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Let's Understand The Devil Covid-19 Disease And It's Impact

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Abstract:

In December 2019, a cluster of fatal acute atypical respiratory disease cases seen in Wuhan, China. They were caused by a noval corona virus, now named as SARS-CoV-2. Based on clinical criteria and available serological and molecular information, the new disease was called corona virus disease of 2019 (COVID-19), and the novel corona virus was called SARS Coronavirus-2 (SARS-CoV-2), emphasizing its close relationship to the 2002 SARS virus (SARS-CoV). The scientific community raced to uncover the origin of the virus, its epidemiological data , transmission rate, incubation period, invasion of host, host response to Sars Cov-2, treatment and development of vaccination probability. Lack of targeted therapy continues to be a problem. Epidemiological studies showed that elder patients were more susceptible to this severe disease, while children tend to have milder symptoms. Here we tried to review the current knowledge about this disease and considered the potential explanation of the different symptomatology between children and adults .

Keywords : SARS-COV-2 , COVID-19

Introduction

A series of fatal acute atypical respiratory disease was seen in Wuhan, China in December 2019,. It was soon discovered that a novel corona virus was responsible for this severe disease. The novel corona virus was named as the severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2, 2019-nCoV) due to its more similarity (around 80%) to SARS-CoV, that caused acute respiratory distress syndrome (ARDS) and more deaths during 2002-2003 [1]**.** The outbreak of SARS-CoV-2 was considered to have originally started via a zoonotic transmission associated with the Wuhan Whole food market, where seafood and live animals are sold. The virus spread rapidly and public health authorities in China initiated a containment effort. However, by that time, travellers had carried the virus to many countries, sparking memories of the previous corona virus epidemics, severe acute respiratory syndrome (SARS) and Middle East respiratory syndrome (MERS), causing panic and widespread media attention . Later it was recognized that human to human transmission played a major role in the disease outbreak [2]. The disease caused by this virus was called Corona virus disease 19 (COVID-19) and was declared a global pandemic by the World Health Organization (WHO) on January 12th, 2020. COVID-19 has been impacting a large number of people worldwide, being reported in approximately 200 countries and territories [3,4]. As of June 8th, around 6,912,751 confirmed cases and 400,469 deaths worldwide have been reported according to the WHO Covid-19 dashboard [5]. SARS-CoV-2 virus primarily affects the respiratory system, mainly lower respiratory tract infection related symptoms including fever, dry cough and dyspnoea were reported in the initial cases noticed in Wuhan, China [6]. Other symptoms associated were headache, dizziness, generalized weakness, vomiting and diarrhoea [7]. Oral mucosa and nasal mucosa are the primary contact epithelium through which COVID-19 enters the host cells.. It is now widely recognized that respiratory symptoms of COVID-19 are extremely heterogeneous, ranging from minimal symptoms to significant hypoxia with ARDS. In the report from Wuhan mentioned above, the time between the onset of symptoms and the development of ARDS was as short as 9 days, suggesting that the respiratory symptoms could progress rapidly and could also be fatal [8]. Epidemiological studies have shown that mortalities are high in elder population [9] and the incidence is much lower in children [10]. Current medical management is largely supportive with no targeted therapy available. A large number of countries have implemented social distancing and lockdown to mitigate further spread of the virus. Here we will review our current knowledge of COVID-19 and consider the underlying mechanism to explain the heterogeneous symptomatology, particularly focusing on the difference between children and adult patients [11].

Epidemiological data of COVID-19:

Within a month of the outbreak at Wuhan, the SARS-CoV-2 virus extended rapidly all over China in December 2019. The virus was not limited to a country. It was highly contagious and spread to more than 100 countries in the last 2–3 months and affected more than 300,000 people worldwide. Initial data suggests that the majority of patients (73%) were over age 40 years, and that the risk of death increases with age. No deaths were reported in patients younger than 10 years old, and only 2.6% of the total fatalities were in patients younger than 40 years of age. After mainland China, the next area with the highest number of confirmed cases is Italy, where as of 16 March 2020, there were 24,747 reported cases, and Iran where 13,938 cases have been confirmed. As on March 24, 2020, the affected population is as follows : The Western Pacific Region under which China, Republic of Korea, Australia, Malaysia, Japan, Singapore, New Zealand, etc. come reported a total of 96,580 confirmed cases and 3502 deaths. On March 24, 2020, 943 new cases and 29 deaths were registered on a single day. The European Region (Italy, Spain, Germany, the United Kingdom, Norway, etc.) accounted for a total of 195,511 positive cases, out of which 24,087 were registered just in 1 day. The numbers peaked up to 10,189 confirmed cases and 1447 deaths in 1 day. In the Southeast Asia Region, 1990 confirmed cases were reported with 65 deaths. In the Eastern Mediterranean Region, a total of 27,215 people were affected and 1877 died due to this epidemic. In the Americas, 49,444 confirmed cases and 565 deaths were reported, with 12,428 new cases and 100 deaths registered in a day. Finally, in the African Region, 1305 confirmed cases and 26 deaths were reported. As per WHO situation reports, the coronavirus started with a few positive cases but due to its highly contagious nature increased more than tenfold within 10 days' time [12]. As of April 7th, 2020, around 1,400,000 cases worldwide have been reported according to the Center for Systems Science and Engineering (CSSE) at John Hopkins University [13].

Recent epidemiological data:[14]

Africa: 189 598 cases; the five countries reporting most cases are South Africa (48 285), Egypt (34 079), Nigeria (12 486), Algeria (10 154) and Ghana (9 638).

Asia: 1 343 166 cases; the five countries reporting most cases are India (256 611), Iran (171 789), Turkey (170 132), Pakistan (103 671) and Saudi Arabia (101 914).

America: 3 349 334 cases; the five countries reporting most cases are United States (1 942 363), Brazil (672 846), Peru (196 515), Chile (134 150) and Mexico (117 103).

Europe: 2 068 739 cases; the five countries reporting most cases are Russia (467 673), United Kingdom (286 194), Spain (241 550), Italy (234 998) and Germany (184 193).

Oceania: 8 721 cases; the five countries reporting most cases are Australia (7 255), New Zealand (1 154), Guam (179), French Polynesia (60) and Northern Mariana Islands (27).

Other: 696 cases have been reported from an international conveyance in Japan.

To assess the magnitude of the risk posed by the SARS-CoV-2, we review following parameters that we believe important: the transmission rate, the incubation period, pathogenesis, potential explanation for the difference between children and adults, treatment and development vaccination probably.

Transmission Rate

The reproduction number (R0), is a mathematical term that defines contagiousness[15]. Specifically, it is the number of people that one sick host can infect. If the R0 is less than one the disease will disappear. If the R0 _ 1 then the disease will spread between people. Estimates of the R0 of SARS-CoV-2 have ranged from 2.24 to as high as 3.58 [16] although the World Health Organization estimates it is between 1.4 and 2.5 [17]. For the purposes of comparison, the mean R0 for seasonal influenza is between 1.1 and 2.3 (variable by region and immunization rates), whereas for SARS was between 1 and 2.75. The slightly higher R0 for SARS-CoV-2 may be because it has a longer prodromal period, increasing the period during which the infected host is contagious. Corona viruses are generally thought to be spread most often by respiratory droplets, not to be confused with airborne transmission [18]. Droplets are larger and tend to fall to the ground close to the infected host and only infect others if the droplet is intercepted by a susceptible host prior to landing. Droplet transmission is typically limited to short distances, generally less than 2 m. This airborne route occurs, for example, in measles (R0 between 12 and 18 [19] and chicken pox (R0s between 3.7 and 5.0 [20]. Once infected droplets have landed on surfaces, their survivability on those surfaces determines if contact transmission is possible. Based on our current understanding from other beta corona viruses, including SARS and MERS, corona viruses can survive, and remain infectious, from 2 h up to 9 days on inanimate surfaces such as metal, glass, or plastic, with increased survival in colder and dryer environments [21,22]. For this reason, the Chinese government has been reported to be disinfecting and even destroying cash in an effort to contain the virus [23]. Reassuringly, cleansing of surfaces with common biocidals such as ethanol and sodium hypochlorite is very effective at inactivation of the coronaviruses within 1 min of exposure [24].

