Clinical Rheumatology (2021) 40:2611–2619
https://doi.org/10.1007/s10067-021-05691-x

REVIEW ARTICLE

COVID-19 and the clinical course of rheumatic manifestations

Sakir Ahmed[1] · Olena Zimba[2] · Armen Yuri Gasparyan[3]

Received: 22 February 2021 / Revised: 5 March 2021 / Accepted: 10 March 2021 / Published online: 17 March 2021

Abstract

The manifestations of COVID-19 have been evolving over time. Various post-COVID-19 syndromes are being recognised. Various viruses have been implicated in the pathogenesis of autoimmune diseases, and we expect a similar outcome with the severe acute respiratory syndrome-associated coronavirus-2 (SARS-CoV-2). The SARS-CoV-2 virus penetrates various tissues and organs and has a predisposition to lead to endotheliitis that may cause vascular manifestations including thrombosis. SARS-CoV-2 has been shown to activate Toll-like receptors and the complement system. It perpetuates NETosis and leads to autoantibody formation. These predispose to systemic autoimmunity. Both reactive arthritis and connective tissue disorders such as lupus and inflammatory myositis have been reported after COVID-19. Other reported autoimmune disorders include haemolytic anaemia, immune thrombocytopenia, cutaneous vasculitis, and Guillain Barré–like acute demyelinating disorders. The multisystem inflammatory syndrome in children and its adult counterpart are another post-COVID-19 entity that presents as an admixture of Kawasaki disease and staphylococcal toxic shock syndrome. Patients with preexisting rheumatic diseases may flare during the SARS-CoV-2 infection. They may develop novel autoimmune features also. The immune-suppressants used during the acute COVID-19 illness may confound the outcomes whereas comorbidities present in patients with rheumatic diseases may mask them. There is an urgent need to follow-up patients recovering from COVID and monitor autoantibody production in the context of rheumatic manifestations.

Key Points

- *COVID-19 is associated with both innate and acquired immune reactions and production of various autoantibodies.*
- *Various immune-mediated manifestations such as arthritis, myositis, haemolytic anaemia, thrombocytopenia, and acute demyelination may develop after COVID-19.*
- *Longitudinal cohort data are warranted to describe, predict, and test prevent various rheumatic manifestations in post-COVID-19 subjects.*

Keywords Induced autoimmunity · Post-COVID-19 · Rheumatic diseases

Introduction

Since its first detection at Wuhan in China, SARS-CoV-2 (novel coronavirus 2019) has engulfed the world with rapidly accumulating mutations and variants emerging at frequent intervals [1]. More than 100 million infections and 2.4 million deaths have been reported to the World Health Organization [2]. Various countries have experienced more than 1 wave of the epidemic, and it seems to be becoming endemic. Hence, future waves and seasonal outbreaks may be expected.

There is some evidence for the seasonality of coronavirus disease 2019 (COVID-19) [3]. The patterns of regional outbreaks along latitudes and regions of similar temperature and humidity seem to mirror those of a seasonal respiratory virus. In the initial year, the effect of seasonality was weak due to the rate of global spread but is likely to become more prominent from 2021 onwards [4].

✉ Armen Yuri Gasparyan
a.gasparyan@gmail.com

Sakir Ahmed
sakir005@gmail.com

Olena Zimba
zimbaolena@gmail.com

[1] Department of Clinical Immunology & Rheumatology, Kalinga Institute of Medical Sciences (KIMS), KIIT University, Bhubaneswar, India

[2] Department of Internal Medicine No. 2, Danylo Halytsky Lviv National Medical University, Lviv, Ukraine

[3] Departments of Rheumatology and Research and Development, Russells Hall Hospital, Dudley, Dudley Group NHS Foundation Trust (Teaching Trust of the University of Birmingham, UK), Pensnett Road, Dudley, West Midlands DY1 2HQ, UK

The implications of the novel virus variants and seasonality are that the infection can re-emerge from time to time in the near future. Also, the evolution of the virus would be towards less virulence and more prolonged infectivity as it becomes endemic. The latter may result in the prolonged exposure to the host immune system, increasing the likelihood of autoimmunity.

A powerful factor associated with both COVID-19 and autoimmunity is vitamin D. The vitamin D receptor has a role in innate cell activation, and low levels of vitamin D are associated with various autoimmune diseases [5]. A meta-analysis has confirmed the association between low vitamin D and severity of COVID-19 [6]. The latitude effect on COVID-19 mortality can be due to serum vitamin D levels [7].

COVID-19 is a heterogeneous disease ranging from asymptomatic course to multi-organ failure. The duality of inflammation and autoimmunity in COVID-19 has been compared with the two-faced Roman god Janus [8]. Although COVID-19 mortality seems to be decreasing, Europe is still battling the third wave. Vaccination has begun in most countries to safely achieve herd immunity.

The aftermath of the initial infections is being gradually recognised. Post-COVID-19 complications may manifest as pulmonary, cardiac, arthritic, cutaneous, and other affections [9]. It is unknown what proportion of these complications is reversible.

The likelihood of autoimmune and rheumatic diseases in COVID-19 survivors is a big issue. It is critically important to timely identify subjects with autoimmune and rheumatic manifestations. The acute SARS-CoV-2 infection may unmask previously undiagnosed rheumatic conditions and precipitate de novo disease, both of which may persist after resolution of the infection.

Various viral infections have been postulated to induce autoimmunity, including parvovirus B19, Epstein-Barr virus (EBV), cytomegalovirus (CMV), herpes virus-6, HTLV-1, hepatitis A and C virus, and rubella virus [10]. SARS-CoV-2 has been shown to induce activation of different aspects of the immune system. It can activate interleukin-6 (IL-6)-dependent pathways, leading to cytokine storm and macrophage activation syndromes [11, 12]. It can also alter interferon signalling [13] and affect antigen presentation.

The NETosis (formation of neutrophilic extracellular traps) in COVID-19 [14] can provide a fertile ground for autoantibody formation, especially against intra-nuclear components (anti-nuclear antibody) [15].

Also, various autoantibodies have been reported in the serum of patients with COVID-19, including anti-nuclear antibodies such as anti–52 kDa SSA/Ro and anti–60 kDa SSA/Ro [16], and various anti-phospholipid antibodies [17]. Immune-mediated thrombocytopenia [18] and haemolytic anaemia [19] have also been reported in COVID-19.

The aim of this article is to overview some of the pathophysiological mechanisms in COVID-19 that may lead to rheumatic manifestations and propose strategies to prevent rheumatic diseases in the long-term.

