminotransferase (ALT). Plasma glucose and HbA1c are measured in all inpatients with COVID-19, and plasma glucose is monitored during dexamethasone treatment. Arterial puncture analysis should be done if there is respiratory distress. Fibrin d-dimer, coronary markers such as Troponin-I and ferritin may be considered in COVID-19 patients due to the risk of cardiovascular events and hyperinflammation. These markers have all been associated with disease progression, severity and outcome.\(^\text{16,17}\)

Imaging is not pivotal for the diagnosis, but chest X-ray is a relevant examination for all and is used to determine severity and treatment need. Chest X-rays may be normal, but are often seen with bilateral peripheral interstitial infiltrates. Chest Computerized Tomography (CT) images are not routinely used, but has been used to aid the diagnostic process and determine the need for continued isolation early on in the pandemic when test assays were less sensitive. Manifestations are similar to what is seen in other viral pneumonias and not specific for COVID-19 disease, hence the diagnostic value of chest CT imaging for COVID-19 is low and variable with radiographic interpretation but abnormal findings on CT scans are revealed in more than 80% of hospitalised patients.\(^\text{19}\) Another study found that 56% of patients presenting within two days of diagnosis had a normal CT.\(^\text{20}\) Frequent manifestations are peripheral ground-glass opacity and bilateral patchy shadowing each found in more than 50% of hospitalised patients.\(^\text{19}\) Consolidation is typically seen later in the process.

### Treatment

**Oxygen and fluid therapy.** The main area of focus within treatment options is to maintain an Respiratory Frequency (RF) of <24/min, a SAT\(_2\) above 94%, and/or a pO\(_2\) above 8,5kPa. If the patient fails to keep these levels, oxygen therapy is initiated and is scaled up according to the severity of the respiratory hypoxia. Target levels may vary in patients with comorbidities such as COPD where the habitual SAT\(_2\) can be lower than otherwise healthy subjects. A restrictive approach is taken with regard to fluid therapy unless the patient presents with signs of hypoperfusion or shock.\(^\text{21}\)

**Antibiotics** should not be administered routinely to patients with COVID-19 where early co-infection is rare.\(^\text{22}\) In case of reasonable suspicion of bacterial infection and need for intravenous treatment, a broad spectrum antibiotics such i.v. Piperacillin / Tazobactam may be initiated or treatment according to microbiological test results.

**Anticoagulation therapy.** A known and serious condition caused by COVID-19 is a hyperinflammatory response which gives a significantly increased risk of thrombosis in the large vessels (DVT, pulmonary embolism) and in smaller vessels as part of the disease.\(^\text{23}\) The pathogenesis for COVID-19-associated hypercoagulability is not clear, but hypothesized to
involve hypoxia and systemic inflammation secondary to COVID-19 which may lead to high levels of inflammatory cytokines and activation of the coagulation pathway. In order to combat this, patients at-risk should have administered Heparin as thromboprophylaxis. In patients where COVID-19 is the primary cause of hospitalization, a daily dosage of Fragmin 5000 ie x 1 should be given, dose reductions apply in case of renal impairment. In intensive care COVID-19 patients, a higher dosage (twice daily) should be given. Active bleeding and a platelet count <30 × 10^9/L are contraindications of heparin treatment.

Steroid treatment. Dexamethasone should be administered to patients with confirmed COVID-19 pneumonia and in need of oxygen therapy due to hypoxia (SATO2 < 94%) without oxygen therapy or lung infiltration on x-ray and in need of oxygen therapy or patients in need of mechanical ventilation or extracorporeal membrane oxygenation (ECMO). Dexamethasone has been shown to reduce mortality among patients in need of oxygen therapy. No effect has been shown in patients without need of oxygen therapy. Daily dosages are 6 mg Dexamethasone orally or 8mg Dexavit intravenously in up to 10 days. Pregnant women can as a substitute receive 40 mg Prednisolon a day, 50mg Hydrocortison three times a day or 100mg two times a day. As steroids can promote a reduction in bone density, 400 mg calcium is given with 19 µg vitamin D as supplements two times a day. If steroids are used for more than five days, the supplements are continued for eight weeks unless there are contraindications. Plasma glucose is continually monitored during this treatment.

