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.

extra toxicity of this regimen might prevent its implementation, particularly in earlier lines of therapy. Unlike many patients with solid tumours who are receiving combination immune checkpoint regimens, patients with relapsed or refectory Hodgkin lymphoma have a number of other treatment options, including curative ones. First, anti-PD-1 therapy (alone or in combination with brentuximab vedotin) offers long-term remission (and a potential cure in some patients), with low toxicity. Second, in patients who have disease progression after single or doublet nivolumab therapy, many can be rescued with salvage therapies; anti-PD-1 therapy might resensitise the tumour to chemotherapy and thus offer a new chance of remission with conventional chemotherapy.[7,8] Furthermore, other novel therapies have shown encouraging preliminary results, including CD25 antibody-drug conjugates, and cellular therapies, like CD30 chimeric antigen receptor T cells and Epstein-Barr virus-directed cytotoxic T cells. Finally, autologous stem cell transplantation could be very effective after anti-PD-1 therapy,[9] and allogeneic stem cell transplantation—which was initially reported to be very toxic after PD-1 blockade—appears to be safer with the use of post-transplant cyclophosphamide.[10]

The ongoing phase 2 trial should offer more evidence about how best to use these novel therapies. Since the triplet regimen might increase the risk of severe, life-threatening toxicities (like pneumonitis and myocarditis), it would need to be significantly more effective than doublet therapy with higher response rates and, more importantly, improved duration of response and survival. Ideally, this trial and other ongoing studies can identify predictive biomarkers to select patients who are more likely to benefit from the addition of ipilimumab or are less likely to develop severe toxicity, or both. If such biomarkers could identify patients who can achieve long-term remissions with doublet or triplet therapy without the need for consolidative stem cell transplantation, more upfront toxicity would be easier to accept. With so many novel drugs, the optimal strategy for patients with relapsed or refractory disease is not yet clear. Although much work remains, combination approaches, if safely wielded, might offer improved outcomes for patients with Hodgkin lymphoma.

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Coagulation disorder in COVID-19

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See **Articles** page e671

The COVID-19 pandemic has had a major impact on health care globally. More than 10·1 million cases of COVID-19 have been reported worldwide, with more than 502 000 deaths. The severity of COVID-19 varies considerably from asymptomatic to life threatening. In severe cases, the host response to severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) leads to sepsis or septic shock as defined by the international consensus definitions for sepsis and septic shock (sepsis-3), including life-threatening organ dysfunction.[1]

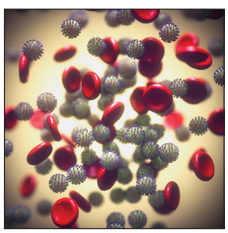
SARS-CoV-2 appears to enter host cells in the respiratory tract through the angiotensin-converting enzyme 2 receptor.[2] In COVID-19-induced sepsis or septic shock, the respiratory manifestations such as severe dyspnoea and hypoxaemia are particularly obvious and pertinent and are also the basis for the grading of mild, moderate, severe, and critical COVID-19 infection, as suggested by the diagnosis and treatment protocol for novel coronavirus pneumonia published by National Health Commission in China.[3] Further, COVID-19 infection is associated with coagulopathy of varying degrees, similar to the changes observed in sepsis induced coagulopathy (SIC) or disseminated intravascular coagulopathy (DIC).

The initial coagulopathy of COVID-19 has been characterised as increased D-dimer and fibrinogen or fibrin degradation products, but also abnormalities of prothrombin time, acute partial thromboplastin time, and platelet counts. Furthermore, severe COVID-19 infection might also lead to a cytokine storm similar to the cytokine profile present in secondary haemophagocytic lymphohistiocytosis, including increased ferritin level, IL-1, IL-2, IL-6, IL-7, granulocyte-colony stimulating factor, interferon-γ inducible protein 10, monocyte chemoattractant protein 1, macrophage inflammatory protein 1-α, and tumour necrosis factor-α.[4,5]

In *The Lancet Haematology*, Danying Liao and colleagues[6] present a retrospective observational cohort study, in which the coagulation profiles of 380 patients with COVID-19 admitted to hospital in Wuhan, China, are described (median age 64 years [53–73]; 174 [46%] women). The patients were classified as having moderate, severe, or critical COVID-19; notably, the severity of coagulopathy was associated with the severity of COVID-19. Thrombocytopenia, defined as platelet count less than 100×10^9 cells per L (odds ratio 8·33 [95% CI 2·56–27·15]), neutrophil to lymphocyte ratio of 9·13 or greater (5·39 [1·70–17·13]), prothrombin time longer than 16 s (4·94 [1·50–16·25]), and D-dimer more than 2 mg/L (4·41 [1·06–18·30]) were independently associated with increased mortality in a linear mixed model comparing survivors and non-survivors. The authors conclude that these routine coagulation tests can be used to help clinicians assess severity and prognosis of patients with COVID-19. The study is a valuable contribution to the knowledge of the coagulation profile of patients with COVID-19 and highlights the established role of routine coagulation tests as predictive variables for mortality and morbidity. However, the question of whether the observed changes in routine coagulation tests are just markers of the severity of illness or whether they show a significant and specific pathophysiology that drives morbidity and mortality in itself is still unanswered. Evidence exists to suggest that the observed coagulopaty is associated with an endotheliopathy that causes a thrombotic microangiopathy and microcirculatory impairment.[7] This association is an interesting and plausible explanation for the observed post-mortem findings of microvascular platelet-rich thrombotic depositions in small vessels of the lungs and other organs of patients with COVID-19.[8] SARS-CoV-2 uses the angiotensin-converting enzyme 2 receptor on endothelial cells for intracellular access to cells in the respiratory tract, with viral replication causing inflammation, endothelial cell apoptosis, and microvascular thrombosis. This pathophysiological course of events is consistent with the finding of microcirculatory clot formation and endothelial apoptosis in the post-mortems of patients with COVID-19,[9] and it is a plausible explanation of sudden cerebrovascular complications, myocardial ischaemia, and the increasing reports of both microcirculatory and macrocirculatory thromboembolic complications in these patients.