Search strategy

MEDLINE/PubMed and Scopus were searched with the keywords—COVID-19 and rheumatology/rheumatic disease/autoimmunity as per standard recommendations for a biomedical review [20]. Relevant articles were chosen and bibliographies of these articles were also explored.

Multi-systemic penetrance and endotheliitis in COVID-19

SARS-CoV-2 entry into the human cells is enabled by the angiotensin-converting enzyme receptor 2 (ACE2) [21]. This is a rather ubiquitous receptor present in the respiratory epithelium, renal glomerular cells, gastrointestinal tract, endothelial cells, immune cells, and even nervous tissue [22].

Clinical manifestations associated with the infection may include acute respiratory distress syndrome, acute kidney injury, heart failure, diarrhoea, and thrombosis [23, 24]. While canonical ACE2 is not affected by interferon (IFN), an inducible (termed MIRb-ACE2) isoform can be upregulated by IFN [25]. STimulator of INterferon Genes (STING) has been postulated to overly activate late in the pathogenesis of severe COVID-19 [26].

The ACE2 receptor is present on endothelial cells, and endotheliitis with virion particle has been reported [27]. SARS-CoV-2 can invade artificially engineered in vitro blood vessel organoid [28]. The endothelial invasion can amplify with apoptosis and pyroptosis leading to vasculitis-like features [29]. This has led to the hypothesis that endotheliitis can induce immune reactions with thrombosis [30]. Although one study could not demonstrate SARS-CoV-2 invasion in human endothelial cells [31], it may be premature to reject this hypothesis.

Persistence of SARS-CoV-2

Although viral illnesses are self-limiting, some viruses can persist in the host for years and decades. The persistent virus may be reactivated during periods of immune suppression as in the case of shingles or play a role in maintaining autoimmunity [32]. In the case of chikungunya infection, autoimmune chronic arthritis can develop and mimic rheumatoid arthritis [33].

The seasonality of autoimmunity is, at least partly, associated with viral infections [34]. Whether this is true for SARS-CoV-2 infection is unknown. Some patients have been found to shed the SARS-CoV-2 virion in their stool for weeks [35].

Younger children seem to shed the virus for longer periods [36]. Some patients test positive for SARS-CoV-2 for a long time, making it difficult to distinguish re-infection from virus persistence [37]. If there is a long-term persistence of the dormant virus, it may be completely harmless, or it may make a person prone to autoimmunity by prolonged innate immunity activation.

Innate immunity and autoinflammation in COVID-19

Autoinflammatory diseases predominantly affect innate immunity pathways [38]. COVID-19 has been associated with activation of innate immunity via Toll-like receptors (TLRs), mostly TLR-3, 4, 7, and 8 [39]. Complement activation in COVID-19 has been shown to activate platelets and neutrophil extracellular traps (NETs) [40]. Such reactions may transform into autoimmunity.

Beyond molecular mimicry, this (hyper)inflammation and dysregulated immune responses seem to be a viable mechanism by which COVID-19 can bring on autoimmunity [41]. It has been shown that innate activation by viral infections can cause flares of diseases with predominant autoinflammatory pathogenesis like psoriasis [42]. NETosis has been proposed in the causation of post-COVID-19 syndrome [43]. Also, there is some evidence that the SARS-CoV-2 infection is aided by autoantibodies such as anti-interferon antibodies that are found in about 10% of severe COVID-19 cases [44].

Thrombosis in COVID-19

Thrombosis is an integral part of COVID-19. Conversely, the mortality benefit of heparin in COVID-19 seems to extend beyond the conventional anti-coagulation properties [45]. The various roles of endothelial cells, turbulent blood flow, and platelet dysfunction included in Virchow's triad are discussed in detail elsewhere [24].

Antiphospholipid antibodies (APLA) found in COVID-19 are a sign of autoimmunity. Initially, these were presumed to be pathological [46]. In cohorts of severe COVID-19, it was shown that almost half had at least one APLA [47]. At least 30% are above stringent cut-offs (> 40 IU) [48] required in the classification criteria for the anti-phospholipid syndrome (APS). More recent studies have shown that APLA in COVID-19 have different epitope specificities as opposed to the ones in classic APS [49]. One target of antibodies in APS could be annexin-A2. Antibodies to this phospholipid-binding protein have been shown to correlate with mortality in COVID-19 [50]. The persistence of these antibodies can herald an increased predisposition to thrombosis and may be indistinguishable from APS [48].

The timing of pro-thrombotic effects of COVID-19 is still uncertain. Although there is no evidence of highly prevalent thrombotic disease among COVID-19 survivors, it may take some time before sufficient data emerge to rule out this possibility.

Antinuclear antibodies in COVID-19

About 30% of COVID-19 patients have at least one antibody against a nuclear antigen. Most of these are detectable at low titre without high specificity [51]. However, considering the number of COVID-19 patients worldwide, it is likely that some patients may develop a persistent autoantibody response resulting in autoimmunity.

The entire "autoantigenome" of SARS-CoV-2-positive patients has been mapped [52]. This has provided valuable links of autoimmunity with thrombosis, fibrosis, and smooth muscle dysfunction in COVID-19. Also, there is a lot of overlap of these antibodies with various neural antigens pointing towards future neurological sequelae.

Rheumatic manifestations in COVID-19

Some of the initially reported autoimmune manifestations of COVID-19 include haemolytic anaemia [19] and immune thrombocytopenia [53]. There are reports of Guillain-Barré syndrome associated with COVID-19 [54, 55]. Even cranial nerve palsies have been reported [56].

Also, autoimmune endocrine disorders have been reported [57]. A variety of arthritic and other musculoskeletal affections in COVID-19 are described in case studies summarized in Table 1.

Cutaneous vasculitis in association with COVID-19 is also reported in case reports [64, 65]. There are two published cases of urticarial vasculitis [66]. However, a couple of systematic reviews have pointed out that most cutaneous manifestations could be traced to various drugs the patients were on [67, 68]. The cause of purpura could be traced to thrombosis in several cases, and these would usually appear early in the disease onset. Thus, the association of cutaneous vasculitis with COVID-19 is not strong.

Three cases of lupus have been diagnosed with the onset of COVID-19 (Table 2). Other COVID-19-related rheumatic conditions include inflammatory myositis [72]. Myalgia has been commonly reported in various cohorts of COVID-19 [73].