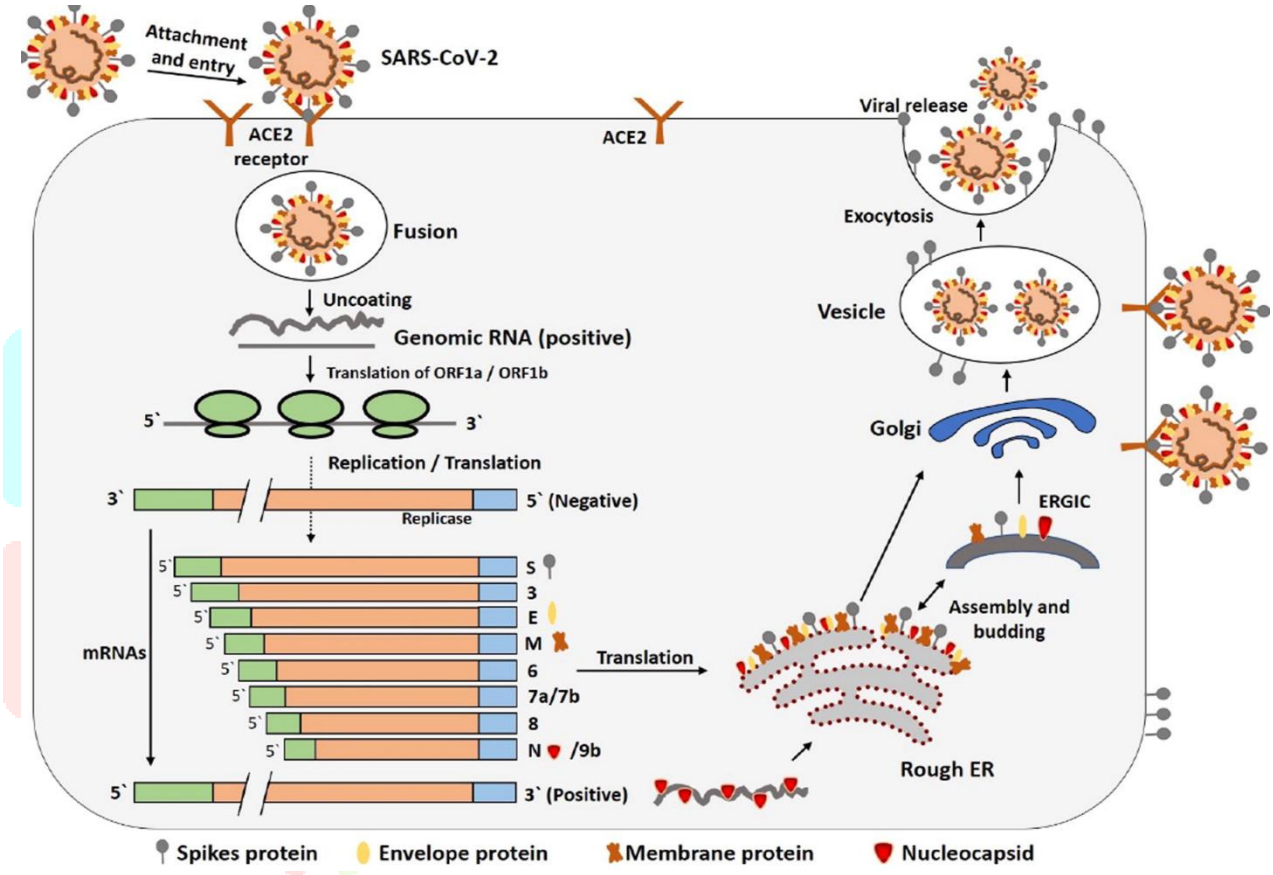
Incubation Period

Understanding incubation periods is very important as it allows health authorities to introduce
more effective quarantine systems for suspected cases. The best current estimates of the SARS-CoV-2 infection range from 2 to 14 days. Analysis of the first 425 cases of COVID-19 in Wuhan a mean incubation period of 5.2 days [25]. A later report, based on 1324 cases, reported

a mean incubation period of 3.0 days [26]. Yet another report, on 88 cases who traveled to Wuhan between 20 and 28 January, had incubation period ranges from 2.1 to 11.1 days, with a mean of 6.4 days [27].

