**COVID-19 and pulmonary circulation**

**The audience/context:** For a professor/consultant who wanted to understand the pathophysiology of COVID-19 and the pulmonary circulation. He wanted to use this as a background to research on forms of oxygen administration in COVID-19.

Was given this background info: Hypoxia could happen through the following mechanisms: 1) thrombotic occlusion of capillaries in pulmonary tree (microthrombosis) 2) damage of endothelium leading to impaired gaseous exchange 3) combination of the two causing pulmonary artery resistance and pressure?

Happy to expand to SARS and MERS.

**Date search conducted:** 24th April 2020

**Source(s):** PubMed, Medline, Embase

**Search strategy**: At end of document. Single lines for HDAS: [Reviewers Note 11/5/20: Consider also using exp CORONAVIRUS/ and exp “CORONAVIRUS INFECTIONS”/ subject headings in Medline and Pubmed]

**PubMed** ((pulmonary).ti AND ((physiolog\* OR patholog\* OR pathophysiolog\*).ti,ab OR (circulat\* OR circuit\* OR system OR "blood flow" OR tree).ti,ab OR (capillar\* OR arter\* OR vein\* OR venous OR vessel\*).ti,ab OR (thromb\* OR occlusion\* OR microthromb\*).ti,ab OR (endothelium).ti,ab OR (resist\* OR pressure\* OR hypertensi\*).ti,ab OR ("gas exchange" OR "gaseous exchange").ti,ab)) AND ((Coronavirus\*).af OR (COVID\*).af OR ("SARS-CoV-2").af OR ("2019-nCoV").af OR (ncov).af OR ("novel betacov").af OR ("novel betacoronavirus").af OR (SARS OR "severe acute respiratory syndrome").af OR (MERS OR "middle east respiratory syndrome").af)

**Medline** ((Coronavirus\*).ti,ab OR (COVID\*).ti,ab OR ("SARS-CoV-2").ti,ab OR ("2019-nCoV").af OR (ncov).af OR ("novel betacov").af OR ("novel betacoronavirus").af OR "SARS VIRUS"/ OR "MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS"/ OR BETACORONAVIRUS/) AND ((pulmonary AND (physiolog\* OR patholog\* OR pathophysiolog\*)).ti,ab OR (pulmonary ADJ2 (circulat\* OR circuit\* OR system\* OR "blood flow" OR tree)).ti,ab OR (pulmonary ADJ3 (capillar\* OR arter\* OR vein\* OR venous OR vessel\*)).ti,ab OR (pulmonary ADJ2 (thromb\* OR occlusion\* OR microthromb\*)).ti,ab OR (pulmonary ADJ5 endothelium).ti,ab OR (gas\* ADJ2 exchange\*).ti,ab OR (pulmonary ADJ3 (resist\* OR pressure\* OR hypertension\*)).ti,ab OR (endothelium ADJ2 (damag\* OR impair\*)).ti,ab OR (alveol\*).ti,ab OR (PA ADJ2 pressure\*).ti,ab OR (pulmonary ADJ3 (parameter\* OR measurement\*)).ti,ab OR "PULMONARY VEINS"/ OR exp "PULMONARY EMBOLISM"/ OR "PULMONARY ARTERIAL HYPERTENSION"/ OR "HYPERTENSION, PULMONARY"/ OR exp "PULMONARY GAS EXCHANGE"/ OR exp "PULMONARY ALVEOLI"/ OR "PULMONARY ARTERY"/ OR "PULMONARY CIRCULATION"/ OR ((lung\* OR respiratory) ADJ2 circulat\*).ti,ab OR ((lung\* OR pulmonary) ADJ2 (emblous OR emboli\*)).ti,ab OR ((lung\* OR pulmonary OR respiratory) ADJ2 perfusion).ti,ab OR (hypoxic ADJ2 vasoconstriction).ti,ab)

**Embase**

((Coronavirus\*).ti,ab OR (COVID\*).ti,ab OR ("SARS-CoV-2").ti,ab OR ("2019-nCoV").af OR (ncov).af OR ("novel betacov").af OR ("novel betacoronavirus").af OR "MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS"/ OR "SARS-RELATED CORONAVIRUS"/ OR BETACORONAVIRUS/ OR CORONAVIRINAE/) AND ((pulmonary AND (physiolog\* OR patholog\* OR pathophysiolog\*)).ti,ab OR (pulmonary ADJ2 (circulat\* OR circuit\* OR system\* OR "blood flow" OR tree)).ti,ab OR (pulmonary ADJ3 (capillar\* OR arter\* OR vein\* OR venous OR vessel\*)).ti,ab OR (pulmonary ADJ2 (thromb\* OR occlusion\* OR microthromb\*)).ti,ab OR (pulmonary ADJ5 endothelium).ti,ab OR (gas\* ADJ2 exchange\*).ti,ab OR (pulmonary ADJ3 (resist\* OR pressure\* OR hypertension\*)).ti,ab OR (endothelium ADJ2 (damag\* OR impair\*)).ti,ab OR (alveol\*).ti,ab OR (PA ADJ2 pressure\*).ti,ab OR (pulmonary ADJ3 (parameter\* OR measurement\*)).ti,ab OR "LUNG CIRCULATION"/ OR "PULMONARY VEIN"/ OR exp "PULMONARY ARTERY"/ OR "LUNG EMBOLISM"/ OR exp "PULMONARY VASCULAR DISEASE"/ OR "LUNG GAS EXCHANGE"/ OR exp "LUNG ALVEOLUS"/ OR ((lung\* OR respiratory) ADJ2 circulat\*).ti,ab OR ((lung\* OR pulmonary) ADJ2 (emblous OR emboli\*)).ti,ab OR ((lung\* OR pulmonary OR respiratory) ADJ2 perfusion).ti,ab OR (hypoxic ADJ2 vasoconstriction).ti,ab)

24 Apr 20 - 11:37

HDAS Export

Strategy COVID-19 and pulmonary circulation

[See full search strategy](#historyanchor)

Strategy 841548/saved

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[3. Pathological evidence of pulmonary thrombotic phenomena in severe COVID-19.](#38841d8b-b601-274c-b3a1-c0645de93362-3)

[4. Pulmonary thrombosis in 2019-nCoV pneumonia?](#3ec8739e-89aa-5bd1-64f9-15c90d89a5eb-4)

[5. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be harmful in patients with diabetes during COVID-19 pandemic.](#fda2c160-255d-f619-3c8c-267f9fc86026-5)

[6. Angiotensin Converting Enzyme 2: SARS-CoV-2 Receptor and Regulator of the Renin-Angiotensin System.](#e3a080d9-70b3-044f-852c-15ab11f9e3e2-6)

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[12. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases.](#3001ecb1-5e3d-ecd0-79ae-7a8bff45e21b-12)

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[14. Why is Coronavirus Disease 2019 not as severe in children?-A look at type 2 alveolar cells.](#3e88b752-1227-b3f4-363b-f6ddd764f55c-14)

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[16. Severe Acute Proximal Pulmonary Embolism and COVID-19: A Word of Caution.](#4b617bda-5146-8cb7-0768-f30254f7e8c7-16)

[17. COVID-19 complicated by Acute Pulmonary Embolism and Right-Sided Heart Failure.](#90dd1c89-0cbc-6d0a-1615-8115ecaf70c9-17)

[18. COVID-19 pneumonia with hemoptysis: Acute segmental pulmonary emboli associated with novel coronavirus infection.](#0e4471bd-a64a-f918-3d19-a533ce413d72-18)

[19. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection.](#6db0e2f1-a364-c3fb-6df3-cc6919d0b736-19)

[20. Ultra-high-resolution computed tomography can demonstrate alveolar collapse in novel coronavirus (COVID-19) pneumonia.](#ad49e943-4dac-c958-6ba4-dafa75957bd3-20)

[21. Covid-19 Does Not Lead to a "Typical" Acute Respiratory Distress Syndrome](#5925bae3-73e8-81af-e165-401e4a9b7816-21)

[22. Acute pulmonary embolism and COVID-19 pneumonia: a random association?](#22ec6416-ad7c-a635-a4b4-e303518aee32-22)

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[25. Middle East Respiratory Syndrome Coronavirus Causes Multiple Organ Damage and Lethal Disease in Mice Transgenic for Human Dipeptidyl Peptidase 4.](#06e45c11-3f26-75ee-6c8e-c00cc483a633-25)

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**1. Acute pulmonary embolism in a patient with COVID-19 pneumonia**

**Author(s):** Cellina M.; Oliva G.

**Source:** Diagnostic and Interventional Imaging; 2020

**Publication Date:** 2020

**Publication Type(s):** Article

Available at [Diagnostic and Interventional Imaging](https://doi.org/10.1016/j.diii.2020.04.001) - from Unpaywall

**Database:** EMBASE

**2. The Role of Cytokines including Interleukin-6 in COVID-19 induced Pneumonia and Macrophage Activation Syndrome-Like Disease**