Multi-system inflammatory syndrome associated with COVID-19

Kawasaki disease (KD)–like syndrome was first reported in association with COVID-19 in children [74]. The incidence of this syndrome was almost 10 times the incidence of the usual KD [74]. It was termed as multi-system inflammatory syndrome associated with COVID-19 in children (MIS-C) and found to have clinical features overlapping with vasculitis of KD and cutaneous manifestation and cardiovascular collapse

Table 1 Post-COVID-19 reactive arthritis

Place	Age, sex	Joints affected	Lab parameters	Treatment	Outcome
Turkey [58]	73, male	Metatarso-phalangeal, proximal, and distal interphalangeal of toes	RF, ACPA were negative	NSAIDs	Resolved
Japan [59]	50s, male	Bilateral ankles arthritis, with mild enthesitis	ANA, RF, and ACPA were negative; No crystals on arthrocentesis HLA-B27 negative	NSAID and intra-articular steroids	Moderate improvement
Jeddah, SAU [60]	39, female	Distal interphalangeal (DIP) and proximal interphalangeal (PIP) joints of the hands	ANA, RF, ACPA were negative	NSAIDs (celecoxib)	Resolved
Norwich, UK [61]	53, male	Inflammatory back pain	HLA-B27-positive	Intra-muscular methylprednisolone 120 mg and oral diclofenac 75 mg	Resolved at 3 months
Erlangen, Germany [62]	65, female	Ankles, wrists, and knee joints; Associated with cutaneous vasculitis	Auto-antibody tests were negative. HLA-B27 was positive	Oral prednisolone	Resolved
Singapore [63]	47, male	Right knee; with "swelling" of penis	No crystals on arthrocentesis	Etoricoxib and intra-articular triamcinolone	Not mentioned

ACPA anti-citrullinated peptide antibody, *ANA* antinuclear antibodies, *HLA* human leukocyte antigen, *IAS* intra-articular steroids, *NSAID* non-steroidal anti-inflammatory drugs, *RF* rheumatoid factor

of staphylococcal toxic shock syndrome [75]. Later on, the adult counterpart was recognised and named as "MIS-A." Variants have been described including a case presenting as status epilepticus [76].

Although the pathogenesis of MIS is unclear, it is likely an (auto)immune manifestation that occurs mostly post-COVID-19 (concomitantly in a very limited number of cases). Unlike most other rheumatic diseases, both KD and MIS are not chronic.

COVID-19 in patients with various autoinflammatory and autoimmune rheumatic diseases

Despite the use of immunosuppressants and intrinsic immune dysfunction in various autoimmune diseases, there has been no report of an increased susceptibility to COVID-19. Initial epidemiological data from the COVID-19 Global Rheumatology Alliance international physician registry has demonstrated that patients on higher glucocorticoid doses have higher chances of hospitalization while those on anti-TNF-alpha inhibitors have lesser chances [77]. In an analysis of data from primary care, patients with a diagnosis of rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), or psoriasis were at higher risk for death during the pandemic [78]. But these data need to be carefully interpreted since there may be confounding by indication.

Overall, the risks of severe COVID-19 in patients with rheumatic diseases have gradually reduced over time [79]. Rheumatic diseases have multiple comorbidities that may predispose to severe disease and worse outcomes [80].

It has been shown that patients with preexisting rheumatic diseases can flare during COVID-19 and develop new manifestations. A male patient with lupus presenting with arthritis and thrombocytopenia developed Coombs' positive haemolytic anaemia along with APLA positivity [81]. A review has found two novel cases of lupus, along with flares in

Table 2 Case reports of de novo post-COVID-19 systemic lupus erythematosus

Place	Age, sex	Clinical features	Lab	Management	Outcome
Italy [69]	85, female	Severe hypotension, thrombocytopenia, pleural effusion	Positivity for ANA; Ku positivity and atypical ANCA	Steroids	Dried gangrene in three fingers; antibodies persistent at 2 months
Connecticut, US [70]	18, female	Fever, pericardial tamponade, acute heart failure, and pleural effusion	Positive anti-nuclear and anti-double-stranded DNA antibodies, lupus anti-coagulant, and anti-cardiolipin B. C3 and C4 levels were low.	Steroids, antibiotics, hydroxychloroquine	ARDS, renal failure and death
Mexico [71]	45, male	Fever, dry cough, myalgia, and arthralgia; oedema; thrombocytopenia	Positive anti-nuclear antibodies	Steroids, IV immunoglobulin, and rituximab	Recovered

another five during COVID-19 [71]. A large multi-centric cohort has shown that patients with autoimmune diseases may be at higher risks for developing COVID-19 than the general population [82].

Immunosuppressant therapy in COVID-19

Although various immune-mediated therapies were initially proposed for COVID-19 [83], only a few have stood the rigour of randomized trials [84]. A much-purported drug, hydroxychloroquine, did not meet endpoints in various RCTs [85]. Colchicine has shown some promise in moderate COVID-19 in an RCT though the primary end-point was not met [86]. Evidence is sparse for various biologic agents such as tocilizumab and anakinra, and current practice guidelines do not support their routine use [87]. It is possible that individuals with autoimmune features might respond to these therapies while others do not. However, to explore such possibilities, a personalised medicine approach is required.

What is interesting is that some of these drugs have been used in the pandemic and such off-label use could have influenced the development of autoimmunity. They may offset the development of autoimmunity. The use and withdrawal may paradoxically induce autoimmunity. It has been hypothesized that transient immunosuppression followed by inappropriate immune reconstitution itself may result in autoimmunity [88].

Moreover, gout can also be precipitated by anti-virals such as favipiravir and lopinavir-ritonavir combination that were initially used for COVID-19 [89]. Similarly, the use of convalescent serum may lead to delayed serum sickness (systematic Arthus-like reaction) [90].

Comorbidities and post-COVID-19 rheumatic manifestations

A survey of COVID-19 survivors has shown a high prevalence of fatigue and various complications such as myocardial ischemia syndromes, stroke, and pulmonary fibrosis [91]. Initially, the manifestation of various autoimmune diseases may be masked by symptoms attributed to these manifestations. For example, large-vessel stroke in the young might be attributed to accelerated thrombosis due to COVID-19 and underlying de novo vasculitis.

Predicting and preventing post-COVID-19 rheumatic diseases

The prediction will depend on genetic susceptibility to vasculitis and prothrombotic diseases. A genome-wide association study in patients with COVID-19 has found the loci 3p21.31 and 9q34.2 associated with severe disease [92]. The 3p21.31 locus contains genes like C–C chemokine receptor type 9; C–X–C motif chemokine receptor 6 and XCR1, the receptor for lymphotactins-1 and -2 [92]. These can be associated with vasculitis, and autoimmune colitis [93]. XCR-1 is associated with antigen cross-presentation and has been reported in RA synovium [94]. The 9q34.2 locus coincides with the ABO group, and there is a hypothesis that stabilization of the von-Willebrand factor can predispose to thrombosis and severe COVID-19 [92]. However, the work done is preliminary and needs to be backed up with more clinical correlations.