Mechanism of SARS-CoV-2 invasion into host cells

Corona viruses are enveloped, positive-sense, single-stranded RNA virus of ~30 kb. They infect a wide variety of host species [28]. They are largely divided into four genera; α, β, γ, and δ based on their genomic structure. α and β corona viruses infect only mammals [29]. Human corona viruses such as 229E and NL63 are responsible for common cold and cough and belong to α corona virus. In contrast, SARS - CoV, Middle East respiratory syndrome corona virus (MERS CoV) and SARS-CoV-2 are classified to β corona viruses. The life cycle of the virus with the host consists of the following 5 steps: attachment, penetration, biosynthesis, maturation and release. Once viruses bind to host receptors (attachment), they enter host cells through endocytosis or membrane fusion (penetration). Once viral contents are released inside the host cells, viral RNA enters the nucleus for replication. Viral mRNA is used to make viral proteins (biosynthesis). Then, new viral particles are made (maturation) and released. Corona viruses consist of four structural proteins; Spike (S), membrane (M), envelop (E) and nsucleocapsid (N) [30]. Spike is composed of a trans membrane trimetric glycoprotein protruding from the viral surface, which determines the diversity of corona viruses and host tropism. Spike comprises two functional subunits; S1 subunit is responsible for binding to the host cell receptor and S2 subunit is for the fusion of the viral and



cellular membranes. Angiotensin converting enzyme 2 (ACE2) was identified as a functional receptor for SARS-CoV [31]. Structural and functional analysis showed that the spike for SARS CoV-2 also bound to ACE2 [32]. ACE2 expression was high in lung, heart, ileum, kidney and bladder [33]. In lung, ACE2 was highly expressed on lung epithelial cells. Whether or not SARS CoV- 2 binds to an additional target needs further investigation.

Host response to SARS-CoV-2

SARS-CoV-2 infected patients show the symptoms ranges from minort to severe respiratory failure with multiple organ system failure. Even in asymptomatic patients On Computerized tomography (CT) scan, the characteristic pulmonary ground glass opacification can be seen [34]. The action of ACE2 is highly expressed on the apical side of epithelial cells of lungs in alveolar space [35], this virus can likely enter and destroy them. This correlate with the fact that the early injury of lungs was often seen in the distal airways. On viral entry and any type of cell infection leads to the activation of the host's immune response, and the inflammatory cascade is triggered by antigen-presenting cells (APC). The process starts with the APC performing two functions: [36] presenting the foreign antigen to CD4 +-T-helper (Th1) cells, and (2) releasing interleukin-12 to further stimulate the Th1 cell. The Th1 cells stimulate CD8 +-T-killer (Tk) cells that will target any cells containing the foreign antigen. In addition, activated Th1 cells stimulate B-cells to produce antigen-specific antibodies. Epithelial cells, alveolar macrophages and dendritic cells (DCs) are three main components for innate immunity in the airway. DCs reside underneath the epithelium. Macrophages are located at the apical side of the epithelium.DCs and macrophages serve as innate immune cells to fight against viruses till adaptive immunity is involved.T cell mediated responses against coronaviruses.[37]

Potential explanation for the difference between children and adults in COVID-19

Infants and young children are typically at high risk for admission to hospitals due to respiratory tract infection with viruses as respiratory syncytial virus and influenza virus. In contrast, pediatric COVID-19 patients have relatively milder symptoms in general compared to elder patients. The recent report suggested the correlation between the severity of COVID-19 and the amount of viral loads [38], children may have less virus loads even if they get COVID-19. In this line, a couple of hypotheses can be considered. The first possibility is that the expression level of ACE2 may differ between adults and children. The second possibility is that children have a qualitatively different response to the SARS-CoV-2 virus to adults. With ageing, continuous antigen stimulation and thymic involution leads to a shift in T cell subset distribution from naïve T cells to central memory T cells, effector T cells and effector memory T cells [39]. Severe COVID-19 infection is characterized by a massive proinflammatory response or cytokine storm that results in ARDS and multi -organ dysfunction (MODS). It has been also suggested that inflammatory responses in adults and children are much different [40]. Ageing is associated with increasing proinflammatory cytokines that govern neutrophil functions and have been correlated with the severity of ARDS. The third possibility is that the simultaneous presence of other viruses in the mucosa lungs and airways, common in young children, can let SARS-CoV-2 virus compete with them and limit its growth [41].

Treatment

As of now there is no treatment against COVID-19 management has been widely supportive

Gautret P et al. studied 20 cases and found a significant decline in the viral carriage and the average carrying duration compared to untreated patients by receiving 600 mg of hydroxychloroquine per day. Furthermore, adding azithromycin to hydroxychloroquine was substantially more effective in virus removal.[42] The convalescent plasma (CP) has been introduced as the primary treatment. In this treatment CP is acquired from a person recovered from COVID-19 by producing humoral immunity against the2019-nCoV [43]. The success of CP is directly potential source of particular antibodies of human origin[44].