**Author(s):** McGonagle D.; Sharif K.; Bridgewood C.; O'Regan A.

**Source:** Autoimmunity Reviews; 2020

**Publication Date:** 2020

**Publication Type(s):** Review

**PubMedID:** 32251717

Available at [Autoimmunity reviews](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

**Abstract:**Severe COVID-19 associated pneumonia patients may exhibit features of systemic hyper-inflammation designated under the umbrella term of macrophage activation syndrome (MAS) or cytokine storm, also known as secondary haemophagocytic lymphohistocytosis (sHLH). This is distinct from HLH associated with immunodeficiency states termed primary HLH -with radically different therapy strategies in both situations. COVID-19 infection with MAS typically occurs in subjects with adult respiratory distress syndrome (ARDS) and historically, non-survival in ARDS was linked to sustained IL-6 and IL-1 elevation. We provide a model for the classification of MAS to stratify the MAS-like presentation in COVID-19 pneumonia and explore the complexities of discerning ARDS from MAS. We discuss the potential impact of timing of anti-cytokine therapy on viral clearance and the impact of such therapy on intra-pulmonary macrophage activation and emergent pulmonary vascular disease.Copyright © 2020

**Database:** EMBASE

**3. Pathological evidence of pulmonary thrombotic phenomena in severe COVID-19.**

**Author(s):** Dolhnikoff M; Duarte-Neto AN; de Almeida Monteiro RA; Ferraz da Silva LF; Pierre de Oliveira E; Nascimento Saldiva PH; Mauad T; Marcia Negri E

**Source:** Journal of thrombosis and haemostasis : JTH; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Letter

**PubMedID:** 32294295

Available at [Journal of thrombosis and haemostasis : JTH](https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14844) - from Wiley Online Library

Available at [Journal of thrombosis and haemostasis : JTH](http://doi.wiley.com/10.1111/jth.14844) - from IngentaConnect Full text ends 1 year ago (1 year embargo)

Available at [Journal of thrombosis and haemostasis : JTH](http://www.uhl-library.nhs.uk/directpages/uhlarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from NULJ library) - click this link for more information Local Print Collection [location] : UHL Libraries On Request (Free).

Available at [Journal of thrombosis and haemostasis : JTH](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

**Abstract:**Between February and March 2020, the Journal of Thrombosis and Hemosthasis has published four papers addressing the intricate, complex and still little understood relation between COVID-19 and thrombogenesis (1-4). ARS-Cov-2 induces in severe cases a cytokine storm that ultimately leads to the activation of the coagulation cascade, causing thrombotic phenomena (5). There is a further strong link between abnormal coagulation parameters (D-dimer and fibrin degradation products) and mortality. Tang et al. described that 71.4% of nonsurvivors and 0.6% of survivors showed evidence of disseminated intravascular coagulation (DIC), suggesting that DIC is a frequent occurrence in severe COVID-19 (4). The frequency of DIC in these patients is much higher than that reported for severe SARS (6).

**Database:** PubMed

**4. Pulmonary thrombosis in 2019-nCoV pneumonia?**

**Author(s):** Marongiu F; Grandone E; Barcellona D

**Source:** Journal of thrombosis and haemostasis : JTH; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Letter

**PubMedID:** 32293083

Available at [Journal of thrombosis and haemostasis : JTH](https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14818) - from Wiley Online Library

Available at [Journal of thrombosis and haemostasis : JTH](http://doi.wiley.com/10.1111/jth.14818) - from IngentaConnect Full text ends 1 year ago (1 year embargo)

Available at [Journal of thrombosis and haemostasis : JTH](http://www.uhl-library.nhs.uk/directpages/uhlarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from NULJ library) - click this link for more information Local Print Collection [location] : UHL Libraries On Request (Free).

Available at [Journal of thrombosis and haemostasis : JTH](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [Journal of thrombosis and haemostasis : JTH](https://doi.org/10.1111/jth.14818) - from Unpaywall

**Database:** PubMed

**5. Angiotensin-converting enzyme inhibitors and angiotensin receptor blockers may be harmful in patients with diabetes during COVID-19 pandemic.**

**Author(s):** Cure, Erkan; Cumhur Cure, Medine

**Source:** Diabetes & metabolic syndrome; Apr 2020; vol. 14 (no. 4); p. 349-350

**Publication Date:** Apr 2020

**Publication Type(s):** Journal Article

**PubMedID:** 32311651

Available at [Diabetes & Metabolic Syndrome: Clinical Research & Reviews](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

**Abstract:**The novel coronavirus disease 2019 (COVID-19) outbreak once again demonstrated the importance of the renin-angiotensin system (RAS) in patients with diabetes. Activation of the RAS increases in patients with diabetes. The virus attaches to the ACE2 enzyme at low cytosolic pH values and enters into the cell and causes infection. Especially in the presence of diabetes mellitus and accompanying comorbid conditions such as hypertension, obesity, old age, and smoking, cytosolic pH is low, thus the virus easily may enter the cell by attaching to ACE2. ACEIs and ARBs lead to a reduction in angiotensin II level by increasing the ACE2 level, thus they cause a low cytosolic pH. Increased cardiac ACE2 levels due to ACEIs and ARBs can trigger cardiac arrhythmias and myocarditis by causing the virus to easily enter the heart tissue. There is ACE2 activity in the rostral ventrolateral medulla in the brain stem. The release of angiotensin 1-7 in the brain stem leads to the activation of the sympathetic nervous system. This activation causes systemic vasoconstriction and the patient's blood pressure increases. The most important event is the increased sympathetic activity via the central stimulation, this activity increases pulmonary capillary leaking, causing the ARDS. As the cytosolic pH, which is already low in patients with diabetes will decrease further with the mechanisms mentioned above, the viral load will increase and the infection will be exacerbated. As a result, the use of ACEIs and ARBs in patients with diabetes can lead to increased morbidity and mortality of COVID-19.

**Database:** Medline

**6. Angiotensin Converting Enzyme 2: SARS-CoV-2 Receptor and Regulator of the Renin-Angiotensin System.**

**Author(s):** Gheblawi, Mahmoud; Wang, Kaiming; Viveiros, Anissa; Nguyen, Quynh; Zhong, Jiu-Chang; Turner, Anthony J; Raizada, Mohan K; Grant, Maria B; Oudit, Gavin Y

**Source:** Circulation research; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Journal Article

**PubMedID:** 32264791

Available at [Circulation research](https://go.openathens.net/redirector/nhs?url=http%3A%2F%2Fovidsp.ovid.com%2Fovidweb.cgi%3FT%3DJS%26PAGE%3Dfulltext%26D%3Dovft%26CSC%3DY%26NEWS%3DN%26SEARCH%3D%2210.1161%2FCIRCRESAHA.120.317015%22.di) - from Ovid (LWW High Impact Collection) - 2019

Available at [Circulation research](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [Circulation research](https://www.ahajournals.org/doi/reader/10.1161/CIRCRESAHA.120.317015) - from Unpaywall

**Abstract:**Angiotensin-converting enzyme (ACE2) has a multiplicity of physiological roles that revolve around its trivalent function: a negative regulator of the renin-angiotensin system (RAS), facilitator of amino acid transport, and the SARS-CoV and SARS-CoV-2 receptor. ACE2 is widely expressed, including, in the lungs, cardiovascular system, gut, kidneys, central nervous system, and adipose tissue. ACE2 has recently been identified as the SARS-CoV-2 receptor, the infective agent responsible for COVID-19, providing a critical link between immunity, inflammation, ACE2, and cardiovascular disease. Although sharing a close evolutionary relationship with SARS-CoV, the receptor-binding domain of SARS-CoV-2 differs in several key amino acid residues, allowing for stronger binding affinity with the human ACE2 receptor, which may account for the greater pathogenicity of SARS-CoV-2. The loss of ACE2 function following binding by SARS-CoV-2 is driven by endocytosis and activation of proteolytic cleavage and processing. The ACE2 system is a critical protective pathway against heart failure with reduced and preserved ejection fraction including, myocardial infarction and hypertension, and against lung disease and diabetes. The control of gut dysbiosis and vascular permeability by ACE2 has emerged as an essential mechanism of pulmonary hypertension and diabetic cardiovascular complications. Recombinant ACE2, gene-delivery of Ace2, Ang 1-7 analogs, and Mas receptor agonists enhance ACE2 action and serve as potential therapies for disease conditions associated with an activated RAS. Recombinant human ACE2 has completed clinical trials and efficiently lowered or increased plasma angiotensin II and angiotensin 1-7 levels, respectively. Our review summarizes the progress over the past 20 years, highlighting the critical role of ACE2 as the novel SARS-CoV-2 receptor and as the negative regulator of the RAS, together with implications for the COVID-19 pandemic and associated cardiovascular diseases.