Antiviral treatment is indicated for patients >12 years old with a COVID-19 pneumonia in need of oxygen therapy but not mechanically ventilated (SATO2 < 94% without oxygen therapy or subjective need of oxygen therapy and lung infiltrations). The viral RNA-dependent RNA-polymerase inhibitor, Remdesivir, has been shown to reduce recovery time as well as mortality in this group of patients within the first 14 days of treatment. The reduced mortality was only found in a subgroup of patients with COVID-19 pneumonia and in need of oxygen therapy, but without the need for invasive mechanical ventilation, within 14 days of starting treatment. No significant effect of Remdesivir has been found in patients without the need for oxygen supplementation, and no effect when initiated in patients already on a ventilator / ECMO. Results from the WHO’s SOLIDARITY study found no effect of Remdesivir on risk of death, and WHO does not recommend Remdesivir as part of standard treatment. The optimal duration of treatment in the patient group that has been shown to have an effect of the treatment in the ACTT-1 study is not clear from the currently available data. If a Remdesivir regimen has been initiated before a patient is moved to the Intensive Care Unit (ICU), it should be continued as planned unless signs of side effects occur (eg, increasing kreatinin or plasma alanin aminotransferase (ALAT)). As for immunocompromised patients, data of Remdesivir treatment is lacking. However, based on expert opinion, these patients may draw the biggest benefits of antiviral treatment. Due to the risk of a rapid and fatal outcome, it may be preferable to give Remdesivir as soon as an immunocompromised patient is tested positive for SARS-CoV-2 instead of waiting for the otherwise needed clinical signs before initiating treatment.

Contraindications include an eGFR of <30 mL/minute or dialysis, ALAT > 5 times the upper limit of normal levels, hypersensitivity to Remdesivir, multi organ failure, usage of >1 vasopressor drugs, and pregnancy and breast feeding due to lack of data in this area.

Intravenous dosages of Remdesivir is 200 mg the first 24 hours followed by 100 mg daily for another four days. The regimen can be extended another five to ten days for patients with significant Immunosuppression. If patients are discharged before the first five days, treatment is discontinued.

Immunosuppressive drugs. Randomized studies of the interleukin-6 (IL-6) antagonist Tocilizumab for the treatment of COVID-19 have not shown completely unambiguous results. Some RCTs, including COVACTA, showed no difference in mortality on day 28, but several of the studies have shown beneficial effects in terms of reduced risk of progression to need for intensive therapy or death. The pragmatic platform studies: REMAP-CAP and RECOVERY included patients who had recently developed a need for intensive therapy, and patients with hyperinflammation and clinical worsening despite treatment with steroids. These studies found slightly lower mortality when treated with IL-6 antagonist (REMAP-CAP, hospitalization mortality: 27% vs 36%; RECOVERY, 28-day mortality: 31% vs 35%).

Tocilizumab treatment may be considered in patients with confirmed SARS-CoV-2 infection, age >18 years, immunocompetent, currently in steroid treatment for COVID-19, need of oxygen supply ≥10 L/min in order to keep SatO2 > 92%, CRP >75mg/L, decline in clinical status despite 2 days of steroid or a rapid rise in oxygen demand or initiation of intensive therapy (vasopressor, mechanical ventilation or highflow >FiO2 40% and flow >30l/min) <1 day after admission to the hospital.

Relative contraindications are an immune defect, diverticulosis, liver disease or ALAT/ASAT >1,5 times the normal upper level. Absolute contraindications are pregnancy, breast feeding, diverticulitis, ALAT/ASAT above 5 times the upper limit of the normal level, thrombocytes < 50 × 10^9/L or neutrophiles < 2 × 10^9/L. Dosages vary according to body weight as 8 mg are given per kilo (up to 800mg) once. Tocilizumab masks super-infections (lack of fever, lack of CRP increase). For patients treated with Tocilizumab, frequent screening should be considered, and a low threshold for microbiological diagnostics applies. Hence, always use procalcitonin instead of CRP, and uphold a low threshold for broad antibiotic treatment. Patients treated with IL-6 antagonist should be offered clinical monitoring as well as control of hematology and liver function.

Other antiviral and anti-inflammatory treatment. There is no evidence to recommend other antiviral or anti-inflammatory therapy. Hydroxychloroquine (+/- Azithromycin) and Lopinavir and/or Ritonavir are not recommended for treatment with COVID-19.
**Other antiviral and anti-inflammatory treatment**

Baricitinib may reduce the time to clinical improvement by 1 day in patients receiving Remdesivir, but as Remdesivir-treated patients will also receive other immunosuppressive therapy with a proven effect on mortality (dexamethasone), there is not yet sufficient evidence to recommend Baricitinib.