Although the features of COVID-19-associated coagulopathy have been considered unique, with very high levels of D-dimer and only moderately decreased platelet counts, the similarities with SIC and DIC are clear. However, in patients with critical COVID-19 infection and a cytokine storm, an extreme hypercoagulable state rarely seen in regular DIC has been observed. The reason for this life-threatening condition is not known but might be driven by an uncontrolled hyperinflammatory response to a novel pathogen without previous immunity.[7]

Regardless, understanding of the effects of this new pathogen is improving, and the guidelines for optimisation of patient management, including thrombosis prophylaxis, are developing. Pending the results of several randomised controlled trials (NCT04345848, NCT04366960, NCT04367831 and NCT04372589), the opinion of the Scientific and Standardization Committee of the International Society on Thrombosis and Haemostasis on thrombosis prophylaxis is that "a change of anticoagulant regimen from prophylactic low molecular weight heparin or intermediate-dose to treatment-dose regimen can be considered in patients without established venous



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For the **Johns Hopkins coronavirus resource center** see https://coronavirus.jhu.edu/map.html

thromboembolism, but deteriorating pulmonary status or acute respiratory distress syndrome".[10]

I declare no competing interests.

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Prognosis of patients with sickle cell disease and COVID-19: a French experience

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France is the country with the highest prevalence of sickle cell disease in Europe, with more than 26 000 patients diagnosed with the condition in 2018. Most of these patients are of sub-Saharan African origin.[1] Patients with sickle cell disease are thought to be at increased risk of COVID-19 complications. Aside from specific COVID-19-related morbidities, infections in patients with sickle cell disease[2] can provoke painful vaso-occlusive crisis and life-threatening acute chest syndrome. Thus, COVID-19 could be devastating for regions such as Africa or India, where an estimated 8–12 million patients with sickle cell disease live, or in the USA and Brazil, with more than 100 000 patients in each country.[3] Nevertheless, there are currently no data on the outcomes of patients with sickle cell disease and COVID-19.

On March 13, 2020, at an early stage of the COVID-19 pandemic in France, we invited all practitioners involved in the management of patients with sickle cell disease to report on all inpatients with sickle cell disease and confirmed COVID-19 by RNA detection of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) from nasal swabs. An email was sent to paediatricians, internists, and haematologists involved in sickle cell disease managment in France by our national consortia — MCGRE (Filière de santé maladies constitutionnelles rares du globule rouge et de l'érythropoïèse) and Laboratory of Excellence GR-Ex network. We prospectively collected data on outcomes in patients with sickle cell disease infected with COVID-19 using a standardised form. We compared the prevalence of intensive care unit (ICU) admission for inpatients with sickle cell disease by age range to that of COVID-19-positive inpatients in France during the same period.[4] Data were collected between March 13, 2020, and April 16, 2020.

83 inpatients with sickle cell disease infected by SARS-CoV-2 from 24 centres were enrolled (table 1). The median age was 33·5 years (range 19–68) for the 66 (80%) adults and 12 years (0·3–17) for the 17 (20%) children (defined as patients <18 years). 48 (58%) of 83 patients had a past medical history of acute chest syndrome, with a median of 2 episodes (range 1–10); 38 (46%) were being treated with hydroxyurea at admission (30 [51%] of 59 patients in the SS/Sβ^0 subpopulation). Vaso-occlusive crisis was associated with COVID-19 in 44 (54%) of 81 inpatients and acute chest syndrome was associated with COVID-19 in 23 (28%) of 82 inpatients (table 1).

17 (20%) of 83 patients were admitted to the ICU. Nine (53%) required mechanical ventilation, including two patients treated with extracorporeal membrane oxygenation. Two patients died in the ICU with COVID-19 pneumopathy: two men with the SC haemoglobin genotype. Five (63%) of the 8 patients with the SC genotype were admitted to the ICU, compared with 12 (17 %) of 71 patients with the SS/Sβ^0 genotype (p=0·0099 by Fisher's