**Database:** Medline

**7. Suspected myocardial injury in patients with COVID-19: Evidence from front-line clinical observation in Wuhan, China.**

**Author(s):** Deng, Qing; Hu, Bo; Zhang, Yao; Wang, Hao; Zhou, Xiaoyang; Hu, Wei; Cheng, Yuting; Yan, Jie; Ping, Haiqin; Zhou, Qing

**Source:** International journal of cardiology; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Journal Article

**PubMedID:** 32291207

Available at [International journal of cardiology](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [International journal of cardiology](https://doi.org/10.1016/j.ijcard.2020.03.087) - from Unpaywall

**Abstract:**BACKGROUNDA novel coronavirus disease (COVID-19) in Wuhan has caused an outbreak and become a major public health issue in China and great concern from international community. Myocarditis and myocardial injury were suspected and may even be considered as one of the leading causes for death of COVID-19 patients. Therefore, we focused on the condition of the heart, and sought to provide firsthand evidence for whether myocarditis and myocardial injury were caused by COVID-19.METHODSWe enrolled patients with confirmed diagnosis of COVID-19 retrospectively and collected heart-related clinical data, mainly including cardiac imaging findings, laboratory results and clinical outcomes. Serial tests of cardiac markers were traced for the analysis of potential myocardial injury/myocarditis.RESULTS112 COVID-19 patients were enrolled in our study. There was evidence of myocardial injury in COVID-19 patients and 14 (12.5%) patients had presented abnormalities similar to myocarditis. Most of patients had normal levels of troponin at admission, that in 42 (37.5%) patients increased during hospitalization, especially in those that died. Troponin levels were significantly increased in the week preceding the death. 15 (13.4%) patients have presented signs of pulmonary hypertension. Typical signs of myocarditis were absent on echocardiography and electrocardiogram.CONCLUSIONSThe clinical evidence in our study suggested that myocardial injury is more likely related to systemic consequences rather than direct damage by the 2019 novel coronavirus. The elevation in cardiac markers was probably due to secondary and systemic consequences and can be considered as the warning sign for recent adverse clinical outcomes of the patients.

**Database:** Medline

**8. Incidence of thrombotic complications in critically ill ICU patients with COVID-19.**

**Author(s):** Klok, F A; Kruip, M J H A; van der Meer, N J M; Arbous, M S; Gommers, D A M P J; Kant, K M; Kaptein, F H J; van Paassen, J; Stals, M A M; Huisman, M V; Endeman, H

**Source:** Thrombosis research; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Journal Article

**PubMedID:** 32291094

Available at [Thrombosis research](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [Thrombosis research](https://doi.org/10.1016/j.thromres.2020.04.013) - from Unpaywall

**Abstract:**INTRODUCTIONCOVID-19 may predispose to both venous and arterial thromboembolism due to excessive inflammation, hypoxia, immobilisation and diffuse intravascular coagulation. Reports on the incidence of thrombotic complications are however not available.METHODSWe evaluated the incidence of the composite outcome of symptomatic acute pulmonary embolism (PE), deep-vein thrombosis, ischemic stroke, myocardial infarction or systemic arterial embolism in all COVID-19 patients admitted to the ICU of 2 Dutch university hospitals and 1 Dutch teaching hospital.RESULTSWe studied 184 ICU patients with proven COVID-19 pneumonia of whom 23 died (13%), 22 were discharged alive (12%) and 139 (76%) were still on the ICU on April 5th 2020. All patients received at least standard doses thromboprophylaxis. The cumulative incidence of the composite outcome was 31% (95%CI 20-41), of which CTPA and/or ultrasonography confirmed VTE in 27% (95%CI 17-37%) and arterial thrombotic events in 3.7% (95%CI 0-8.2%). PE was the most frequent thrombotic complication (n = 25, 81%). Age (adjusted hazard ratio (aHR) 1.05/per year, 95%CI 1.004-1.01) and coagulopathy, defined as spontaneous prolongation of the prothrombin time > 3 s or activated partial thromboplastin time > 5 s (aHR 4.1, 95%CI 1.9-9.1), were independent predictors of thrombotic complications.CONCLUSIONThe 31% incidence of thrombotic complications in ICU patients with COVID-19 infections is remarkably high. Our findings reinforce the recommendation to strictly apply pharmacological thrombosis prophylaxis in all COVID-19 patients admitted to the ICU, and are strongly suggestive of increasing the prophylaxis towards high-prophylactic doses, even in the absence of randomized evidence.

**Database:** Medline

**9. Microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome (MicroCLOTS): an atypical acute respiratory distress syndrome working hypothesis.**

**Author(s):** Ciceri, Fabio; Beretta, Luigi; Scandroglio, Anna Mara; Colombo, Sergio; Landoni, Giovanni; Ruggeri, Annalisa; Peccatori, Jacopo; D'Angelo, Armando; De Cobelli, Francesco; Rovere-Querini, Patrizia; Tresoldi, Moreno; Dagna, Lorenzo; Zangrillo, Alberto

**Source:** Critical care and resuscitation : journal of the Australasian Academy of Critical Care Medicine; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Journal Article

**PubMedID:** 32294809

Available at [Critical care and resuscitation : journal of the Australasian Academy of Critical Care Medicine](http://search.ebscohost.com/login.aspx?direct=true&scope=site&site=ehost-live&db=mdc&AN=32294809) - from EBSCO (MEDLINE Complete)

Available at [Critical care and resuscitation : journal of the Australasian Academy of Critical Care Medicine](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

**Abstract:**We suggest the use of MicroCLOTS (microvascular COVID-19 lung vessels obstructive thromboinflammatory syndrome) as a new name for severe pulmonary coronavirus disease 2019 (COVID-19). We hypothesise that, in predisposed individuals, alveolar viral damage is followed by an inflammatory reaction and by microvascular pulmonary thrombosis. This progressive endothelial thromboinflammatory syndrome may also involve the microvascular bed of the brain and other vital organs, leading to multiple organ failure and death. Future steps in the understanding of the disease and in the identification of treatments may benefit from this definition and hypothesised sequence of events.

**Database:** Medline

**10. Reply to the comment.**

**Author(s):** Tang, Ning

**Source:** Journal of thrombosis and haemostasis : JTH; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Letter

**PubMedID:** 32291906

Available at [Journal of thrombosis and haemostasis : JTH](https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14843) - from Wiley Online Library

Available at [Journal of thrombosis and haemostasis : JTH](http://doi.wiley.com/10.1111/jth.14843) - from IngentaConnect Full text ends 1 year ago (1 year embargo)

Available at [Journal of thrombosis and haemostasis : JTH](http://www.uhl-library.nhs.uk/directpages/uhlarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from NULJ library) - click this link for more information Local Print Collection [location] : UHL Libraries On Request (Free).

Available at [Journal of thrombosis and haemostasis : JTH](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [Journal of thrombosis and haemostasis : JTH](https://doi.org/10.1111/jth.14843) - from Unpaywall

**Abstract:**We appreciate the opportunity to respond to the comments by Dr. Marongiu et al., they presented that as only laboratory findings of Disseminated Intravascular Coagulation (DIC) but no bleeding was mentioned, indicating that there was not an overt DIC in our patients, instead, the abnormal laboratory findings could be an expression of local DIC, i.e. a pulmonary vascular thrombosis. Thus they suggested the anticoagulant treatment in patients with coronavirus disease 2019 (COVID-19).

**Database:** Medline

**11. Tissue Plasminogen Activator (tPA) Treatment for COVID-19 Associated Acute Respiratory Distress Syndrome (ARDS): A Case Series.**

**Author(s):** Wang, Janice; Hajizadeh, Negin; Moore, Ernest E; McIntyre, Robert C; Moore, Peter K; Veress, Livia A; Yaffe, Michael B; Moore, Hunter B; Barrett, Christopher D

**Source:** Journal of thrombosis and haemostasis : JTH; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Case Reports

**PubMedID:** 32267998

Available at [Journal of thrombosis and haemostasis : JTH](https://onlinelibrary.wiley.com/doi/full/10.1111/jth.14828) - from Wiley Online Library

Available at [Journal of thrombosis and haemostasis : JTH](http://doi.wiley.com/10.1111/jth.14828) - from IngentaConnect Full text ends 1 year ago (1 year embargo)

Available at [Journal of thrombosis and haemostasis : JTH](http://www.uhl-library.nhs.uk/directpages/uhlarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from NULJ library) - click this link for more information Local Print Collection [location] : UHL Libraries On Request (Free).

Available at [Journal of thrombosis and haemostasis : JTH](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [Journal of thrombosis and haemostasis : JTH](https://onlinelibrary.wiley.com/doi/pdfdirect/10.1111/jth.14828) - from Unpaywall

**Abstract:**A hallmark of severe COVID-19 is coagulopathy, with 71.4% of patients who die of COVID-19 meeting ISTH criteria for disseminated intravascular coagulation (DIC) while only 0.6% of patients who survive meet these criteria (1). Additionally, it has become clear that this is not a bleeding diathesis but rather a predominantly pro-thrombotic DIC with high venous thromboembolism rates, elevated D-dimer levels, high fibrinogen levels in concert with low anti-thrombin levels, and pulmonary congestion with microvascular thrombosis and occlusion on pathology in addition to mounting experience with high rates of central line thrombosis and vascular occlusive events (e.g. ischemic limbs, strokes, etc.) observed by those who care for critically ill COVID-19 patients (1-7). There is evidence in both animals and humans that fibrinolytic therapy in Acute Lung Injury and ARDS improves survival, which also points to fibrin deposition in the pulmonary microvasculature as a contributory cause of ARDS and would be expected to be seen in patients with ARDS and concomitant diagnoses of DIC on their laboratory values such as what is observed in more than 70% of those who die of COVID-19 (8-10).