At least half of patients with severe COVID-19 develop autoantibodies [95]. There is a need of cohort studies to estimate how long these persist. If they persist, it should be seen whether they predispose to autoimmune disease.

The post-COVID-19 pulmonary syndrome is well recognised [96]. Similarly, there is a possibility of a post-COVID-19 cardiac syndrome [97]. A meta-analysis of cohorts of survivors of severe acute respiratory syndrome and Middle East respiratory syndrome coronavirus outbreaks has shown a low diffusing capacity for carbon monoxide and reduced exercise capacity in at least a quarter [98].

One question that arises is how much of this is due to immune dysregulation and vascular endotheliitis. If this hypothesis is true, there may be a role of DMARDs such as methotrexate and colchicine in the prevention of post-COVID-19 syndromes. These should be explored in the context of clinical trials.

Conclusion

Various autoimmune and rheumatic diseases have been reported among COVID-19 survivors. COVID-19 can also result in flares of preexisting rheumatic diseases. Cohort studies to identify rheumatologic manifestations in the short- and long-terms after surviving COVID-19 are the need of the hour. This will clarify the burden of rheumatic and other manifestations after COVID-19 as well as help to recognise vulnerable groups for screening and preventive strategies.

Author contribution Conceptualisation: Ahmed S, Gasparyan AY, Zimba O. Methodology: Ahmed S, Zimba O. writing—original draft: Ahmed S, Gasparyan AY writing—review and editing: Ahmed S, Zimba O, Gasparyan AY. All the authors have approved the final manuscript and take full responsibility for the integrity of the data and the contents of the manuscript.

Declarations

Disclosures None.

Disclaimer All views and opinions expressed in this article are those of the authors and do not necessarily reflect the official policy or position of any institution or association.

References

1. Flores-Alanis A, Cruz-Rangel A, Rodríguez-Gómez F, González J, Torres-Guerrero CA, Delgado G, Cravioto A, Morales-Espinosa R (2021) Molecular epidemiology surveillance of SARS-CoV-2: mutations and genetic diversity one year after emerging. Pathogens 10: 184. https://doi.org/10.3390/pathogens10020184
2. WHO Coronavirus Disease (COVID-19) Dashboard. https://covid19.who.int. Accessed 13 Feb 2021
3. Sajadi MM, Habibzadeh P, Vintzileos A, Shokouhi S, Miralles-Wilhelm F, Amoroso A (2020) Temperature, humidity, and latitude analysis to estimate potential spread and seasonality of coronavirus disease 2019 (COVID-19). JAMA Netw Open 3:e2011834. https://doi.org/10.1001/jamanetworkopen.2020.11834
4. Smit AJ, Fitchett JM, Engelbrecht FA, Scholes RJ, Dzhivhuho G, Sweijd NA (2020) Winter is coming: a southern hemisphere perspective of the environmental drivers of SARS-CoV-2 and the potential seasonality of COVID-19. Int J Environ Res Public Health 17:5634. https://doi.org/10.3390/ijerph17165634
5. Yamamoto E, Jørgensen TN (2019) Immunological effects of vitamin D and their relations to autoimmunity. J Autoimmun 100:7–16. https://doi.org/10.1016/j.jaut.2019.03.002
6. Pereira M, Dantas Damascena A, Galvão Azevedo LM, de Almeida Oliveira T, da Mota Santana J (2020) Vitamin D deficiency aggravates COVID-19: systematic review and meta-analysis. Crit Rev Food Sci Nutr:1–9. https://doi.org/10.1080/10408398.2020.1841090
7. Whittemore PB (2020) COVID-19 fatalities, latitude, sunlight, and vitamin D. Am J Infect Control 48:1042–1044. https://doi.org/10.1016/j.ajic.2020.06.193
8. Novelli L, Motta F, De Santis M et al (2021) The JANUS of chronic inflammatory and autoimmune diseases onset during COVID-19 - A systematic review of the literature. J Autoimmun 117:102592. https://doi.org/10.1016/j.jaut.2020.102592
9. Davido B, Seang S, Tubiana R, de Truchis P (2020) Post-COVID-19 chronic symptoms: a postinfectious entity? Clin Microbiol Infect 26:1448–1449. https://doi.org/10.1016/j.cmi.2020.07.028
10. Ehrenfeld M, Tincani A, Andreoli L, Cattalini M, Greenbaum A, Kanduc D, Alijotas-Reig J, Zinserling V, Semenova N, Amital H, Shoenfeld Y (2020) Covid-19 and autoimmunity. Autoimmun Rev 19:102597. https://doi.org/10.1016/j.autrev.2020.102597
11. Soy M, Keser G, Atagündüz P, Tabak F, Atagündüz I, Kayhan S (2020) Cytokine storm in COVID-19: pathogenesis and overview of anti-inflammatory agents used in treatment. Clin Rheumatol 39: 2085–2094. https://doi.org/10.1007/s10067-020-05190-5
12. Merad M, Martin JC (2020) Pathological inflammation in patients with COVID-19: a key role for monocytes and macrophages. Nat Rev Immunol 20:355–362. https://doi.org/10.1038/s41577-020-0331-4
