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COVID-19 y la pandemia global causada por un nuevo coronavirus

COVID-19 and the global pandemic caused by a new coronavirus

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Resumen

Introducción: COVID-19 es una enfermedad respiratoria inédita que se reportó inicialmente como una neumonía atípica en diciembre de 2019. SARS-CoV-2, agente etiológico de esta patología, probablemente originado a partir de un virus de murciélago. La inesperada capacidad de transmisión y patogenicidad que adquirió este coronavirus transformó a COVID-19 en una pandemia de sintomatología variada y compleja. **Objetivo:** Analizar aspectos evolutivos, moleculares, biológicos, inmunológicos y epidemiológicos de esta enfermedad. **Materiales y métodos:** Se realizó una revisión narrativa de literatura científica publicada en *Pubmed*, sobre estos aspectos desde enero 2020. **Resultados:** SARS-CoV-2 es un nuevo coronavirus que utiliza su proteína superficial *S* para infectar células humanas que exhiben el receptor ACE2. Este patógeno se transmite por secreciones respiratorias e induce un incremento nocivo de mediadores químicos proinflamatorios en individuos vulnerables, reacción inmune conocida como tormenta de citoquinas. Esta respuesta hiper-inflamatoria es la causante de las lesiones alveolares que desencadenan la insuficiencia respiratoria observada en casos severos de COVID-19. **Conclusiones:** En individuos susceptibles, SARS-CoV-2 puede desencadenar una disfunción pulmonar que requiere soporte ventilatorio asistido y tratamiento con inmunosupresores. Se están desarrollando nuevas estrategias terapéuticas y de prevención para disminuir los elevados índices de contagio y la mortalidad asociados con COVID-19.

Palabras clave: Betacoronavirus; infecciones por coronavirus; glicoproteína de espiga del coronavirus; síndrome respiratorio agudo grave; inflamación. (Fuente: DeCS, Bireme).

Abstract

Introduction: COVID-19 is a new respiratory disease reported initially as an atypical pneumonia in December 2019. SARS-CoV-2, the etiological agent of this pathology, probably originated from a bat viral pathogen. The unexpected transmission and pathogenicity capacities that this coronavirus acquired turned COVID-19 into a pandemic with a wide and complex arrangement of symptoms. **Objective:** To analyze evolutionary, molecular, biological, immunological and epidemiological aspects of this disease. **Materials and methods:** A narrative review of the literature concerning these topics was conducted, which was published in Pubmed mostly from January 2020. **Results:** SARS-CoV-2 is a new coronavirus that uses its surface respiratory secretions and triggers a harmful increase in pro-inflammatory chemical mediators in vulnerable individuals, an immune reaction known as cytokine storm. This hyper-inflammatory response is the cause of the alveolar lesions behind the respiratory failure observed in severe cases of COVID-19. **Conclusions:** In susceptible individuals, SARS-CoV-2 triggers an acute respiratory distress syndrome that requires assisted ventilatory support and immunomodulatory therapy. New therapeutic and prevention strategies are being developed to reduce the high transmission and mortality rates associated with COVID-19.

Key words: Betacoronavirus; coronavirus infections; spike glycoprotein; severe acute respiratory syndrome; inflammation. (Source: DeCS, Bireme).

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Aunque ha habido avances significativos en las áreas descritas anteriormente, virólogos e inmunólogos deben colaborar para enfrentar retos futuros importantes, tales como: (i) caracterizar la estructura ACE2 y su función en la infección de órganos que son frecuentemente lesionados por SARS-CoV-2; (ii) identificar moléculas accesorias de origen celular y viral que contribuyen a la adhesión y penetración de SARS-CoV-2; (iii) descubrir posibles mutaciones del gen humano que codifica ACE2 que incrementan su susceptibilidad al reconocimiento por la proteína viral S; (iv) encontrar y/o diseñar un modelo animal apropiado donde estudiar la dinámica de la interacción entre la proteína S y ACE2; (v) culminar la fase III de pruebas clínicas en humanos donde se pueda cuantificar niveles de inmunogenicidad, de patogenicidad y la dosis efectiva de muchos vacunas que están siendo desarrolladas en la actualidad; y (vi) determinar la duración de la inmunidad inducida por una potencial vacuna.