Interleukin-1 inhibitor, Anakinra, is used only under controlled conditions.

Human granulocyte colony stimulating factor has so far not been shown to be effective and is used only under protocol conditions. Convalescent plasma therapy may reduce the risk of serious COVID-19 pneumonia if given early. Yet, there is no certain effect of giving this treatment among patients already hospitalised with COVID-19. Should primarily be used under protocol conditions. Convalescent plasma may be considered in special situations in patients with severe immune deficiency, and may have a place in hospital outbreaks with a known time of infection among patients with risk factors for severe COVID-19 course.

Monoclonal antibodies (mAb) to Spike protein. For 7-10 days after the onset of COVID-19 symptoms, there is active viral replication. The amount of virus is higher in people who develop severe or critical illness. In few severely immunocompromised patients, especially haematological patients with B-cell defect due to the underlying disease or treatment with anti-CD20 antibody, active viral replication can be detected weeks to months after symptom onset. The same patient population has an increased risk of severe COVID-19. Randomized studies have shown that mAb given to outpatients early in the course of the disease can reduce the relative risk of hospitalization or death by approximately 70%. Among immunocompetent individuals, there is no effect if treatment is started only when patients have developed hypoxia and need hospitalization. For severely immunocompromised patients, it is unknown whether treatment is effective among inpatients with COVID-19, as no data from randomized trials are available. There is currently limited access to mAb, and mAb has only preliminary approval in EMA in the form of REGN-COV2 (casirivimab and imdevimab).

Criteria for treatment are: Confirmed SARS-CoV-2 infection by reverse transcription-polymerase chain reaction (RT-PCR) examination of airway sample within 7 days; age ≥ 12 years; possibility of starting treatment within 10 days after the first sign of COVID-19 (symptom onset or positive PCR; high-risk patient with haematological malignancy and B-cell defect (primarily lymphoma, CLL, multiple myeloma or treatment with B-cell depleting antibodies within 6 months) or hematological malignancy and recent treatment with high-dose chemotherapy or bone marrow transplantation within 2 years or immunosuppressive treatment for graft-versus-host disease or solid organ transplantation. Vaccinated patients without severe immunosuppression by vaccination should have controlled serology before mAb treatment, and in case of positive serology no mAb should be given. Duration of action is at least 1 month and treatment should not be repeated within this period. There is most often an indication for concomitant treatment with Remdesivir for optimal antiviral treatment.

**Discharge**

Isolation can be discontinued 48 hours after symptoms have ended or 10 days after debut of symptoms and 48 hours without a fever. Patients after a severe case of COVID-19 should be evaluated individually in regard to the duration of isolation. Immunosuppressed individuals, in particular patients with impaired B-cell function, may excrete contagious virus for a prolonged time period, hence ceasing isolation may require expert consultation. Patients can be discharged with or without isolation after recovery of acute symptoms.

**Patients With Post Infectious Long-Term COVID-19 Sequelae**

There is no internationally agreed definition of long-term COVID-19 (LTC). Currently COVID-19 signs or symptoms for more than 4 weeks is considered ongoing COVID-19, and signs and symptoms for more than 12 weeks is considered LTC. The most frequent reported symptoms include cognitive impairment, dyspnea, loss of smell and taste, and mental and physical fatigue. Life quality is affected, and patients suffering from LTC experience problems performing daily activities and work.

**Nervous System**

Early reports describe possible involvement of the central nervous system. However SARS-CoV-2 encephalitis has only been reported in few and stroke does not seem to be more common long after COVID-19. Advanced imaging indicates structural changes in the brain relating to specific symptoms. Currently, standard neurological evaluation is recommended when signs and symptoms raise the suspicion of CNS complication or other concomitant disease. MRI or CT of the brain may be needed. Neurophysiological examination has shown signs of myopathy in 11 of 20 consecutively referred patients from a Post COVID-19 Clinic which may explain physical fatigue and muscle aches. As no standard treatment is available for the myopathy clinical suspicion should not necessarily lead to advances investigations in cases where symptoms are improving (expert opinion).