**Database:** Medline

**12. Complement associated microvascular injury and thrombosis in the pathogenesis of severe COVID-19 infection: A report of five cases.**

**Author(s):** Magro, Cynthia; Mulvey, J Justin; Berlin, David; Nuovo, Gerard; Salvatore, Steven; Harp, Joanna; Baxter-Stoltzfus, Amelia; Laurence, Jeffrey

**Source:** Translational research : the journal of laboratory and clinical medicine; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Journal Article

**PubMedID:** 32299776

Available at [Translational research : the journal of laboratory and clinical medicine](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [Translational research : the journal of laboratory and clinical medicine](https://doi.org/10.1016/j.trsl.2020.04.007) - from Unpaywall

**Abstract:**Acute respiratory failure and a systemic coagulopathy are critical aspects of the morbidity and mortality characterizing infection with severe acute respiratory distress syndrome-associated coronavirus-2 (SARS-CoV-2), the etiologic agent of Coronavirus disease 2019 (COVID-19). We examined skin and lung tissues from 5 patients with severe COVID-19 characterized by respiratory failure (n=5) and purpuric skin rash (n=3). The pattern of COVID-19 pneumonitis was predominantly a pauci-inflammatory septal capillary injury with significant septal capillary mural and luminal fibrin deposition and permeation of the inter-alveolar septa by neutrophils. No viral cytopathic changes were observed and the diffuse alveolar damage (DAD) with hyaline membranes, inflammation, and type II pneumocyte hyperplasia, hallmarks of classic ARDS, were not prominent. These pulmonary findings were accompanied by significant deposits of terminal complement components C5b-9 (membrane attack complex), C4d, and mannose binding lectin (MBL)-associated serine protease (MASP)2, in the microvasculature, consistent with sustained, systemic activation of the alternative and lectin-based complement pathways. The purpuric skin lesions similarly showed a pauci-inflammatory thrombogenic vasculopathy, with deposition of C5b-9 and C4d in both grossly involved and normally-appearing skin. In addition, there was co-localization of COVID-19 spike glycoproteins with C4d and C5b-9 in the inter-alveolar septa and the cutaneous microvasculature of two cases examined. In conclusion, at least a subset of sustained, severe COVID-19 may define a type of catastrophic microvascular injury syndrome mediated by activation of complement pathways and an associated procoagulant state. It provides a foundation for further exploration of the pathophysiologic importance of complement in COVID-19, and could suggest targets for specific intervention.

**Database:** Medline

**13. Pathological study of the 2019 novel coronavirus disease (COVID-19) through postmortem core biopsies.**

**Author(s):** Tian, Sufang; Xiong, Yong; Liu, Huan; Niu, Li; Guo, Jianchun; Liao, Meiyan; Xiao, Shu-Yuan

**Source:** Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Journal Article

**PubMedID:** 32291399

Available at [Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [Modern pathology : an official journal of the United States and Canadian Academy of Pathology, Inc](https://www.nature.com/articles/s41379-020-0536-x.pdf) - from Unpaywall

**Abstract:**Data on pathologic changes of the 2019 novel coronavirus disease (COVID-19) are scarce. To gain knowledge about the pathology that may contribute to disease progression and fatality, we performed postmortem needle core biopsies of lung, liver, and heart in four patients who died of COVID-19 pneumonia. The patients' ages ranged from 59 to 81, including three males and one female. Each patient had at least one underlying disease, including immunocompromised status (chronic lymphocytic leukemia and renal transplantation) or other conditions (cirrhosis, hypertension, and diabetes). Time from disease onset to death ranged from 15 to 52 days. All patients had elevated white blood cell counts, with significant rise toward the end, and all had lymphocytopenia except for the patient with leukemia. Histologically, the main findings are in the lungs, including injury to the alveolar epithelial cells, hyaline membrane formation, and hyperplasia of type II pneumocytes, all components of diffuse alveolar damage. Consolidation by fibroblastic proliferation with extracellular matrix and fibrin forming clusters in airspaces is evident. In one patient, the consolidation consists of abundant intra-alveolar neutrophilic infiltration, consistent with superimposed bacterial bronchopneumonia. The liver exhibits mild lobular infiltration by small lymphocytes, and centrilobular sinusoidal dilation. Patchy necrosis is also seen. The heart shows only focal mild fibrosis and mild myocardial hypertrophy, changes likely related to the underlying conditions. In conclusion, the postmortem examinations show advanced diffuse alveolar damage, as well as superimposed bacterial pneumonia in some patients. Changes in the liver and heart are likely secondary or related to the underlying diseases.

**Database:** Medline

**14. Why is Coronavirus Disease 2019 not as severe in children?-A look at type 2 alveolar cells.**

**Author(s):** Im, Daniel D

**Source:** Pediatric pulmonology; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Journal Article

**PubMedID:** 32314538

Available at [Pediatric Pulmonology](https://go.openathens.net/redirector/nhs?url=https%3A%2F%2Fonlinelibrary.wiley.com%2Fdoi%2Ffull%2F10.1002%2Fppul.24786) - from Wiley Online Library Medicine and Nursing Collection 2019 - NHS

Available at [Pediatric Pulmonology](http://www.uhl-library.nhs.uk/directpages/uhlarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from NULJ library) - click this link for more information Local Print Collection [location] : UHL Libraries On Request (Free).

Available at [Pediatric Pulmonology](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

**Database:** Medline

**15. Diagnostic evaluation of pulmonary embolism during the COVID-19 pandemic**

**Author(s):** Zuckier L.S.; Moadel R.M.; Freeman L.; Haramati L.B.

**Source:** Journal of nuclear medicine : official publication, Society of Nuclear Medicine; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Article

**PubMedID:** 32238427

Available at [Journal of nuclear medicine : official publication, Society of Nuclear Medicine](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [Journal of nuclear medicine : official publication, Society of Nuclear Medicine](http://jnm.snmjournals.org/content/early/2020/04/01/jnumed.120.245571.full.pdf) - from Unpaywall

**Database:** EMBASE

**16. Severe Acute Proximal Pulmonary Embolism and COVID-19: A Word of Caution.**

**Author(s):** Fabre, Olivier; Rebet, Olivier; Carjaliu, Ionut; Radutoiu, Mihai; Gautier, Laurence; Hysi, Ilir

**Source:** The Annals of thoracic surgery; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Case Reports

**PubMedID:** 32305287

Available at [The Annals of thoracic surgery](https://linkinghub.elsevier.com/retrieve/pii/S0003497520305701?goto=sd) - from ScienceDirect Please click on 'Sign in' and then on 'OpenAthens' for the site to recognise your Athens account and provide access to the full range of issues.

Available at [The Annals of thoracic surgery](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

**Abstract:**Acute pulmonary embolism is an uncharacteristic presentation in patients with COVID-19. Here we describe the case of a young woman presenting with severe pulmonary embolism, without any associated symptoms of infections. A clot in a patent foramen ovale was noted. Despite emergency surgical embolectomy, her clinical conditions continued to deteriorate. She was put on extracorporeal life support and tested positive for COVID-19. She died of multiorgan failure on day 10. COVID-19 may have a thrombogenic effect and it may need to be considered in cases of pulmonary embolism and in absence of any obvious risk factor.

**Database:** Medline

**17. COVID-19 complicated by Acute Pulmonary Embolism and Right-Sided Heart Failure.**

**Author(s):** Ullah, Waqas; Saeed, Rehan; Sarwar, Usman; Patel, Rajesh; Fischman, David L

**Source:** JACC. Case reports; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Case Reports

**PubMedID:** 32313884

**Abstract:**A patient with Coronavirus Disease-2019 (COVID-19) developed sudden shortness of breath and hypoxia. She was diagnosed with a massive pulmonary embolism (PE) complicated by right sided heart failure, which was successfully managed conservatively. This marks the first report of COVID-19 induced PE in association with acute heart failure.

**Database:** Medline

**18. COVID-19 pneumonia with hemoptysis: Acute segmental pulmonary emboli associated with novel coronavirus infection.**

**Author(s):** Casey K; Iteen A; Nicolini R; Auten J

**Source:** The American journal of emergency medicine; Apr 2020

**Publication Date:** Apr 2020

**Publication Type(s):** Case Reports

**PubMedID:** 32312574

Available at [The American journal of emergency medicine](http://www.uhl-library.nhs.uk/directpages/uhlarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from NULJ library) - click this link for more information Local Print Collection [location] : UHL Libraries On Request (Free).