Contribuciones a corto y largo plazo en las áreas descritas anteriormente acelerarán el desarrollo y uso de métodos preventivos y terapéuticos que protejan eficientemente no sólo a la comunidad en general, sino también al personal de salud, a quienes su trabajo en unidades de cuidado de pacientes con COVID-19 los expone frecuentemente a situaciones de riesgo de contagio.

Los ciclos acelerados de multiplicación y destrucción celular de MERS-CoV, SARS-CoV y SARS-CoV-2 provocan respuestas inflamatorias incontrolables inducidas por una intensa y auto-amplificada tormenta de citoquinas. Se ha demostrado que la insuficiencia respiratoria que desarrollan ciertos pacientes con MERS, SARS y COVID-19 se debe a los efectos adversos de citoquinas inflamatorias que circulan en el cuerpo de pacientes causándoles daño. Sin embargo, las manifestaciones clínicas de COVID-19 son bastante complejas y tienen un desenlace fatal más frecuente en pacientes de edad avanzada, con obesidad y/o con comorbilidades de tipo cardiovascular y respiratoria.

Estudios en el área de la inmunopatología deberán determinar el umbral de citoquinas a partir del cual la tormenta de citoquinas alcanza características perjudiciales de auto-perpetuación y auto-amplificación. De este modo, se haría más fácil diseñar tratamientos que bloqueen citoquinas inflamatorias específicas sin afectar otros componentes esenciales de las respuestas inmunes, mejorando así el pronóstico de COVID-19. También se debe construir un cuadro clínico individualizado de pacientes, de todas las edades, con y sin comorbilidades, el cual incluya marcadores moleculares y predictores clínicos con la capacidad de pronosticar si un paciente es propenso a desencadenar estas tormentas de citoquinas.

Estudios clínicos de pacientes con COVID-19 bajo soporte ventilatorio han demostrado que agentes inmunosupresores de tipo esteroide pueden atenuar los efectos adversos de citoquinas inflamatorias, mejorando de esta manera los índices de mortalidad de COVID-19. Una perspectiva interesante que se desprende de estas observaciones es investigar si pacientes con enfermedades genéticas autoinmunes de tipo inflamatorio y bajo tratamiento con este tipo de inmunosupresores son menos susceptibles a padecer complicaciones clínicas severas si contraen COVID-19. Por último, se debe descifrar si algunos individuos asintomáticos o con sintomatología leve desarrollaron inmunidad cruzada a partir de encuentros anteriores con otros coronavirus, tal y como lo sugieren algunos reportes.

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Referencias

1. World Health Organization. SARS : lessons from a new disease [Internet]. The World Health Report 2003 international. Geneva (Suiza): WHO Library Cataloguing-in-Publication Data; 2003. 71–82 p. Available from: https://www.who.int/whr/2003/en/whr03_en.pdf?ua
2. World Health Organization. SARS outbreak contained worldwide [Internet]. World Health Organization. Geneva (Suiza); 2003. Available from:

https://www.who.int/mediacentre/news/releases/2003/pr56/en/
3. Andersen KG, Rambaut A, Lipkin WI, Holmes EC, Garry RF. The proximal origin of SARS-CoV-2. Nat Med [Internet]. 2020 Apr 17;26(4):450–2. Available from: http://www.nature.com/articles/s41591-020-0820-9
4. Ball P, Maxmen A. The epic battle against coronavirus misinformation and conspiracy theories. Nature [Internet]. 2020 May 27;581(7809):371–4. Available from: http://www.nature.com/articles/d41586-020-01452-z
5. Li Q, Guan X, Wu P, Wang X, Zhou L, Tong Y, et al. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus–Infected Pneumonia. N Engl J Med [Internet]. 2020 Mar 26;382(13):1199–207. Available from: http://www.nejm.org/doi/10.1056/NEJMoa2001316
6. Phelan AL, Katz R, Gostin LO. The Novel Coronavirus Originating in Wuhan, China. JAMA [Internet]. 2020 Feb 25;323(8):709. Available from: https://jamanetwork.com/journals/jama/fullarticle/2760500
7. World Health Organization. Naming the coronavirus disease (COVID-19) and the virus that causes it [Internet]. World Health Organization. Geneva (Suiza); 2020. Available from: https://www.who.int/emergencies/diseases/novel-coronavirus-2019/technical-guidance/naming-the-coronavirus-disease-(covid-2019)-and-the-virus-that-causes-it
8. Lu R, Zhao X, Li J, Niu P, Yang B, Wu H, et al. Genomic characterisation and epidemiology of 2019 novel coronavirus: implications for virus origins and receptor binding. Lancet [Internet]. 2020 Feb;395(10224):565–74. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673620302518
9. Wu F, Zhao S, Yu B, Chen Y-M, Wang W, Song Z-G, et al. A new coronavirus associated with human respiratory disease in China. Nature [Internet]. 2020 Mar 3;579(7798):265–9. Available from: http://www.nature.com/articles/s41586-020-2008-3
10. Zhou P, Yang X-L, Wang X-G, Hu B, Zhang L, Zhang W, et al. A pneumonia outbreak associated with a new coronavirus of probable bat origin. Nature [Internet]. 2020 Mar 12;579(7798):270–3. Available from: http://www.nature.com/articles/s41586-020-2012-7
11. Zhu N, Zhang D, Wang W, Li X, Yang B, Song J, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med [Internet]. 2020 Feb 20;382(8):727–33. Available from: http://www.nejm.org/doi/10.1056/NEJMoa2001017
12. Walls AC, Park Y-J, Tortorici MA, Wall A, McGuire AT, Veesler D. Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. Cell [Internet]. 2020 Apr;181(2):281-292.e6. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0092867420302622
13. Wrapp D, Wang N, Corbett KS, Goldsmith JA, Hsieh C-L, Abiona O, et al. Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation. Science (80-) [Internet]. 2020 Mar 13;367(6483):1260–3. Available from: https://pubmed.ncbi.nlm.nih.gov/32075877/
14. Letko M, Marzi A, Munster V. Functional assessment of cell entry and receptor usage for SARS-CoV-2 and other lineage B betacoronaviruses. Nat Microbiol [Internet]. 2020 Apr 24;5(4):562–9. Available from: http://www.nature.com/articles/s41564-020-0688-y
15. Wang Q, Zhang Y, Wu L, Niu S, Song C, Zhang Z, et al. Structural and Functional Basis of SARS-CoV-2 Entry by Using Human ACE2. Cell [Internet]. 2020 May;181(4):894-904.e9. Available from: https://linkinghub.elsevier.com/retrieve/pii/S009286742030338X
16. Lan J, Ge J, Yu J, Shan S, Zhou H, Fan S, et al. Structure of the SARS-CoV-2 spike receptor-binding domain bound to the ACE2 receptor. Nature [Internet]. 2020 May 30;581(7807):215–20. Available from: http://www.nature.com/articles/s41586-020-2180-5
17. Shang J, Ye G, Shi K, Wan Y, Luo C, Aihara H, et al. Structural basis of receptor recognition by SARS-CoV-2. Nature [Internet]. 2020 May 30;581(7807):221–4. Available from: http://www.nature.com/articles/s41586-020-2179-y
18. Huang C, Wang Y, Li X, Ren L, Zhao J, Hu Y, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet [Internet]. 2020 Feb;395(10223):497–506. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673620301835
19. Zhou F, Yu T, Du R, Fan G, Liu Y, Liu Z, et al. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Lancet. 2020;395(10229):1054–62.
20. Casadevall A, Pirofski L. The convalescent sera option for containing COVID-19. J Clin Invest [Internet]. 2020 Mar 13;130(4):1545–8. Available from: https://www.jci.org/articles/view/138003
21. Stokes EK, Zambrano LD, Anderson KN, Marder EP, Raz KM, El Burai Felix S, et al. Coronavirus Disease 2019 Case Surveillance - United States, January 22-May 30, 2020. MMWR Morb Mortal Wkly Rep [Internet]. 2019;64(24):759–65. Available from: https://www.cdc.gov/mmwr/volumes/69/wr/mm6924e2.htm?s_cid=mm6924e2_w
22. Guan W, Ni Z, Hu Y, Liang W, Ou C, He J, et al. Clinical Characteristics of Coronavirus Disease 2019 in China. N Engl J Med [Internet]. 2020 Apr 30;382(18):1708–20. Available from: http://www.nejm.org/doi/10.1056/NEJMoa2002032
23. Hirano T, Murakami M. COVID-19: A New Virus, but a Familiar Receptor and Cytokine Release Syndrome. Immunity [Internet]. 2020 May;52(5):731–3. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1074761320301618
24. Ong EZ, Chan YFZ, Leong WY, Lee NMY, Kalimuddin S, Haja Mohideen SM, et al. A Dynamic Immune Response Shapes COVID-19 Progression. Cell Host Microbe. 2020;27(6):879-882.e2.
25. Ye Q, Wang B, Mao J. The pathogenesis and treatment of the `Cytokine Storm' in COVID-19. J Infect [Internet]. 2020 Jun;80(6):607–13. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0163445320301651
26. Weston S, Frieman MB. COVID-19: Knowns, Unknowns, and Questions. mSphere [Internet]. 2020 Mar 18;5(2):e00203-20. Available from: https://msphere.asm.org/content/5/2/e00203-20
27. Shereen MA, Khan S, Kazmi A, Bashir N, Siddique R. COVID-19 infection: Origin, transmission, and characteristics of human coronaviruses. J Adv Res. 2020;24:91–8.
28. Yi Y, Lagniton PNP, Ye S, Li E, Xu RH. COVID-19: What has been learned and to be learned about the novel coronavirus disease. Int J Biol Sci. 2020;16(10):1753–1766.