**Cognitive Complaints**

More than 60% of hospitalized patients may experience cognitive problems 3-4 months after hospitalization. Executive functions and verbal learning are some of the areas affected.
It is recommended to use a validated screening tool to evaluate cognitive impairment\(^{14}\) but a specific screening tool for COVID-19 has not been developed.

**Psychiatric Symptoms**

Anxiety and depression are more common in the society overall\(^6\) but also more common in patients who had COVID-19. It has not been established to which extend psychological stress follows the mental and physical long-term effects of COVID-19\(^9,17\). Attention should be on signs of anxiety, depression or stress when caring for patients with LTC.

**Smell and Taste**

Smell and taste are affected in more than 10% of SARS-CoV-2 positive patients 6 months after infection.\(^9\) Smell- and taste impairment may improve by using smell- and taste training\(^76\) and in case of lack of improvement the patients should be offered an evaluation by an ear-nose-throat specialist to rule out other pathology and for guidance.

**Cardiopulmonary Symptoms**

Dyspnoe more than 6 months after COVID-19 has been reported in more than 25% of patients hospitalized due to COVID-19\(^8\) and an increased risk was also found in non-hospitalized patients.\(^10\) Only few develop chronic structural pulmonary manifestations like fibrosis – primarily among patients hospitalized in the acute phase of the disease.\(^67,77\)

Standard evaluation (spirometry, ecg and chest X-ray) is recommended. Physical tests (like 6 min walk test) may aid the evaluation of patients. Diffusion capacity (DLCO), reversibility test, and pulmonary CT scan may be considered but are not recommended as standard investigation for all patients with LTC. Besides dyspnea, tachycardia heart failure and chest pain was also reported to be more common following COVID-19.\(^69\) The contribution of previous peri- or myocarditis to the long term symptoms has not been established.\(^78\) Currently arrhythmia, angina and heart failure should be evaluated according to standard referral criteria.

**General Considerations**

Post-infectious autoimmune manifestations have been reported,\(^79,80\) and attention should be drawn not to overlook these well-known post viral manifestations in patients who present multiple symptoms. Patients with fatigue, neurologically manifestations or dyspnea are recommended biochemical evaluation which may include organ markers (proBNP, liver counts, kidney markers), inflammatory markers, hematology, B12 and folate, thyroid hormones and diabetes screening.

There is no documented specific medication for treating LTC and current treatment is based on symptom relief and rehabilitation. Patientes are observed for improvement during physical rehabilitation and are advised about mental fatigue. Cognitive therapy guidance concerning mental fatigue and physical rehabilitation is effective in rehabilitation of patients with long-term symptoms following other infectious diseases and seems to be of great importance in patients with LTC (expert opinion). Patients’ guidelines on rehabilitation after COVID-19 have been developed.\(^81\)

A multidisciplinary approach is recommended for patients with multiple symptoms following COVID-19.\(^63,64\) It is important that the clinical evaluation is accompanied by registration, evaluation and research in order hopefully to develop an effective treatment strategy. Outpatient clinics with large numbers of patients suffering long-term symptoms are reported from multiple sites.\(^82\)

In summary long-term COVID-19 is a debilitating disease and as numbers of patients with a previous positive SARS-CoV-2 test are still increasing, the human and economical costs are rising. Health politicians should be aware of this planning further preventive measures for COVID-19.