Available at [The American journal of emergency medicine](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [The American journal of emergency medicine](https://doi.org/10.1016/j.ajem.2020.04.011) - from Unpaywall

**Abstract:**Recent retrospective studies from Wuhan, China suggest Novel Coronavirus Disease 2019 (COVID-19) may be associated with a hypercoagulable state and increased risk for venous thromboembolism. The overlap in the signs and symptoms of COVID-19 associated Acute Respiratory Distress Syndrome (ARDS) and COVID-19 with concurrent pulmonary embolism creates a diagnostic challenge for emergency medicine physicians in patients already at risk for renal impairment. However, identifying features atypical for COVID-19 alone may play a role in the judicious use of Computed Tomography Angiography among these patients. Hemoptysis is seen in roughly 13% of pulmonary embolism cases and infrequently reported among COVID-19 infections. Additionally, the presence of right heart strain on electrocardiography (EKG) is a well described clinical presentations of pulmonary embolism not reported commonly with COVID-19 infections.

**Database:** PubMed

**19. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection.**

**Author(s):** Zou, Xin; Chen, Ke; Zou, Jiawei; Han, Peiyi; Hao, Jie; Han, Zeguang

**Source:** Frontiers of medicine; Mar 2020

**Publication Date:** Mar 2020

**Publication Type(s):** Journal Article

**PubMedID:** 32170560

Available at [Frontiers of medicine](https://link.springer.com/content/pdf/10.1007/s11684-020-0754-0.pdf) - from Unpaywall

**Abstract:**It has been known that, the novel Coronavirus, 2019-nCoV, which is considered similar to SARS-CoV and originated from Wuhan (China), invades human cells via the receptor angiotensin converting enzyme II (ACE2). Moreover, lung cells that have ACE2 expression may be the main target cells during 2019-nCoV infection. However, some patients also exhibit non-respiratory symptoms, such as kidney failure, implying that 2019-nCoV could also invade other organs. To construct a risk map of different human organs, we analyzed the single-cell RNA sequencing (scRNA-seq) datasets derived from major human physiological systems, including the respiratory, cardiovascular, digestive, and urinary systems. Through scRNA-seq data analyses, we identified the organs at risk, such as lung, heart, esophagus, kidney, bladder, and ileum, and located specific cell types (i.e., type II alveolar cells (AT2), myocardial cells, proximal tubule cells of the kidney, ileum and esophagus epithelial cells, and bladder urothelial cells), which are vulnerable to 2019-nCoV infection. Based on the findings, we constructed a risk map indicating the vulnerability of different organs to 2019-nCoV infection. This study may provide potential clues for further investigation of the pathogenesis and route of 2019-nCoV infection.

**Database:** Medline

**20. Ultra-high-resolution computed tomography can demonstrate alveolar collapse in novel coronavirus (COVID-19) pneumonia.**

**Author(s):** Iwasawa, Tae; Sato, Midori; Yamaya, Takafumi; Sato, Yozo; Uchida, Yoshinori; Kitamura, Hideya; Hagiwara, Eri; Komatsu, Shigeru; Utsunomiya, Daisuke; Ogura, Takashi

**Source:** Japanese journal of radiology; Mar 2020

**Publication Date:** Mar 2020

**Publication Type(s):** Journal Article

**PubMedID:** 32236856

Available at [Japanese journal of radiology](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [Japanese journal of radiology](https://link.springer.com/content/pdf/10.1007/s11604-020-00956-y.pdf) - from Unpaywall

**Abstract:**PURPOSETo review the chest computed tomography (CT) findings on the ultra-high-resolution CT (U-HRCT) in patients with the Novel coronavirus disease 2019 (COVID-19).MATERIALS AND METHODSIn February 2020, six consecutive patients with COVID-19 pneumonia (median age, 69 years) underwent U-HR CT imaging. U-HR-CT has a larger matrix size of 1024 × 1024 thinner slice thickness of 0.25 mm and can demonstrate terminal bronchioles in the normal lungs; as a result, Reid's secondary lobules and their abnormalities can be identified. The distribution and hallmarks (ground-glass opacity, consolidation with or without architectural distortion, linear opacity, crazy paving) of the lung opacities on U-HRCT were visually evaluated on a 1 K monitor by two experienced reviewers. The CT lung volume was measured, and the ratio of the measured lung volume to the predicted total lung capacity (predTLC) based on sex, age and height was calculated.RESULTSAll cases showed crazy paving pattern in U-HRCT. In these lesions, the secondary lobules were smaller than those in the un-affected lungs. CT lung volume decreased in two cases comparing predTLC.CONCLUSIONU-HRCT can evaluate not only the distribution and hallmarks of COVID-19 pneumonia but also visualize local lung volume loss.

**Database:** Medline

**21. Covid-19 Does Not Lead to a "Typical" Acute Respiratory Distress Syndrome**

**Author(s):** Gattinoni L.; Coppola S.; Chiumello D.; Cressoni M.; Busana M.

**Source:** American journal of respiratory and critical care medicine; Mar 2020

**Publication Date:** Mar 2020

**Publication Type(s):** Article

**PubMedID:** 32228035

Available at [American journal of respiratory and critical care medicine](http://www.uhl-library.nhs.uk/directpages/uhlarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from NULJ library) - click this link for more information Local Print Collection [location] : UHL Libraries On Request (Free).

Available at [American journal of respiratory and critical care medicine](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [American journal of respiratory and critical care medicine](http://www.atsjournals.org/doi/pdf/10.1164/rccm.202003-0817LE) - from Unpaywall

**Database:** EMBASE

**22. Acute pulmonary embolism and COVID-19 pneumonia: a random association?**

**Author(s):** Danzi G.B.; Loffi M.; Galeazzi G.; Gherbesi E.

**Source:** European heart journal; Mar 2020

**Publication Date:** Mar 2020

**Publication Type(s):** Article

**PubMedID:** 32227120

Available at [European heart journal](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [European heart journal](https://academic.oup.com/eurheartj/advance-article-pdf/doi/10.1093/eurheartj/ehaa254/32977101/ehaa254.pdf) - from Unpaywall

**Database:** EMBASE

**23. 2019-novel Coronavirus severe adult respiratory distress syndrome in two cases in Italy: An uncommon radiological presentation.**

**Author(s):** Albarello, Fabrizio; Pianura, Elisa; Di Stefano, Federica; Cristofaro, Massimo; Petrone, Ada; Marchioni, Luisa; Palazzolo, Claudia; Schininà, Vincenzo; Nicastri, Emanuele; Petrosillo, Nicola; Campioni, Paolo; Eskild, Petersen; Zumla, Alimuddin; Ippolito, Giuseppe; COVID 19 INMI Study Group

**Source:** International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases; Feb 2020; vol. 93 ; p. 192-197

**Publication Date:** Feb 2020

**Publication Type(s):** Journal Article

**PubMedID:** 32112966

Available at [International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [International journal of infectious diseases : IJID : official publication of the International Society for Infectious Diseases](https://doi.org/10.1016/j.ijid.2020.02.043) - from Unpaywall

**Abstract:**INTRODUCTIONSeveral recent case reports have described common early chest imaging findings of lung pathology caused by 2019 novel Coronavirus (SARS-COV2) which appear to be similar to those seen previously in SARS-CoV and MERS-CoV infected patients.OBJECTIVEWe present some remarkable imaging findings of the first two patients identified in Italy with COVID-19 infection travelling from Wuhan, China. The follow-up with chest X-Rays and CT scans was also included, showing a progressive adult respiratory distress syndrome (ARDS).RESULTSModerate to severe progression of the lung infiltrates, with increasing percentage of high-density infiltrates sustained by a bilateral and multi-segmental extension of lung opacities, were seen. During the follow-up, apart from pleural effusions, a tubular and enlarged appearance of pulmonary vessels with a sudden caliber reduction was seen, mainly found in the dichotomic tracts, where the center of a new insurgent pulmonary lesion was seen. It could be an early alert radiological sign to predict initial lung deterioration. Another uncommon element was the presence of mediastinal lymphadenopathy with short-axis oval nodes.CONCLUSIONSAlthough only two patients have been studied, these findings are consistent with the radiological pattern described in literature. Finally, the pulmonary vessels enlargement in areas where new lung infiltrates develop in the follow-up CT scan, could describe an early predictor radiological sign of lung impairment.