29. Fehr AR, Perlman S. Coronaviruses: an overview of their replication and pathogenesis. Methods Mol Biol [Internet]. 2015;1282:1–23. Available from: http://link.springer.com/10.1007/978-1-4939-2438-7_1
30. Gilbert GL. Commentary: SARS, MERS and COVID-19—new threats; old lessons. Int J Epidemiol [Internet]. 2020 Jun 1;49(3):726–8. Available from: https://academic.oup.com/ije/article/49/3/726/5828441
31. Kang S, Yang M, Hong Z, Zhang L, Huang Z, Chen X, et al. Crystal structure of SARS-CoV-2 nucleocapsid protein RNA binding domain reveals potential unique drug targeting sites. Acta Pharm Sin B. 2020;10(7):1228–38.
32. McBride R, van Zyl M, Fielding BC. The coronavirus nucleocapsid is a multifunctional protein. Viruses. 2014;6(8):2991–3018.
33. Mousavizadeh L, Ghasemi S. Genotype and phenotype of COVID-19: Their roles in pathogenesis. J Microbiol Immunol Infect. 2020;S1684-1182(20):0–4.
34. Wu A, Peng Y, Huang B, Ding X, Wang X, Niu P, et al. Genome Composition and Divergence of the Novel Coronavirus (2019-nCoV) Originating in China. Cell Host Microbe. 2020;27(3):325–8.
35. Zhang YZ, Holmes EC. A Genomic Perspective on the Origin and Emergence of SARS-CoV-2. Cell. 2020;181(2):223–7.
36. McBride R, Fielding BC. The role of severe acute respiratory syndrome (SARS)-coronavirus accessory proteins in virus pathogenesis. Viruses [Internet]. 2012;4(11):2902–2923. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC3509677/pdf/viruses-04-02902.pdf
37. Kim D, Lee JY, Yang JS, Kim JW, Kim VN, Chang H. The Architecture of SARS-CoV-2 Transcriptome. Cell. 2020;181(4):914-921.e10.
38. Astuti I, Ysrafil Y. Severe Acute Respiratory Syndrome Coronovairus 2 (SARS-CoV-2): An Overview of Viral Structure and Host Response. Diabetes Metab Syndr. 2020;14(4):407–412.
39. Hamming I, Timens W, Bulthuis M, Lely A, Navis G, Van Goor H. Tissue distribution of ACE" protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. J Pathol [Internet]. 2004;203(2):631–7. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7167720/
40. Li MY, Li L, Zhang Y, Wang XS. Expression of the SARS-CoV-2 cell receptor gene ACE2 in a wide variety of human tissues. Infect Dis Poverty. 2020;9(45):1–7.
41. Wan Y, Shang J, Graham R, Baric RS, Li F. Receptor Recognition by the Novel Coronavirus from Wuhan: an Analysis Based on Decade-Long Structural Studies of SARS Coronavirus. J Virol. 2020;94(7):1–9.
42. Wang, C., Li, W., Drabek, D. *et al.* A human monoclonal antibody blocking SARS-CoV-2 infection. Nat Commun [Internet]. 2020 May; 11;2251:e1-e6. Available from: https://www.nature.com/articles/s41467-020-16256-y#citeas
43. Wrapp, D., De Vlieger, D., Corbett, K. *et al.* Structural Basis for Potent Neutralization of Betacoronaviruses by Single-Domain Camelid Antibodies. Cell [Internet]. 2020 May; 181(5):1004-1015. Available from: https://www.cell.com/cell/pdf/S0092-8674(20)30494-3.pdf