**References**

1. Weekly Epidemiological Update on COVID-19. Switzerland: WHO Geneva, 2021
2. Chen N, Zhou M, Dong X, et al: Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. Lancet 395:507-513, 2020
3. Guan W-J, Ni Z-Y, Hu, Y, et al: Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med: 1-13, 2020
4. World Health Organization. Report of the WHO-China Joint Mission on Coronavirus Disease 2019 (COVID-19). Switzerland: WHO Geneva, 2020
5. Wu Z, McGoogan JM. Characteristics of and important lessons from the Coronavirus Disease 2019 (COVID-19) outbreak in China. JAMA 323:1239-1242, 2020
6. Relev M, Kristensen KB, Portegård A, et al: Characteristics and predictors of hospitalization and death in the first 11 122 cases with a positive RT-PCR test for SARS-CoV-2 in Denmark: a nationwide cohort. Int J Epidemiol 49:1468-1481, 2020
7. Simonsen L, Ørskov S, Pedersen RK, Andreasen V: Beregning af Worst_Case_Scenario for COVID-19 i Danmark. Roskilde University, Denmark: Roskilde University, 2021. https://ruc.forsk.dk/wsportalfiles/portal/76207998/Worst_Case_Covid_19_Final.pdf. Accessed May 30, 2021.
8. Alene M, Yismaw L, Assemie MA, et al: Magnitude of asymptomatic COVID-19 cases throughout the course of infection: A systematic review and meta-analysis. PLoS One 16:e0249090, 2020
9. Huang C, Huang L, Wang Y, et al: 6-month consequences of COVID-19 in patients discharged from hospital: a cohort study. Lancet 397:220-232, 2021
10. Havervall S, Rosell A, Phillipson M, et al: Symptoms and functional impairment assessed 8 months after mild COVID-19 among health care workers. JAMA 325:2015-2016, 2021
11. Sudre CH, Murray B, Varsavsky T, et al: Attributes and predictors of long COVID. Nat Med 27:626-631, 2021
12. Docherty AB, Harrison EM, Green CA, et al: Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO clinical characterisation protocol: Prospective observational cohort study. BMJ 369: m1985, 2020
13. Struyf T, Deeks JJ, Dinnes J, et al: Signs and symptoms to determine if a patient presenting in primary care or hospital outpatient settings has COVID-19. Cochrane Database Syst Rev 2:1-52, 2021. Feb 23CD013665
14. Baker TL, Greiner JV, Maxwell-Schmidt E, et al: Guidelines for Frontline Health Care Staff Safety for COVID-19. J Prim Care Community Health 13, 2020. Jan-Dec, 1.501.3272.0938.0546
15. Sethuraman N, Jeremiah SS, Ryo A: Interpreting diagnostic tests for SARS-CoV-2. JAMA 323:2249-2251, 2020
16. Danwang C, Endomba FT, Nkeck JR, et al: A meta-analysis of potential biomarkers associated with severity of coronavirus disease 2019 (COVID-19). Biomark Res 8:37, 2020
17. Stauning MA, Altintas I, Kallemose T, et al: Soluble urokinase plasminogen activator receptor as a decision marker for early discharge of patients with COVID-19 symptoms in the emergency department. J Emerg Med 2021. https://doi.org/10.1016/j.jemermed.2021.03.012
18. Bai BX, Hsieh B, Xiong Z, et al: Performance of radiologists in differentiating COVID-19 from viral pneumonia on chest CT. Radiology 296: E46-E54, 2020
19. Guan WJ, Ni ZY, Hu Y, et al: Clinical characteristics of coronavirus disease 2019 in China. N Engl J Med 382:1708-1720, 2020
20. Berheim A, Mei X, Huang M, et al: Chest CT findings in Coronavirus Disease-19 (COVID-19): Relationship to duration of infection. Radiology 295:685-691, 2020
21. World Health Organization (WHO): COVID-19 Clinical management: Living Guidance; 2021. https://www.who.int/publications-detail-redirect/WHO-2019-nCoV-clinical-2021-1. Accessed May 30, 2021
22. Langford BJ, So M, Raybardhan S, et al: Bacterial co-infection and secondary infection in patients with COVID-19: a living rapid review and meta-analysis. Clin Microbiol Infect 26:1622-1629, 2020. Dec
23. Helms J, Tacquird C, Severa F, et al: High risk of thrombosis in patients with severe SARS-CoV-2 infection: A multicenter prospective cohort study. Intensive Care Med 46:1089-1094, 2020
24. Merad M, Martin JC: Pathological inflammation in patients with COVID-19: A key role for monocytes and macrophages. Nat Rev Immunol 20:355-362, 2020