13. Hadjadj J, Yatim N, Barnabei L, Corneau A, Boussier J, Smith N, Péré H, Charbit B, Bondet V, Chenevier-Gobeaux C, Breillat P, Carlier N, Gauzit R, Morbieu C, Pène F, Marin N, Roche N, Szwebel TA, Merkling SH, Treluyer JM, Veyer D, Mouthon L, Blanc C, Tharaux PL, Rozenberg F, Fischer A, Duffy D, Rieux-Laucat F, Kernéis S, Terrier B (2020) Impaired type I interferon activity and inflammatory responses in severe COVID-19 patients. Science 369:718–724. https://doi.org/10.1126/science.abc6027
14. Barnes BJ, Adrover JM, Baxter-Stoltzfus A, Borczuk A, Cools-Lartigue J, Crawford JM, Daßler-Plenker J, Guerci P, Huynh C, Knight JS, Loda M, Looney MR, McAllister F, Rayes R, Renaud S, Rousseau S, Salvatore S, Schwartz RE, Spicer JD, Yost CC, Weber A, Zuo Y, Egeblad M (2020) Targeting potential drivers of COVID-19: Neutrophil extracellular traps. J Exp Med 217: e20200652. https://doi.org/10.1084/jem.20200652
15. Gupta S, Kaplan MJ (2016) The role of neutrophils and NETosis in autoimmune and renal diseases. Nat Rev Nephrol 12:402–413. https://doi.org/10.1038/nrneph.2016.71
16. Zhou Y, Han T, Chen J, Hou C, Hua L, He S, Guo Y, Zhang S, Wang Y, Yuan J, Zhao C, Zhang J, Jia Q, Zuo X, Li J, Wang L, Cao Q, Jia E (2020) Clinical and autoimmune characteristics of severe and critical cases of COVID-19. Clin Transl Sci 13:1077–1086. https://doi.org/10.1111/cts.12805
17. Xiao M, Zhang Y, Zhang S, Qin X, Xia P, Cao W, Jiang W, Chen H, Ding X, Zhao H, Zhang H, Wang C, Zhao J, Sun X, Tian R, Wu W, Wu D, Ma J, Chen Y, Zhang D, Xie J, Yan X, Zhou X, Liu Z, Wang J, du B, Qin Y, Gao P, Lu M, Hou X, Wu X, Zhu H, Xu Y, Zhang W, Li T, Zhang F, Zhao Y, Li Y, Zhang S (2020) Antiphospholipid antibodies in critically ill patients with COVID-19. Arthritis Rheumatol 72:1998–2004. https://doi.org/10.1002/art.41425
18. Bomhof G, Mutsaers PGNJ, Leebeek FWG, Boekhorst PAW, Hofland J, Croles FN, Jansen AJG (2020) COVID-19-associated immune thrombocytopenia. Br J Haematol 190:e61–e64. https://doi.org/10.1111/bjh.16850
19. Lazarian G, Quinquenel A, Bellal M, Siavellis J, Jacquy C, Re D, Merabet F, Mekinian A, Braun T, Damaj G, Delmer A, Cymbalista F (2020) Autoimmune haemolytic anaemia associated with COVID-19 infection. Br J Haematol 190:29–31. https://doi.org/10.1111/bjh.16794
20. Gasparyan AY, Ayvazyan L, Blackmore H, Kitas GD (2011) Writing a narrative biomedical review: considerations for authors, peer reviewers, and editors. Rheumatol Int 31:1409–1417. https://doi.org/10.1007/s00296-011-1999-3
21. Hoffmann M, Kleine-Weber H, Schroeder S et al (2020) SARS-CoV-2 Cell entry depends on ACE2 and TMPRSS2 and is blocked by a clinically proven protease inhibitor. Cell 181:271–280.e8. https://doi.org/10.1016/j.cell.2020.02.052
22. Hamming I, Timens W, Bulthuis MLC, Lely AT, Navis GJ, van Goor H (2004) Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol 203:631–637. https://doi.org/10.1002/path.1570
23. Tu H, Tu S, Gao S, Shao A, Sheng J (2020) Current epidemiological and clinical features of COVID-19; a global perspective from China. J Infect 81:1–9. https://doi.org/10.1016/j.jinf.2020.04.011
24. Ahmed S, Zimba O, Gasparyan AY (2020) Thrombosis in coronavirus disease 2019 (COVID-19) through the prism of Virchow's triad. Clin Rheumatol 39:2529–2543. https://doi.org/10.1007/s10067-020-05275-1
25. Ng KW, Attig J, Bolland W, Young GR, Major J, Wrobel AG, Gamblin S, Wack A, Kassiotis G (2020) Tissue-specific and interferon-inducible expression of nonfunctional ACE2 through endogenous retroelement co-option. Nat Genet 52:1294–1302. https://doi.org/10.1038/s41588-020-00732-8
26. Berthelot J-M, Lioté F, Maugars Y, Sibilia J (2020) Lymphocyte changes in severe COVID-19: delayed over-activation of STING? Front Immunol 11:607069. https://doi.org/10.3389/fimmu.2020.607069
27. Ackermann M, Verleden SE, Kuehnel M, Haverich A, Welte T, Laenger F, Vanstapel A, Werlein C, Stark H, Tzankov A, Li WW, Li VW, Mentzer SJ, Jonigk D (2020) Pulmonary vascular endothelialitis, thrombosis, and angiogenesis in Covid-19. N Engl J Med 383:120–128. https://doi.org/10.1056/NEJMoa2015432
28. Monteil V, Kwon H, Prado P et al (2020) Inhibition of SARS-CoV-2 infections in engineered human tissues using clinical-grade soluble human ACE2. Cell 181:905–913.e7. https://doi.org/10.1016/j.cell.2020.04.004
29. Varga Z, Flammer AJ, Steiger P, Haberecker M, Andermatt R, Zinkernagel AS, Mehra MR, Schuepbach RA, Ruschitzka F, Moch H (2020) Endothelial cell infection and endotheliitis in