44. Pinto D, Park Y, Beltramello M, Walls AC, Tortorici MA, Bianchi S, et al. Cross-neutralization of SARS-CoV-2 by a human monoclonal SARS-CoV antibody. Nature. 2020;583:290–295.
45. Wu, Y., Wang, F., Shen, C. *et al.* A noncompeting pair of human neutralizing antibodies block COVID-19 virus binding to its receptor ACE2. Science [Internet]. 2020 Jun; 368(6496):1274-1278. Available from: https://science.sciencemag.org/content/368/6496/1274?utm_campaign=fr_sci_2020-05-13&et_rid=33950910&et_cid=3325009
46. Deng L, Li C, Zeng Q, Liu X, Li X, Zhang H, Hong Z, Xia J. Arbidol combined with LPV/r versus LPV/r alone against Corona Virus Disease 2019: A retrospective cohort study. J Infect [Internet]. 2020 Jul;81(1):e1-e5. Available from: https://www.journalofinfection.com/article/S0163-4453(20)30113-4/pdf
47. Wang, M., Cao, R., Zhang, L. *et al.* Remdesivir and chloroquine effectively inhibit the recently emerged novel coronavirus (2019-nCoV) in vitro. Cell Res [Internet]. 2020 Jan; 30**:** 269–271. Available from: https://www.nature.com/articles/s41422-020-0282-0#citeas
48. Chu CM, Cheng VC, Hung IF, *et al.* Role of lopinavir/ritonavir in the treatment of SARS: initial virological and clinical findings. Thorax [Internet]. 2004 Mar; 59(3):252-256. doi:10.1136/thorax.2003.012658 Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC1746980/pdf/v059p00252.pdf
49. Hoffmann M, Kleine-Weber H, Schroeder S, Krüger N, Herrler T, Erichsen S, et al. SARS-CoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Cell [Internet]. 2020 Apr;181(2):271-280.e8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0092867420302294
50. Academy of Medical Sciences, Brithish Society of Immunology. COVID-19 immunology research What do we know and what are the research priorities? [Internet]. Reino Unido; 2020. Available from: https://www.immunology.org/sites/default/files/Final_COVID-19_Immunology_report.pdf
51. Prompetchara E, Ketloy C, Palaga T. Immune responses in COVID-19 and potential vaccines: Lessons learned from SARS and MERS epidemic. Asian Pac J Allergy Immunol. 2020;38(1):1–9.
52. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: consider cytokine storm syndromes and immunosuppression. Lancet [Internet]. 2020 Mar;395(10229):1033–4. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673620306280
53. Ruan Q, Yang K, Wang W, Jiang L, Song J. Clinical predictors of mortality due to COVID-19 based on an analysis of data of 150 patients from Wuhan, China. Intensive Care Med [Internet]. 2020;46(5):846–8. Available from: https://doi.org/10.1007/s00134-020-05991-x
54. Niu P, Zhang S, Zhou P, Huang B, Deng Y, Qin K, et al. Ultrapotent Human Neutralizing Antibody Repertoires Against Middle East Respiratory Syndrome Coronavirus From a Recovered Patient. J Infect Dis [Internet]. 2018 Sep 8;218(8):1249–60. Available from: https://academic.oup.com/jid/article/218/8/1249/5017222
55. Traggiai E, Becker S, Subbarao K, Kolesnikova L, Uematsu Y, Gismondo MR, et al. An efficient method to make human