25. Interim clinical guidance for management of patients with Confirmed Coronavirus Disease (COVID-19). Center of Disease Control, Atlanta USA: 2021. https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinical-guidance-management-patients.html. Accessed May 20, 2021
26. World Health Organization (WHO): Corticosteroids for COVID-19. Living Guidance. WHO, Geneva, Switzerland: 2020. https://www.who.int/publications-detail/WHO-2019-nCoV-Corticosteroids-2020-1. Accessed May 30, 2021
27. RECOVERY Collaborative Group, Horby P, Lim WS, et al: Dexamethasone in hospitalized patients with severe Covid-19 pneumonia. N Engl J Med 22:1503-1516, 2020. April 384
28. REMAP-CAP Investigators, Gordon AC, Mouncey PR, et al: Interleukin-6 receptor antagonists in critically ill patients with Covid-19. N Engl J Med 384:1491-1502, 2021. April 22. April
29. RECOVERY Collaborative Group: Tocilizumab in patients admitted to hospital with COVID-19 (RECOVERY). A randomised, controlled, open-label, platform trial. Lancet 397:1637-1645, 2021
30. Cavalcanti AB, Zampieri FG, Rosa RG, et al: Hydroxychloroquine with or without azithromycin in mild-to-moderate Covid-19. N Engl J Med 383:2041-2052, 2020
31. Tang W, Cao Z, Han M, et al: Hydroxychloroquine in patients with mainly mild to moderate coronavirus disease 2019: Open label, randomised controlled trial. BMJ 369:m1849, 2020
32. Furtado RH, Berwanger O, Fonseca HA, et al: Azithromycin in addition to standard of care versus standard of care alone in the treatment of patients admitted to the hospital for severe COVID-19 in Brazil (COALITION II): A randomised controlled trial. Lancet 396:950-967, 2020
33. RECOVERI Collaborative Group, Horby P, Matham M, et al: Effect of hydroxychloroquine in hospitalized patients with Covid-19. N Engl J Med 383:2030-2040, 2020
34. Cao B, Wang Y, Wen D, et al: A trial of lopinavir-ritonavir in adults hospitalized with severe Covid-19. N Engl J Med 382:1787-1799, 2020
35. Kalil AC, Patterson TF, Mehta AK, et al: Baricitinib plus remdesivir for hospitalized adults with Covid-19. N Engl J Med 384:795-807, 2020. April 6
36. Cheng L-L, Guan W-J, Duan C-Y, et al: m. Effect of recombinant human granulocyte colony-stimulating factor for patients with coronavirus disease 2019 (COVID-19) and lymphopenia: A randomised clinical trial. JAMA Intern Med 181:71-78, 2021
37. Agarwal A, Mukherjee A, Kumar G, et al: Convalescent plasma in the management of moderate covid-19 in adults in India: Open label phase II multicentre randomised controlled trial (PLACID Trial). BMJ 371: m232, 2020
38. Rerlich FJ, Tomashke KM, Dodd LE, et al: ACTT-1 study group members: remdesivir for the treatment of Covid-19 - Final report. N Engl J Med 383:1813-1826, 2020
39. REMAP-CAP Investigators, Gordon AC, Mouncey PR, et al: Interleukin-6 receptor antagonists in critically ill patients with Covid-19. N Engl J Med 384:1491-1502, 2021. April 22. April
40. Fajnzylber J, Regan J, Coxen K, et al: SARS-CoV-2 viral load is associated with increased disease severity and mortality. Nat Commun 11:5493, 2020
57. Aydillo T, Gonzalez-Reiche AS, Aslam S, et al: Shedding of Viable SARS-CoV-2 after immunosuppressive therapy for cancer. N Engl J Med 383:2586-2588, 2020
58. Thakkar A, Pradhan K, Jindal S, et al: Patterns of seroconversion for SARS-CoV-2 IgG in patients with malignant disease and association with anticancer therapy. Nat Cancer 2:392-399, 2021
59. Phase 3 Treatment Trial in Recently Infected Asymptomatic Patients Showed REGEN-COVTM (casirivimab with imdevimab) Significantly Reduced Progression to Symptomatic COVID-19 | Regeneron Pharmaceuticals Inc. Regeneron Pharmaceuticals, New York, USA: 2021. https://investor.regeneron.com/index.php/news-releases/news-release-details/phase-3-treatment-trial-recently-infected-asymptomatic-patients/. Accessed May 30, 2021