COVID-19. Lancet 395:1417–1418. https://doi.org/10.1016/S0140-6736(20)30937-5
30. Bilgin E, Ertenli AI (2021) Proposal of a new nomenclature for the underlying pathogenetic mechanism of severe coronavirus disease-19: "inflammatory thrombosis with immune endotheliitis—ITIE". Rheumatol Int 41:679–680. https://doi.org/10.1007/s00296-020-04768-1
31. McCracken IR, Gaye S, He L et al (2021) Lack of evidence of angiotensin-converting enzyme 2 expression and replicative infection by SARS-CoV-2 in human endothelial cells. Circulation 143: 865–868. https://doi.org/10.1161/CIRCULATIONAHA.120.052824
32. Smatti MK, Cyprian FS, Nasrallah GK, al Thani AA, Almishal RO, Yassine HM (2019) Viruses and autoimmunity: a review on the potential interaction and molecular mechanisms. Viruses 11:762. https://doi.org/10.3390/v11080762
33. Tanay A (2017) Chikungunya virus and autoimmunity. Curr Opin Rheumatol 29:389–393. https://doi.org/10.1097/BOR.0000000000000396
34. Watad A, Azrielant S, Bragazzi NL, Sharif K, David P, Katz I, Aljadeff G, Quaresma M, Tanay G, Adawi M, Amital H, Shoenfeld Y (2017) Seasonality and autoimmune diseases: the contribution of the four seasons to the mosaic of autoimmunity. J Autoimmun 82:13–30. https://doi.org/10.1016/j.jaut.2017.06.001
35. Kipkorir V, Cheruiyot I, Ngure B, Misiani M, Munguti J (2020) Prolonged SARS-CoV-2 RNA detection in anal/rectal swabs and stool specimens in COVID-19 patients after negative conversion in nasopharyngeal RT-PCR test. J Med Virol 92:2328–2331. https://doi.org/10.1002/jmv.26007
36. Cai J, Wang X, Zhao J, Ge Y, Xu J, Tian H, Chang H, Xia A, Wang J, Zhang J, Wei Z, Li J, Wang C, Wang J, Zhu Q, Zhai X, Zeng M (2020) Comparison of clinical and epidemiological characteristics of asymptomatic and symptomatic SARS-CoV-2 infection in children. Virol Sin 35:803–810. https://doi.org/10.1007/s12250-020-00312-4
37. Kang H, Wang Y, Tong Z, Liu X (2020) Retest positive for SARS-CoV-2 RNA of "recovered" patients with COVID-19: persistence, sampling issues, or re-infection? J Med Virol 92:2263–2265. https://doi.org/10.1002/jmv.26114
38. Krainer J, Siebenhandl S, Weinhäusel A (2020) Systemic autoinflammatory diseases. J Autoimmun 109:102421. https://doi.org/10.1016/j.jaut.2020.102421
39. Birra D, Benucci M, Landolfi L, Merchionda A, Loi G, Amato P, Licata G, Quartuccio L, Triggiani M, Moscato P (2020) COVID 19: a clue from innate immunity. Immunol Res 68:161–168. https://doi.org/10.1007/s12026-020-09137-5
40. Skendros P, Mitsios A, Chrysanthopoulou A, Mastellos DC, Metallidis S, Rafailidis P, Ntinopoulou M, Sertaridou E, Tsironidou V, Tsigalou C, Tektonidou M, Konstantinidis T, Papagoras C, Mitroulis I, Germanidis G, Lambris JD, Ritis K (2020) Complement and tissue factor-enriched neutrophil extracellular traps are key drivers in COVID-19 immunothrombosis. J Clin Invest 130:6151–6157. https://doi.org/10.1172/JCI141374
41. Galeotti C, Bayry J (2020) Autoimmune and inflammatory diseases following COVID-19. Nat Rev Rheumatol 16:413–414. https://doi.org/10.1038/s41584-020-0448-7
42. Sbidian E, Madrange M, Viguier M, Salmona M, Duchatelet S, Hovnanian A, Smahi A, le Goff J, Bachelez H (2019) Respiratory virus infection triggers acute psoriasis flares across different clinical subtypes and genetic backgrounds. Br J Dermatol 181:1304–1306. https://doi.org/10.1111/bjd.18203
43. Sawadogo SA, Dighero-Kemp B, Ouédraogo D-D, Hensley L, Sakandé J (2020) How NETosis could drive "post-COVID-19 syndrome" among survivors. Immunol Lett 228:35–37. https://doi.org/10.1016/j.imlet.2020.09.005
44. Bastard P, Rosen LB, Zhang Q et al (2020) Autoantibodies against type I IFNs in patients with life-threatening COVID-19. Science 370:eabd4585. https://doi.org/10.1126/science.abd4585
45. Ahmed S, Anirvan P (2020) Reply to Rheumatologists' perspective on coronavirus disease 19: is heparin the dark horse for COVID-19? Clin Rheumatol 39:2099–2100. https://doi.org/10.1007/s10067-020-05145-w
46. Zhang Y, Xiao M, Zhang S, Xia P, Cao W, Jiang W, Chen H, Ding X, Zhao H, Zhang H, Wang C, Zhao J, Sun X, Tian R, Wu W, Wu D, Ma J, Chen Y, Zhang D, Xie J, Yan X, Zhou X, Liu Z, Wang J, du B, Qin Y, Gao P, Qin X, Xu Y, Zhang W, Li T, Zhang F, Zhao Y, Li Y, Zhang S (2020) Coagulopathy and antiphospholipid antibodies in patients with COVID-19. N Engl J Med 382:e38. https://doi.org/10.1056/NEJMc2007575
47. Amezcua-Guerra LM, Rojas-Velasco G, Brianza-Padilla M, Vázquez-Rangel A, Márquez-Velasco R, Baranda-Tovar F, Springall R, Gonzalez-Pacheco H, Juárez-Vicuña Y, Tavera-Alonso C, Sanchez-Muñoz F, Hernández-Salas M (2020) Presence of antiphospholipid antibodies in COVID-19: case series study. Ann Rheum Dis:annrheumdis-2020-218100. https://doi.org/10.1136/annrheumdis-2020-218100
48. Zuo Y, Estes SK, Ali RA et al (2020) Prothrombotic autoantibodies in serum from patients hospitalized with COVID-19. Sci Transl Med 12:eabd3876. https://doi.org/10.1126/scitranslmed.abd3876
49. Borghi MO, Beltagy A, Garrafa E, Curreli D, Cecchini G, Bodio C, Grossi C, Blengino S, Tincani A, Franceschini F, Andreoli L, Lazzaroni MG, Piantoni S, Masneri S, Crisafulli F, Brugnoni D, Muiesan ML, Salvetti M, Parati G, Torresani E, Mahler M, Heilbron F, Pregnolato F, Pengo M, Tedesco F, Pozzi N, Meroni PL (2020) Anti-phospholipid antibodies in COVID-19 are different from those detectable in the anti-phospholipid syndrome. Front Immunol 11:584241. https://doi.org/10.3389/fimmu.2020.584241
50. Zuniga M, Gomes C, Carsons SE, et al (2021) Autoimmunity to the lung protective phospholipid-binding protein annexin A2 predicts mortality among hospitalized COVID-19 patients. medRxiv 2020.12.28.20248807. https://doi.org/10.1101/2020.12.28.20248807
51. Lerma LA, Chaudhary A, Bryan A, Morishima C, Wener MH, Fink SL (2020) Prevalence of autoantibody responses in acute coronavirus disease 2019 (COVID-19). J Transl Autoimmun 3:100073. https://doi.org/10.1016/j.jtauto.2020.100073
52. Wang JY, Zhang W, Roehrl MW et al (2021) An autoantigen atlas from human lung HFL1 cells offers clues to neurological and diverse autoimmune manifestations of COVID-19. bioRxiv. https://doi.org/10.1101/2021.01.24.427965
53. Zulfiqar A-A, Lorenzo-Villalba N, Hassler P, Andrès E (2020) Immune thrombocytopenic purpura in a patient with Covid-19. N Engl J Med 382:e43. https://doi.org/10.1056/NEJMc2010472
54. Toscano G, Palmerini F, Ravaglia S, Ruiz L, Invernizzi P, Cuzzoni MG, Franciotta D, Baldanti F, Daturi R, Postorino P, Cavallini A, Micieli G (2020) Guillain-Barré syndrome associated with SARS-CoV-2. N Engl J Med 382:2574–2576. https://doi.org/10.1056/NEJMc2009191
55. Scheidl E, Canseco DD, Hadji-Naumov A, Bereznai B (2020) Guillain-Barré syndrome during SARS-CoV-2 pandemic: a case report and review of recent literature. J Peripher Nerv Syst 25: 204–207. https://doi.org/10.1111/jns.12382
56. Dinkin M, Gao V, Kahan J, Bobker S, Simonetto M, Wechsler P, Harpe J, Greer C, Mints G, Salama G, Tsiouris AJ, Leifer D (2020) COVID-19 presenting with ophthalmoparesis from cranial nerve palsy. Neurology 95:221–223. https://doi.org/10.1212/WNL.0000000000009700
57. Speer G, Somogyi P (2021) Thyroid complications of SARS and coronavirus disease 2019 (COVID-19). Endocr J 68:129–136. https://doi.org/10.1507/endocrj.EJ20-0443