monoclonal antibodies from memory B cells: Potent neutralization of SARS coronavirus. Nat Med. 2004;10:871–875.
56. Amanat F, Krammer F. SARS-CoV-2 Vaccines: Status Report. Immunity [Internet]. 2020 Apr;52(4):583–9. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1074761320301205
57. Thanh Le T, Andreadakis Z, Kumar A, Gómez Román R, Tollefsen S, Saville M, et al. The COVID-19 vaccine development landscape. Nat Rev Drug Discov [Internet]. 2020;19(5):305–6. Available from: http://dx.doi.org/10.1038/d41573-020-00073-5
58. Cheng Y, Luo R, Wang K, Zhang M, Wang Z, Dong L, et al. Kidney disease is associated with in-hospital death of patients with COVID-19. Kidney Int [Internet]. 2020 May;97(5):829–38. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0085253820302556
59. World Health Organization. Landscape analysis of therapeutics as 21st March 2020 [Internet]. Geneva (Suiza); 2020. Available from: https://www.who.int/blueprint/priority-diseases/key-action/Table_of_therapeutics_Appendix_17022020.pdf
60. Casillo GM, Mansour AA, Raucci F, Saviano A, Mascolo N, Iqbal AJ, et al. Could IL-17 represent a new therapeutic target for the treatment and/or management of COVID-19-related respiratory syndrome? Pharmacol Res [Internet]. 2020 Jun;156(104791):104791. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1043661820310999
61. Lu C-C, Chen M-Y, Lee W-S, Chang Y-L. Potential therapeutic agents against COVID-19: What we know so far. J Chinese Med Assoc [Internet]. 2020 Jun 1;83(6):534–6. Available from: https://journals.lww.com/10.1097/JCMA.0000000000000318
62. Risitano AM, Mastellos DC, Huber-Lang M, Yancopoulou D, Garlanda C, Ciceri F, et al. Complement as a target in COVID-19? Nat Rev Immunol [Internet]. 2020;20(6):343–4. Available from: http://dx.doi.org/10.1038/s41577-020-0320-7
63. World Health Organization. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19 [Internet]. Geneva (Suiza); 2020 Feb. Available from: https://www.who.int/news-room/commentaries/detail/multisystem-inflammatory-syndrome-in-children-and-adolescents-with-covid-19
64. Burns JC, Glodé MP. Kawasaki syndrome. Lancet [Internet]. 2004 Aug;364(9433):533–44. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673604168141
65. Newburger JW, Takahashi M, Burns JC. Kawasaki Disease. J Am Coll Cardiol [Internet]. 2016 Apr;67(14):1738–49. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0735109716007130
66. Deza Leon MP, Redzepi A, McGrath E, Abdel-Haq N, Shawaqfeh A, Sethuraman U, et al. COVID-19–Associated Pediatric Multisystem Inflammatory Syndrome. J Pediatric Infect Dis Soc [Internet]. 2020 Jul 13;9(3):407–8. Available from: https://pesquisa.bvsalud.org/global-literature-on-novel-coronavirus-2019-ncov/resource/en/covidwho-343299
67. DeBiasi RL, Song X, Delaney M, Bell M, Smith K, Pershad J, et al. Severe COVID-19 in Children and Young Adults in the Washington, DC Metropolitan Region. J Pediatr. 2020;223:199–203.e1.