**Database:** Medline

**24. Inflammatory Responses Regulating Alveolar Ion Transport during Pulmonary Infections.**

**Author(s):** Peteranderl C; Sznajder JI; Herold S; Lecuona E

**Source:** Frontiers in immunology; 2017; vol. 8 ; p. 446

**Publication Date:** 2017

**Publication Type(s):** Journal Article; Review

**PubMedID:** 28458673

Available at [Frontiers in immunology](http://europepmc.org/search?query=(DOI:10.3389/fimmu.2017.00446)) - from Europe PubMed Central - Open Access

Available at [Frontiers in immunology](https://www.frontiersin.org/articles/10.3389/fimmu.2017.00446/pdf) - from Unpaywall

**Abstract:**The respiratory epithelium is lined by a tightly balanced fluid layer that allows normal O2 and CO2 exchange and maintains surface tension and host defense. To maintain alveolar fluid homeostasis, both the integrity of the alveolar-capillary barrier and the expression of epithelial ion channels and pumps are necessary to establish a vectorial ion gradient. However, during pulmonary infection, auto- and/or paracrine-acting mediators induce pathophysiological changes of the alveolar-capillary barrier, altered expression of epithelial Na,K-ATPase and of epithelial ion channels including epithelial sodium channel and cystic fibrosis membrane conductance regulator, leading to the accumulation of edema and impaired alveolar fluid clearance. These mediators include classical pro-inflammatory cytokines such as TGF-β, TNF-α, interferons, or IL-1β that are released upon bacterial challenge with Streptococcus pneumoniae, Klebsiella pneumoniae, or Mycoplasma pneumoniae as well as in viral infection with influenza A virus, pathogenic coronaviruses, or respiratory syncytial virus. Moreover, the pro-apoptotic mediator TNF-related apoptosis-inducing ligand, extracellular nucleotides, or reactive oxygen species impair epithelial ion channel expression and function. Interestingly, during bacterial infection, alterations of ion transport function may serve as an additional feedback loop on the respiratory inflammatory profile, further aggravating disease progression. These changes lead to edema formation and impair edema clearance which results in suboptimal gas exchange causing hypoxemia and hypercapnia. Recent preclinical studies suggest that modulation of the alveolar-capillary fluid homeostasis could represent novel therapeutic approaches to improve outcomes in infection-induced lung injury.

**Database:** PubMed

**25. Middle East Respiratory Syndrome Coronavirus Causes Multiple Organ Damage and Lethal Disease in Mice Transgenic for Human Dipeptidyl Peptidase 4.**

**Author(s):** Li, Kun; Wohlford-Lenane, Christine; Perlman, Stanley; Zhao, Jincun; Jewell, Alexander K; Reznikov, Leah R; Gibson-Corley, Katherine N; Meyerholz, David K; McCray, Paul B

**Source:** The Journal of infectious diseases; Mar 2016; vol. 213 (no. 5); p. 712-722

**Publication Date:** Mar 2016

**Publication Type(s):** Research Support, Non-u.s. Gov't Research Support, N.i.h., Extramural Journal Article

**PubMedID:** 26486634

Available at [The Journal of infectious diseases](http://www.uhl-library.nhs.uk/directpages/uhlarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from NULJ library) - click this link for more information Local Print Collection [location] : UHL Libraries On Request (Free).

Available at [The Journal of infectious diseases](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [The Journal of infectious diseases](https://academic.oup.com/jid/article-pdf/213/5/712/17411043/jiv499.pdf) - from Unpaywall

**Abstract:**Middle East respiratory syndrome coronavirus (MERS-CoV) causes life-threatening disease. Dipeptidyl peptidase 4 (DPP4) is the receptor for cell binding and entry. There is a need for small-animal models of MERS, but mice are not susceptible to MERS because murine dpp4 does not serve as a receptor. We developed transgenic mice expressing human DPP4 (hDPP4) under the control of the surfactant protein C promoter or cytokeratin 18 promoter that are susceptible to infection with MERS-CoV. Notably, mice expressing hDPP4 with the cytokeratin 18 promoter developed progressive, uniformly fatal disease following intranasal inoculation. High virus titers were present in lung and brain tissues 2 and 6 days after infection, respectively. MERS-CoV-infected lungs revealed mononuclear cell infiltration, alveolar edema, and microvascular thrombosis, with airways generally unaffected. Brain disease was observed, with the greatest involvement noted in the thalamus and brain stem. Animals immunized with a vaccine candidate were uniformly protected from lethal infection. These new mouse models of MERS-CoV should be useful for investigation of early disease mechanisms and therapeutic interventions.

**Database:** Medline

**26. Differentiated phenotypes of primary murine alveolar epithelial cells and their susceptibility to infection by respiratory viruses.**

**Author(s):** Kebaabetswe, Lemme P; Haick, Anoria K; Miura, Tanya A

**Source:** Virus research; Aug 2013; vol. 175 (no. 2); p. 110-119

**Publication Date:** Aug 2013

**Publication Type(s):** Research Support, Non-u.s. Gov't Research Support, N.i.h., Extramural Journal Article

**PubMedID:** 23639425

Available at [Virus research](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [Virus research](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3683362) - from Unpaywall

**Abstract:**Severe respiratory viral infections are associated with spread to the alveoli of the lungs. There are multiple murine models of severe respiratory viral infections that have been used to identify viral and host factors that contribute to disease severity. Primary cultures of murine alveolar epithelial cells provide a robust in vitro model to perform mechanistic studies that can be correlated with in vivo studies to identify cell type-specific factors that contribute to pathology within the alveoli of the lung during viral infection. In this study, we established an in vitro model to compare the responses of type I (ATI) and type II (ATII) alveolar epithelial cells to infection by respiratory viruses used in murine models: mouse-adapted severe acute respiratory syndrome-associated coronavirus (SARS-CoV, v2163), murine coronavirus MHV-1, and influenza A (H1N1) virus, strain PR8. Murine alveolar cells cultured to maintain an ATII cell phenotype, determined by expression of LBP180, were susceptible to infection by all three viruses. In contrast, ATII cells that were cultured to trans-differentiate into an ATI-like cell phenotype were susceptible to MHV-1 and PR8, but not mouse-adapted SARS-CoV. Epithelial cells produce cytokines in response to viral infections, thereby activating immune responses. Thus, virus-induced cytokine expression was quantified in ATI and ATII cells. Both cell types had increased expression of IL-1β mRNA upon viral infection, though at different levels. While MHV-1 and PR8 induced expression of a number of shared cytokines in ATI cells, there were several cytokines whose expression was induced uniquely by MHV-1 infection. In summary, ATI and ATII cells exhibited differential susceptibilities and cytokine responses to infection by respiratory viruses. This in vitro model will be critical for future studies to determine the roles of these specialized cell types in the pathogenesis of respiratory viral infection.

**Database:** Medline

**27. Local renin-angiotensin II systems, angiotensin-converting enzyme and its homologue ACE2: their potential role in the pathogenesis of chronic obstructive pulmonary diseases, pulmonary hypertension and acute respiratory distress syndrome.**

**Author(s):** Kaparianos A; Argyropoulou E

**Source:** Current medicinal chemistry; 2011; vol. 18 (no. 23); p. 3506-3515

**Publication Date:** 2011

**Publication Type(s):** Journal Article; Review

**PubMedID:** 21756232

Available at [Current medicinal chemistry](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

**Abstract:**Renin-angiotensin II-aldosterone axis has long been known as a regulator of blood pressure and fluid homeostasis. Yet, local renin-angiotensin II systems have been discovered and novel actions of angiotensin II (AngII) have emerged among which its ability to act as a immunomodulator and profibrotic molecule. The enzyme responsible for its synthesis, Angiotensin-converting-enzyme (ACE), is present in high concentrations in lung tissue. In the present paper, we review data from studies of the past decade that implicate AngII and functional polymorphisms of the ACE gene that increase ACE activity with increased susceptibility for asthma and chronic obstructive pulmonary disease (COPD) and for pulmonary hypertension. Moreover, drugs that inhibit the synthesis of AngII (ACE inhibitors) or that antagonize its actions on its receptors (Angiotensin II receptor blockers -ARBs) have been shown to provide beneficial effects. Another recent discovery reviewed is the presence of a homologue of ACE, ACE2, which cleaves a single amino acid from AngII and forms a heptapeptide with vasodilatory actions, Ang 1-7. The balance between ACE and ACE2 is crucial for controlling AngII levels. ACE and ACE2 also appear to modify the severity of Acute Respiratory Distress Syndrome (ARDS), with ACE2 playing a protective role. Finally, mention is made to the recent discovery of ACE2 as a receptor for the SARS Corona Virus.