58. Saricaoglu EM, Hasanoglu I, Guner R (2020) The first reactive arthritis case associated with COVID-19. J Med Virol 93:192–193. https://doi.org/10.1002/jmv.26296
59. Ono K, Kishimoto M, Shimasaki T, Uchida H, Kurai D, Deshpande GA, Komagata Y, Kaname S (2020) Reactive arthritis after COVID-19 infection. RMD Open 6:e001350. https://doi.org/10.1136/rmdopen-2020-001350
60. Jali I (2020) Reactive arthritis after COVID-19 infection. Cureus 12:e11761. https://doi.org/10.7759/cureus.11761
61. Coath FL, Mackay J, Gaffney JK (2021) Axial presentation of reactive arthritis secondary to Covid-19 infection. Rheumatology (Oxford):keab009. https://doi.org/10.1093/rheumatology/keab009
62. Schenker HM, Hagen M, Simon D, Schett G, Manger B (2021) Reactive arthritis and cutaneous vasculitis after SARS-CoV-2 infection. Rheumatology (Oxford) 60:479–480. https://doi.org/10.1093/rheumatology/keaa689
63. Liew IY, Mak TM, Cui L, Vasoo S, Lim XR (2020) A case of reactive arthritis secondary to coronavirus disease 2019 infection. J Clin Rheumatol 26:233. https://doi.org/10.1097/RHU.0000000000001560
64. Castelnovo L, Capelli F, Tamburello A, Faggioli PM, Mazzone A (2020) Symmetric cutaneous vasculitis in COVID-19 pneumonia. J Eur Acad Dermatol Venereol 34:e362–e363. https://doi.org/10.1111/jdv.16589
65. Caputo V, Schroeder J, Rongioletti F (2020) A generalized purpuric eruption with histopathologic features of leucocytoclastic vasculitis in a patient severely ill with COVID-19. J Eur Acad Dermatol Venereol 34:e579–e581. https://doi.org/10.1111/jdv.16737
66. de Perosanz-Lobo D, Fernandez-Nieto D, Burgos-Blasco P, Selda-Enriquez G, Carretero I, Moreno C, Fernández-Guarino M (2020) Urticarial vasculitis in COVID-19 infection: a vasculopathy-related symptom? J Eur Acad Dermatol Venereol 34:e566–e568. https://doi.org/10.1111/jdv.16713
67. Najar Nobari N, Seirafianpour F, Mashayekhi F, Goodarzi A (2020) A systematic review on treatment-related mucocutaneous reactions in COVID-19 patients. Dermatol Ther:e14662. https://doi.org/10.1111/dth.14662
68. Perna A, Passiatore M, Massaro A, Terrinoni A, Bianchi L, Cilli V, D'Orio M, Proietti L, Taccardo G, de Vitis R (2021) Skin manifestations in COVID-19 patients, state of the art. A systematic review. Int J Dermatol. https://doi.org/10.1111/ijd.15414
69. Bonometti R, Sacchi MC, Stobbione P et al (2020) The first case of systemic lupus erythematosus (SLE) triggered by COVID-19 infection. Eur Rev Med Pharmacol Sci 24:9695–9697. https://doi.org/10.26355/eurrev_202009_23060
70. Mantovani Cardoso E, Hundal J, Feterman D, Magaldi J (2020) Concomitant new diagnosis of systemic lupus erythematosus and COVID-19 with possible antiphospholipid syndrome. Just a coincidence? A case report and review of intertwining pathophysiology. Clin Rheumatol 39:2811–2815. https://doi.org/10.1007/s10067-020-05310-1
71. Gracia-Ramos AE, Saavedra-Salinas MÁ (2021) Can the SARS-CoV-2 infection trigger systemic lupus erythematosus? A case-based review. Rheumatol Int 4:1–11. https://doi.org/10.1007/s00296-021-04794-7
72. Beydon M, Chevalier K, Tabaa OA et al (2020) Myositis as a manifestation of SARS-CoV-2. Ann Rheum Dis 80:e42. https://doi.org/10.1136/annrheumdis-2020-217573
73. Abdullahi A, Candan SA, Abba MA, Bello AH, Alshehri MA, Afamefuna Victor E, Umar NA, Kundakci B (2020) Neurological and musculoskeletal features of COVID-19: a systematic review and meta-analysis. Front Neurol 11. https://doi.org/10.3389/fneur.2020.00687
74. Toubiana J, Poirault C, Corsia A, Bajolle F, Fourgeaud J, Angoulvant F, Debray A, Basmaci R, Salvador E, Biscardi S, Frange P, Chalumeau M, Casanova JL, Cohen JF, Allali S (2020) Kawasaki-like multisystem inflammatory syndrome in children during the COVID-19 pandemic in Paris, France: prospective observational study. BMJ 369:m2094. https://doi.org/10.1136/bmj.m2094
75. Pouletty M, Borocco C, Ouldali N, Caseris M, Basmaci R, Lachaume N, Bensaid P, Pichard S, Kouider H, Morelle G, Craiu I, Pondarre C, Deho A, Maroni A, Oualha M, Amoura Z, Haroche J, Chommeloux J, Bajolle F, Beyler C, Bonacorsi S, Carcelain G, Koné-Paut I, Bader-Meunier B, Faye A, Meinzer U, Galeotti C, Melki I (2020) Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease (Kawa-COVID-19): a multicentre cohort. Ann Rheum Dis 79:999–1006. https://doi.org/10.1136/annrheumdis-2020-217960
76. Carroll E, Neumann H, Aguero-Rosenfeld ME, Lighter J, Czeisler BM, Melmed K, Lewis A (2020) Post-COVID-19 inflammatory syndrome manifesting as refractory status epilepticus. Epilepsia 61:e135–e139. https://doi.org/10.1111/epi.16683
77. Gianfrancesco M, Hyrich KL, Al-Adely S et al (2020) Characteristics associated with hospitalisation for COVID-19 in people with rheumatic disease: data from the COVID-19 Global Rheumatology Alliance physician-reported registry. Ann Rheum Dis 79:859–866. https://doi.org/10.1136/annrheumdis-2020-217871
78. Williamson EJ, Walker AJ, Bhaskaran K, Bacon S, Bates C, Morton CE, Curtis HJ, Mehrkar A, Evans D, Inglesby P, Cockburn J, McDonald HI, MacKenna B, Tomlinson L, Douglas IJ, Rentsch CT, Mathur R, Wong AYS, Grieve R, Harrison D, Forbes H, Schultze A, Croker R, Parry J, Hester F, Harper S, Perera R, Evans SJW, Smeeth L, Goldacre B (2020) Factors associated with COVID-19-related death using OpenSAFELY. Nature 584:430–436. https://doi.org/10.1038/s41586-020-2521-4
79. Jorge A, D'Silva KM, Cohen A et al (2021) Temporal trends in severe COVID-19 outcomes in patients with rheumatic disease: a cohort study. Lancet Rheumatol 3:e131–e137. https://doi.org/10.1016/S2665-9913(20)30422-7
80. Ahmed S, Gasparyan AY, Zimba O (2021) Comorbidities in rheumatic diseases need special consideration during the COVID-19 pandemic. Rheumatol Int 41:243–256. https://doi.org/10.1007/s00296-020-04764-5
81. Raghavan S, Gonakoti S, Asemota IR, Mba B (2020) A case of systemic lupus erythematosus flare triggered by severe coronavirus disease 2019. J Clin Rheumatol 26:234–235. https://doi.org/10.1097/RHU.0000000000001531
82. Ferri C, Giuggioli D, Raimondo V et al (2020) COVID-19 and rheumatic autoimmune systemic diseases: report of a large Italian patients series. Clin Rheumatol 39:3195–3204. https://doi.org/10.1007/s10067-020-05334-7
83. Gasparyan AY, Misra DP, Yessirkepov M, Zimba O (2020) Perspectives of immune therapy in coronavirus disease 2019. J Korean Med Sci 35:e176. https://doi.org/10.3346/jkms.2020.35.e176
84. WHO Solidarity Trial Consortium, Pan H, Peto R et al (2021) Repurposed antiviral drugs for Covid-19 - interim WHO solidarity trial results. N Engl J Med 384:497–511. https://doi.org/10.1056/NEJMoa2023184
85. Elavarasi A, Prasad M, Seth T, Sahoo RK, Madan K, Nischal N, Soneja M, Sharma A, Maulik SK, Shalimar, Garg P (2020) Chloroquine and hydroxychloroquine for the treatment of COVID-19: a systematic review and meta-analysis. J Gen Intern Med 35:3308–3314. https://doi.org/10.1007/s11606-020-06146-w
86. Tardif J-C, Bouabdallaoui N, L'Allier PL, et al (2021) Efficacy of colchicine in non-hospitalized patients with COVID-19. medRxiv 2021.01.26.21250494. https://doi.org/10.1101/2021.01.26.21250494