68. Jones VG, Mills M, Suarez D, Hogan CA, Yeh D, Segal JB, et al. COVID-19 and Kawasaki Disease: Novel Virus and Novel Case. Hosp Pediatr [Internet]. 2020 Jun;10(6):537–40. Available from: http://hosppeds.aappublications.org/lookup/doi/10.1542/hpeds.2020-0123
69. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. Lancet [Internet]. 2020 May;395(10237):1607–8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673620310941
70. Halfmann PJ, Hatta M, Chiba S, Maemura T, Fan S, Takeda M, et al. Transmission of SARS-CoV-2 in Domestic Cats. N Engl J Med [Internet]. 2020 Aug 6;383(6):592–4. Available from: http://www.nejm.org/doi/10.1056/NEJMc2013400
71. Asadi S, Bouvier N, Wexler AS, Ristenpart WD. The coronavirus pandemic and aerosols: Does COVID-19 transmit via expiratory particles? Aerosol Sci Technol [Internet]. 2020 Jun 2;54(6):635–8. Available from: https://www.tandfonline.com/doi/full/10.1080/02786826.2020.1749229
72. Van Doremalen N, Bushmaker T, Morris DH, Holbrook MG, Gamble A, Williamson BN, et al. Aerosol and Surface Stability of SARS-CoV-2 as Compared with SARS-CoV-1. N Engl J Med [Internet]. 2020 Apr 16;382(16):1564–7. Available from: http://www.nejm.org/doi/10.1056/NEJMc2004973
73. Liu Y, Ning Z, Chen Y, Guo M, Liu Y, Gali NK, et al. Aerodynamic analysis of SARS-CoV-2 in two Wuhan hospitals. Nature [Internet]. 2020 Jun 27;582(7813):557–60. Available from: http://www.nature.com/articles/s41586-020-2271-3
74. Ningthoujam R. COVID 19 can spread through breathing, talking, study estimates. Curr Med Res Pract [Internet]. 2020 May;10(3):132–3. Available from: https://linkinghub.elsevier.com/retrieve/pii/S235208172030057X
75. Böhmer MM, Buchholz U, Corman VM, Hoch M, Katz K, Marosevic D V, et al. Investigation of a COVID-19 outbreak in Germany resulting from a single travel-associated primary case: a case series. Lancet Infec Dis [Internet]. 2020 Aug;20(8):920–8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S1473309920303145
76. He X, Lau EHY, Wu P, Deng X, Wang J, Hao X, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. Nat Med [Internet]. 2020 May 15;26(5):672–5. Available from: http://www.nature.com/articles/s41591-020-0869-5
77. Li D, Jin M, Bao P, Zhao W, Zhang S. Clinical Characteristics and Results of Semen Tests Among Men With Coronavirus Disease 2019. JAMA Netw Open [Internet]. 2020 May 7;3(5):e208292. Available from: https://jamanetwork.com/journals/jamanetworkopen/fullarticle/2765654
78. Groß R, Conzelmann C, Müller JA, Stenger S, Steinhart K, Kirchhoff F, et al. Detection of SARS-CoV-2 in human breastmilk. Lancet [Internet]. 2020 Jun;395(10239):1757–8. Available from: https://linkinghub.elsevier.com/retrieve/pii/S0140673620311818

79. Lamers MM, Beumer J, van der Vaart J, Knoops K, Puschhof J, Breugem TI, et al. SARS-CoV-2 productively infects human gut enterocytes. Science (80-) [Internet]. 2020 Jul 3;369(6499):50–4. Available from: https://www.sciencemag.org/lookup/doi/10.1126/science.abc1669