**Database:** PubMed

**28. Pulmonary artery thrombosis in a patient with severe acute respiratory syndrome.**

**Author(s):** Ng KH; Wu AK; Cheng VC; Tang BS; Chan CY; Yung CY; Luk SH; Lee TW; Chow L; Yuen KY

**Source:** Postgraduate medical journal; Jun 2005; vol. 81 (no. 956); p. e3

**Publication Date:** Jun 2005

**Publication Type(s):** Case Reports; Journal Article

**PubMedID:** 15937197

Available at [Postgraduate Medical Journal](https://go.openathens.net/redirector/nhs?url=https%3A%2F%2Fpmj.bmj.com%2Flookup%2Fdoi%2F10.1136%2Fpgmj.2004.030049) - from BMJ Journals - NHS

Available at [Postgraduate Medical Journal](http://europepmc.org/search?query=(DOI:10.1136/pgmj.2004.030049)) - from Europe PubMed Central - Open Access

Available at [Postgraduate Medical Journal](http://pmj.bmj.com/cgi/doi/10.1136/pgmj.2004.030049) - from HighWire - Free Full Text

Available at [Postgraduate Medical Journal](http://gateway.proquest.com/openurl?ctx_ver=Z39.88-2004&res_id=xri:pqm&req_dat=xri:pqil:pq_clntid=47856&rft_val_fmt=ori/fmt:kev:mtx:journal&genre=article&issn=0032-5473&volume=81&issue=956&spage=e3) - from ProQuest (Health Research Premium) - NHS Version

Available at [Postgraduate Medical Journal](http://www.uhl-library.nhs.uk/directpages/lgh.html) - from Leicester General Hospital Library Local Print Collection [location] : Leicester General Library. [title\_notes] : Issues before 2000 held in Archive.

Available at [Postgraduate Medical Journal](http://www.uhl-library.nhs.uk/directpages/uhlarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from NULJ library) - click this link for more information Local Print Collection [location] : UHL Libraries On Request (Free).

Available at [Postgraduate Medical Journal](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

Available at [Postgraduate Medical Journal](https://pmj.bmj.com/content/postgradmedj/81/956/e3.full.pdf) - from Unpaywall

**Abstract:**Severe acute respiratory syndrome (SARS) is an emerging infectious disease with both pulmonary and extra-pulmonary manifestations. Although coagulation abnormalities are common in these patients, clinically overt thromboembolic events are rarely reported. This report describes the first case of pulmonary artery thrombosis in a patient with laboratory confirmed SARS.

**Database:** PubMed

**29. Acute respiratory distress syndrome.**

**Author(s):** Chen, Hsing I; Kao, Shang Jyh; Wang, David; Lee, Ru Ping; Su, Chain Fa

**Source:** Journal of biomedical science; 2003; vol. 10 (no. 6); p. 588-592

**Publication Date:** 2003

**Publication Type(s):** Research Support, Non-u.s. Gov't Journal Article Review

**PubMedID:** 14576460

Available at [Journal of biomedical science](http://search.ebscohost.com/login.aspx?direct=true&scope=site&site=ehost-live&db=mdc&AN=14576460) - from EBSCO (MEDLINE Complete)

Available at [Journal of biomedical science](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

**Abstract:**Acute respiratory distress syndrome (ARDS) can be associated with various disorders. Among these, coronavirus infection may cause life-threatening severe acute respiratory syndrome (SARS). In this review, we present animal models and techniques for the study of ARDS, and discuss the roles and possible mechanisms of various chemical factors, including nitric oxide (NO). Our early work revealed that cerebral compression elicits severe hemorrhagic pulmonary edema (PE), leading to central sympathetic activation that results in systemic vasoconstriction. The consequence of systemic vasoconstriction is volume and pressure loading in the pulmonary circulation. Vasodilators, but not oxidant radical scavengers, are effective in the prevention of centrogenic PE. In isolated perfused lung, exogenous and endogenous NO enhances lung injury following air embolism and ischemia/reperfusion. In contrast, NO synthase (NOS) inhibitors reverse such lung injury. Although NO is important in maintaining vasodilator tone, hypoxia-induced pulmonary vasoconstriction is accompanied by an increase instead of a decrease in NO release. In animal and isolated lung studies, endotoxin produces acute lung injury that is associated with increases in cytokines and inducible NOS mRNA expression, suggesting that NO is toxic to the lung in endotoxin shock. Recently, we reported several rare cases that indicate that ARDS in patients with Japanese B encephalitis, lymphangitis with breast cancer and fat embolism is caused by different mechanisms. Our early and recent studies on ARDS and PE may provide information for clinical practice and the understanding of the pathogenesis of SARS.

**Database:** Medline

**30. Lung pathology of fatal severe acute respiratory syndrome.**

**Author(s):** Nicholls, John M; Poon, Leo L M; Lee, Kam C; Ng, Wai F; Lai, Sik T; Leung, Chung Y; Chu, Chung M; Hui, Pak K; Mak, Kong L; Lim, Wilina; Yan, Kin W; Chan, Kwok H; Tsang, Ngai C; Guan, Yi; Yuen, Kwok Y; Peiris, J S Malik

**Source:** Lancet (London, England); May 2003; vol. 361 (no. 9371); p. 1773-1778

**Publication Date:** May 2003

**Publication Type(s):** Research Support, Non-u.s. Gov't Case Reports Journal Article Research Support, U.s. Gov't, P.h.s.

**PubMedID:** 12781536

Available at [Lancet (London, England)](http://gateway.proquest.com/openurl?ctx_ver=Z39.88-2004&res_id=xri:pqm&req_dat=xri:pqil:pq_clntid=47856&rft_val_fmt=ori/fmt:kev:mtx:journal&genre=article&issn=0140-6736&volume=361&issue=9371&spage=1773) - from ProQuest (Health Research Premium) - NHS Version

Available at [Lancet (London, England)](http://search.ebscohost.com/login.aspx?direct=true&scope=site&site=ehost-live&db=mdc&AN=12781536) - from EBSCO (MEDLINE Complete)

Available at [Lancet (London, England)](http://www.uhl-library.nhs.uk/directpages/gh.html) - from Glenfield Hospital Library Local Print Collection [location] : Glenfield Library. [title\_notes] : The Lancet pre 1980 are stored in Glenfield Library Office, please ask library staff for assistance.

Available at [Lancet (London, England)](http://www.uhl-library.nhs.uk/directpages/lgh.html) - from Leicester General Hospital Library Local Print Collection [location] : Leicester General Library. [title\_notes] : Issues before 2000 held in Archive.

Available at [Lancet (London, England)](http://www.uhl-library.nhs.uk/directpages/uhlarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from NULJ library) - click this link for more information Local Print Collection [location] : UHL Libraries On Request (Free).

Available at [Lancet (London, England)](http://www.uhl-library.nhs.uk/directpages/lri.html) - from LRI Library Local Full Text Collection [location] : LRI Library.

Available at [Lancet (London, England)](http://www.uhl-library.nhs.uk/directpages/uhlblarticles.html) - from Available to NHS staff on request from UHL Libraries & Information Services (from non-NHS library) - click this link for more information Local Print Collection [location] : British Library via UHL Libraries - please click link to request article.

**Abstract:**BACKGROUNDSevere acute respiratory syndrome (SARS) is a novel infectious disease with global impact. A virus from the family Coronaviridae has been identified as the cause, but the pathogenesis is still unclear.METHODSPost-mortem tissue samples from six patients who died from SARS in February and March, 2003, and an open lung biopsy from one of these patients were studied by histology and virology. Only one full autopsy was done. Evidence of infection with the SARS-associated coronavirus (SARS-CoV) and human metapneumovirus was sought by reverse-transcriptase PCR and serology. Pathological samples were examined by light and electron microscopy and immunohistochemistry.FINDINGSAll six patients had serological evidence of recent infection with SARS-CoV. Diffuse alveolar damage was common but not universal. Morphological changes identified were bronchial epithelial denudation, loss of cilia, and squamous metaplasia. Secondary bacterial pneumonia was present in one case. A giant-cell infiltrate was seen in four patients, with a pronounced increase in macrophages in the alveoli and the interstitium of the lung. Haemophagocytosis was present in two patients. The alveolar pneumocytes also showed cytomegaly with granular amphophilic cytoplasm. The patient for whom full autopsy was done had atrophy of the white pulp of the spleen. Electron microscopy revealed viral particles in the cytoplasm of epithelial cells corresponding to coronavirus.INTERPRETATIONSARS is associated with epithelial-cell proliferation and an increase in macrophages in the lung. The presence of haemophagocytosis supports the contention that cytokine dysregulation may account, at least partly, for the severity of the clinical disease. The case definition of SARS should acknowledge the range of lung pathology associated with this disease.