60. Phase 3 Trial Shows REGEN-COVTM (casirivimab with imdevimab) Antibody Cocktail Reduced Hospitalization or Death by 70% in Non-hospitalized COVID-19 Patients | Regeneron Pharmaceuticals Inc. 2021. https://investor.regeneron.com/news-releases/news-release-details/phase-3-trial-shows-regen-covtm-casirivimab-imdevimab-antibody/. Accessed May 29, 2021
61. CASIRIVIMAB WITH IMDEVIMAB ANTIBODY COCKTAIL FOR COVID-19 PREVENTION: INTERIM RESULTS [Internet]. CROI Conference. 2021. https://www.croiconference.org/abstract/casirivimab-with-imdevimab-antibody-cocktail-for-covid-19-prevention-interim-results/. Accessed May 22, 2021
62. Helleberg M, Niemann CU, Moestrup KS, et al: Persistent COVID-19 in an immunocompromised patient temporarily responsive to two courses of remdesivir therapy. J Infect Dis 222:1103-1107, 2020
63. Senfølger efter COVID-19, Sundhedsstyrelsen 2021, https://www.sst.dk/da/Udgivelser/2020/Senfoelger-efter-COVID-19. Accessed May 22, 2021
64. COVID-19 Rapid Guideline: Managing the Long-Term Effects of COVID-19. National Institute for Health and Care Excellence. NICE, London, UK: 2021. https://www.nice.org.uk/guidance/ng188. Accessed May 25, 2021
65. Svan M, Taylor S. NICE guideline on long covid. Research must be done urgently to fill the many gaps in this new ‘living guideline. BMJ 371:m4938, 2020
66. Leth S, Gunst JD, Mathiasen V, et al: Persistent symptoms in patients recovering from COVID-19 in Denmark. Open Forum Infect Dis 8:ofab042, 2021
67. Johansen S, Sattler SM, Miskowiak KW, et al: Descriptive analysis of long COVID sequelae identified in a multidisciplinary clinic serving hospitalised and non-hospitalised patients. ERJ Open Res 2021. https://doi.org/10.1183/23120541.00205-2021
68. Ellul MA, Benjamin L, Singh B, et al: Neurological associations of COVID-19. Lancet Neurol 19:767-783, 2020
69. Al-Aly Z, Xie Y, Bowe B: High-dimensional characterization of post-acute sequelae of COVID-19. Nature 594:259-264, 2021
70. Greijd P, Campoon JF, Dudoet P, et al: F-FDG brain PET hypometabolism in patients with long COVID. Eur J Nucl Med Mol Imaging: 1-11, 2021
71. Lu Y, Li X, Geng D, et al: Cerebral micro-structural changes in COVID-19 patients – An MRI-based 3-month follow-up study. EClinicalMedicine 25:100484, 2020
72. Agergaard J, Leth S, Pedersen TH, et al: Myopathies in patients with long-term fatigue after COVID-19. Cln Neuropsychopharmacol 46:39-48, 2021
73. Miskowiak KW, Johansen S, Sattler S, et al: Cognitive impairments four months after COVID-19 hospital discharge: Pattern, severity and association with illness variables. Eur Neuropsychopharmacol 46:39-48, 2021
74. Taquet M, Luciano S, Geddes JR, et al: Bidirectional associations between COVID-19 and psychiatric disorder: Retrospective cohort studies of 62 354 COVID-19 cases in the USA. Lancet Psychiatry 8:130-140, 2021
75. Taquet M, Geddes JR, Husain M: 6-month neurological and psychiatric outcomes in 236 379 survivors of COVID-19: A retrospective cohort study using electronic health records. Lancet Psychiatry 8:416-427, 2021
76. Alfred B Addison AB, Wong B, Ahmed T, et al: Clinical Olfactory Working Group consensus statement on the treatment of postinfectious olfactory dysfunction. J Allergy Clin Immunol 147:1704-1719, 2021
77. Dorst B, Peters J, Brink M, et al: Comprehensive health assessment three months after recovery from acute COVID-19. Cln Infect Dis 2020. Nov; ciaa1750
78. Puntmann VO, Carerj ML, Wieters I, et al: Outcomes of cardiovascular magnetic resonance imaging in patients recently recovered from Coronavirus Disease 2019 (COVID-19). JAMA Cardiol 2020
79. Restivo DA, Centonze D, Alesina A, et al: Myasthenia gravis associated with SARS-CoV-2 infection. Ann Intern Med 173:1027-1028, 2020
80. Dworakowska D, Grossman AB: Thyroid disease in the time of COVID-19. Endocrine 68:471, 2020
81. Support for Rehabilitation: Self-Management after COVID-19 Related Illness. Geneva, Switzerland: World health Organisation, 2020. https://www.who.int/publications/m/item/support-for-rehabilitation-self-management-after-covid-19-related-illness
82. CDC guidelines coming along 2021. https://www.medscape.com/view-article/950159. Accessed May 28, 2021