87. Alunno A, Najm A, Machado PM, Bertheussen H, Burmester GR, Carubbi F, de Marco G, Giacomelli R, Hermine O, Isaacs JD, Koné-Paut I, Magro-Checa C, McInnes I, Meroni PL, Quartuccio L, Ramanan AV, Ramos-Casals M, Rodríguez Carrio J, Schulze-Koops H, Stamm TA, Tas SW, Terrier B, McGonagle DG, Mariette X (2021) EULAR points to consider on pathophysiology and use of immunomodulatory therapies in COVID-19. Ann Rheum Dis: annrheumdis-2020-219724. https://doi.org/10.1136/annrheumdis-2020-219724
88. Cañas CA (2020) The triggering of post-COVID-19 autoimmunity phenomena could be associated with both transient immunosuppression and an inappropriate form of immune reconstitution in susceptible individuals. Med Hypotheses 145:110345. https://doi.org/10.1016/j.mehy.2020.110345
89. Shah S, Danda D, Kavadichanda C, Das S, Adarsh MB, Negi VS (2020) Autoimmune and rheumatic musculoskeletal diseases as a consequence of SARS-CoV-2 infection and its treatment. Rheumatol Int 40:1539–1554. https://doi.org/10.1007/s00296-020-04639-9
90. Lachmann PJ (2012) The use of antibodies in the prophylaxis and treatment of infections. Emerg Microbes Infect 1:e11. https://doi.org/10.1038/emi.2012.2
91. Kamal M, Abo Omirah M, Hussein A, Saeed H (2020) Assessment and characterisation of post-COVID-19 manifestations. Int J Clin Pract:e13746. https://doi.org/10.1111/ijcp.13746
92. Severe Covid-19 GWAS Group, Ellinghaus D, Degenhardt F et al (2020) Genomewide association study of severe Covid-19 with respiratory failure. N Engl J Med 383:1522–1534. https://doi.org/10.1056/NEJMoa2020283
93. Bekker P, Ebsworth K, Walters MJ, Berahovich RD, Ertl LS, Charvat TT, Punna S, Powers JP, Campbell JJ, Sullivan TJ, Jaen JC, Schall TJ (2015) CCR9 Antagonists in the treatment of ulcerative colitis. Mediat Inflamm 2015:628340–628310. https://doi.org/10.1155/2015/628340
94. Wang C-R, Liu M-F, Huang Y-H, Chen H-C (2004) Up-regulation of XCR1 expression in rheumatoid joints. Rheumatology (Oxford) 43:569–573. https://doi.org/10.1093/rheumatology/keh147
95. Umbrello M, Nespoli S, Pisano E et al Autoantibodies in severe COVID-19-related acute respiratory distress syndrome: just innocent bystanders? Int J Rheum Dis. https://doi.org/10.1111/1756-185X.14077
96. Shaw B, Daskareh M, Gholamrezanezhad A (2021) The lingering manifestations of COVID-19 during and after convalescence: update on long-term pulmonary consequences of coronavirus disease 2019 (COVID-19). Radiol Med 126:40–46. https://doi.org/10.1007/s11547-020-01295-8
97. Mitrani RD, Dabas N, Goldberger JJ (2020) COVID-19 cardiac injury: implications for long-term surveillance and outcomes in survivors. Heart Rhythm 17:1984–1990. https://doi.org/10.1016/j.hrthm.2020.06.026
98. Ahmed H, Patel K, Greenwood DC et al (2020) Long-term clinical outcomes in survivors of severe acute respiratory syndrome and Middle East respiratory syndrome coronavirus outbreaks after hospitalisation or ICU admission: a systematic review and meta-analysis. J Rehabil Med 52:jrm00063. https://doi.org/10.2340/16501977-2694