**Database:** Medline

Strategy 841548

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| --- | --- | --- | --- |
| **#** | **Database** | **Search term** | **Results** |
| 1 | PubMed | (Coronavirus\*).af | 13920 |
| 2 | PubMed | (COVID\*).af | 2232 |
| 3 | PubMed | ("SARS-CoV-2").af | 377 |
| 4 | PubMed | ("2019-nCoV").af | 362 |
| 5 | PubMed | (ncov).af | 376 |
| 6 | PubMed | ("novel betacov").af | 0 |
| 7 | PubMed | ("novel betacoronavirus").af | 22 |
| 8 | PubMed | (1 OR 2 OR 3 OR 4 OR 5 OR 6 OR 7) | 20548 |
| 9 | PubMed | (pulmonary).ti | 253257 |
| 10 | PubMed | (physiolog\* OR patholog\* OR pathophysiolog\*).ti,ab | 7841053 |
| 11 | PubMed | (circulat\* OR circuit\* OR system OR "blood flow" OR tree).ti,ab | 3877507 |
| 12 | PubMed | (capillar\* OR arter\* OR vein\* OR venous OR vessel\*).ti,ab | 1391707 |
| 13 | PubMed | (thromb\* OR occlusion\* OR microthromb\*).ti,ab | 318882 |
| 14 | PubMed | (endothelium).ti,ab | 157506 |
| 15 | PubMed | (resist\* OR pressure\* OR hypertensi\*).ti,ab | 2552123 |
| 16 | PubMed | ("gas exchange" OR "gaseous exchange").ti,ab | 26953 |
| 17 | PubMed | (10 OR 11 OR 12 OR 13 OR 14 OR 15 OR 16) | 12350645 |
| 18 | PubMed | (8 AND 9 AND 17) | 45 |
| 19 | PubMed | (SARS OR "severe acute respiratory syndrome").af | 13315 |
| 20 | PubMed | (MERS OR "middle east respiratory syndrome").af | 16037 |
| 21 | PubMed | (8 OR 19 OR 20) | 30375 |
| 22 | PubMed | (9 AND 17 AND 21) | 103 |
| 23 | Medline | (Coronavirus\*).ti,ab | 13458 |
| 24 | Medline | (COVID\*).ti,ab | 5674 |
| 25 | Medline | ("SARS-CoV-2").ti,ab | 1371 |
| 26 | Medline | ("2019-nCoV").af | 534 |
| 27 | Medline | (ncov).af | 556 |
| 28 | Medline | ("novel betacov").af | 0 |
| 29 | Medline | ("novel betacoronavirus").af | 27 |
| 31 | Medline | "SARS VIRUS"/ | 2961 |
| 32 | Medline | "MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS"/ | 1005 |
| 33 | Medline | BETACORONAVIRUS/ | 1071 |
| 34 | Medline | (23 OR 24 OR 25 OR 26 OR 27 OR 28 OR 29 OR 31 OR 32 OR 33) | 18569 |
| 35 | Medline | (pulmonary AND (physiolog\* OR patholog\* OR pathophysiolog\*)).ti,ab | 46940 |
| 36 | Medline | (pulmonary ADJ2 (circulat\* OR circuit\* OR system\* OR "blood flow" OR tree)).ti,ab | 25096 |
| 37 | Medline | (pulmonary ADJ3 (capillar\* OR arter\* OR vein\* OR venous OR vessel\*)).ti,ab | 107257 |
| 38 | Medline | (pulmonary ADJ2 (thromb\* OR occlusion\* OR microthromb\*)).ti,ab | 10025 |
| 39 | Medline | (pulmonary ADJ5 endothelium).ti,ab | 1850 |
| 40 | Medline | (gas\* ADJ2 exchange\*).ti,ab | 21085 |
| 41 | Medline | (pulmonary ADJ3 (resist\* OR pressure\* OR hypertension\*)).ti,ab | 71732 |
| 42 | Medline | (endothelium ADJ2 (damag\* OR impair\*)).ti,ab | 4200 |
| 43 | Medline | (alveol\*).ti,ab | 103531 |
| 44 | Medline | (PA ADJ2 pressure\*).ti,ab | 1805 |
| 45 | Medline | (pulmonary ADJ3 (parameter\* OR measurement\*)).ti,ab | 6569 |
| 46 | Medline | "PULMONARY VEINS"/ | 13867 |
| 47 | Medline | exp "PULMONARY EMBOLISM"/ | 38374 |
| 48 | Medline | "PULMONARY ARTERIAL HYPERTENSION"/ | 186 |
| 49 | Medline | "HYPERTENSION, PULMONARY"/ | 33993 |
| 50 | Medline | exp "PULMONARY GAS EXCHANGE"/ | 20146 |
| 51 | Medline | exp "PULMONARY ALVEOLI"/ | 25854 |
| 52 | Medline | "PULMONARY ARTERY"/ | 45700 |
| 53 | Medline | "PULMONARY CIRCULATION"/ | 22006 |
| 54 | Medline | (35 OR 36 OR 37 OR 38 OR 39 OR 40 OR 41 OR 42 OR 43 OR 44 OR 45 OR 46 OR 47 OR 48 OR 49 OR 50 OR 51 OR 52 OR 53) | 364180 |
| 55 | Medline | (34 AND 54) | 247 |
| 56 | EMBASE | (Coronavirus\*).ti,ab | 13930 |
| 57 | EMBASE | (COVID\*).ti,ab | 5696 |
| 58 | EMBASE | ("SARS-CoV-2").ti,ab | 1087 |
| 59 | EMBASE | ("2019-nCoV").af | 511 |
| 60 | EMBASE | (ncov).af | 533 |
| 61 | EMBASE | ("novel betacov").af | 0 |
| 62 | EMBASE | ("novel betacoronavirus").af | 30 |
| 63 | EMBASE | "MIDDLE EAST RESPIRATORY SYNDROME CORONAVIRUS"/ | 1965 |
| 64 | EMBASE | "SARS-RELATED CORONAVIRUS"/ | 150 |
| 65 | EMBASE | BETACORONAVIRUS/ | 337 |
| 66 | EMBASE | CORONAVIRINAE/ | 1965 |
| 67 | EMBASE | (56 OR 57 OR 58 OR 59 OR 60 OR 61 OR 62 OR 63 OR 64 OR 65 OR 66) | 19241 |
| 68 | EMBASE | (pulmonary AND (physiolog\* OR patholog\* OR pathophysiolog\*)).ti,ab | 81273 |
| 69 | EMBASE | (pulmonary ADJ2 (circulat\* OR circuit\* OR system\* OR "blood flow" OR tree)).ti,ab | 25934 |
| 70 | EMBASE | (pulmonary ADJ3 (capillar\* OR arter\* OR vein\* OR venous OR vessel\*)).ti,ab | 151562 |
| 71 | EMBASE | (pulmonary ADJ2 (thromb\* OR occlusion\* OR microthromb\*)).ti,ab | 20378 |
| 72 | EMBASE | (pulmonary ADJ5 endothelium).ti,ab | 2232 |
| 73 | EMBASE | (gas\* ADJ2 exchange\*).ti,ab | 24319 |
| 74 | EMBASE | (pulmonary ADJ3 (resist\* OR pressure\* OR hypertension\*)).ti,ab | 107415 |
| 75 | EMBASE | (endothelium ADJ2 (damag\* OR impair\*)).ti,ab | 4373 |
| 76 | EMBASE | (alveol\*).ti,ab | 127914 |
| 77 | EMBASE | (PA ADJ2 pressure\*).ti,ab | 2951 |
| 78 | EMBASE | (pulmonary ADJ3 (parameter\* OR measurement\*)).ti,ab | 7554 |
| 79 | EMBASE | "LUNG CIRCULATION"/ | 11254 |
| 80 | EMBASE | "PULMONARY VEIN"/ | 14609 |
| 81 | EMBASE | exp "PULMONARY ARTERY"/ | 38603 |
| 82 | EMBASE | "LUNG EMBOLISM"/ | 90567 |
| 83 | EMBASE | exp "PULMONARY VASCULAR DISEASE"/ | 100870 |
| 84 | EMBASE | "LUNG GAS EXCHANGE"/ | 12123 |
| 85 | EMBASE | exp "LUNG ALVEOLUS"/ | 60670 |
| 86 | EMBASE | (68 OR 69 OR 70 OR 71 OR 72 OR 73 OR 74 OR 75 OR 76 OR 77 OR 78 OR 79 OR 80 OR 81 OR 82 OR 83 OR 84 OR 85) | 529179 |
| 87 | EMBASE | (67 AND 86) | 400 |
| 88 | Medline | ((lung\* OR respiratory) ADJ2 circulat\*).ti,ab | 4329 |
| 89 | Medline | ((lung\* OR pulmonary) ADJ2 (emblous OR emboli\*)).ti,ab | 36996 |
| 90 | Medline | ((lung\* OR pulmonary OR respiratory) ADJ2 perfusion).ti,ab | 6417 |
| 91 | Medline | (hypoxic ADJ2 vasoconstriction).ti,ab | 1928 |
| 92 | Medline | (88 OR 89 OR 90 OR 91) | 47949 |
| 93 | Medline | (34 AND 92) | 37 |
| 94 | EMBASE | ((lung\* OR respiratory) ADJ2 circulat\*).ti,ab | 3822 |
| 95 | EMBASE | ((lung\* OR pulmonary) ADJ2 (emblous OR emboli\*)).ti,ab | 56508 |
| 96 | EMBASE | ((lung\* OR pulmonary OR respiratory) ADJ2 perfusion).ti,ab | 7444 |
| 97 | EMBASE | (hypoxic ADJ2 vasoconstriction).ti,ab | 2316 |
| 98 | EMBASE | (94 OR 95 OR 96 OR 97) | 68076 |
| 99 | EMBASE | (67 AND 98) | 48 |

[Reviewers Note 11/5/20: Consider also using exp CORONAVIRUS/ and exp “CORONAVIRUS INFECTIONS”/ subject headings in Medline and Pubmed]