So the main goal should be controlling the infection source and preventing the spread and also to minimize the risk of transmission by developing an easy and early detection methods along with proper quarantining of infected individuals.

Vaccine

Development Vaccination probably offers the best option for COVID-19 control. Epitopes, mRNA, and S protein-RBD structure-based vaccines have been widely proposed and started[45]. Rapid reconstruction of SARS-CoV-2 using a synthetic genomics platform has been reported, and this technical advance is helpful for vaccine development . Human ACE2 transgenic mouse and rhesus monkey models of COVID-19 have been well established for vaccine development and some SARS-CoV-2 vaccines are already under clinical trial [46] to determine this possibility.

Conclusions

The pandemic by COVID-19 is a live issue affecting people worldwide. Without fundamental
therapeutic interventions, current management is to reduce the virus spread and provide appropriate supportive care for diseased patients. There is an urgent need to develop targeted therapies. Understanding the difference in pediatric and adult responses to this virus may help to direct immune based therapeutics.

References:

1. WJ Bellini, LJ Anderson and SW Group. 2003. A novel coronavirus associated with severe acute respiratory syndrome. Journal 348:1953-66.
2. B Yang, GM Leung and Z Feng. 2020. Early Transmission Dynamics in Wuhan, China, of Novel Coronavirus-Infected Pneumonia. Journal 382:1199-1207.
3. M Zheng, Y Gao, G Wang, G Song, S Liu, D Sun, Y Xu and Z Tian. 2020. Functional exhaustion of antiviral lymphocytes in COVID-19 patients. Journal.
4. S Merler, C Viboud, A Vespignani, M Ajelli and H Yu. 2020. Evolving epidemiology and transmission dynamics of coronavirus disease 2019 outside Hubei province, China: a descriptive and modelling study. Journal.
5. Covid19.who.int/
6. C Huang, Y Wang, Z Gao, Q Jin, J Wang and B Cao. 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Journal 395:497-506
7. H Shi, X Han, N Jiang, Y Cao, O Alwalid, J Gu, Y Fan and C Zheng. 2020. Radiological findings from 81 patients with COVID-19 pneumonia in Wuhan, China: a descriptive study Journal 20:425-434.
8. C Huang, Y Wang, Z Gao, Q Jin, J Wang and B Cao. 2020. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Journal 395:497-506
9. F Zhou, T Yu, Y Zhang, H Chen and B Cao. 2020. Clinical course and risk factors for mortality of adult inpatients with COVID-19 in Wuhan, China: a retrospective cohort study. Journal 395:1054-1062.
10. X Lu, S Xu, GWK Wong and T Chinese Pediatric Novel Coronavirus Study. 2020. SARS-CoV-2 Infection in Children. Journal.
11. H Qiu, J Wu, L Hong, Y Luo, Q Song and D Chen. 2020. Clinical and epidemiological features of 36 children with coronavirus disease 2019 (COVID-19) in Zhejiang, China: an observational cohort study. Journal.

12. Coronavirus Disease 2019 (COVID-19) – Epidemiology, Pathogenesis, Diagnosis and Therapeutics by Shailendra K. Saxsena.
13. JHUoMCr center. Journal 2020.
14. who dashboard
15. W Li, MJ Moore, et al 2003 ACE is a functional receptor for coronavirus. Journal 426:450-4.
16. Y Chen, Y Guo, Y Pan and ZJ Zhao. 2020. Structure analysis of the receptor binding of 2019-nCoV. Journal.
17. AC Walls, YJ Park, MA Tortorici, A Wall, AT McGuire and D Veesler. 2020. Structure, Function, and Antigenicity of the SARS-CoV-2 Spike Glycoprotein. Journal.
18. M Letko, A Marzi and V Munster. 2020. Functional assessment of cell entry and accept or usage for SARS-CoV-2 and other lineage B betacoronaviruses. Journal 5:562-569.
19. X Zou, K Chen, J Zou, P Han, J Hao and Z Han. 2020. Single-cell RNA-seq da analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Journal.
20. S Belouzard, VC Chu and GR Whittaker. 2009. Activation of the SARS coronaviru spike protein via sequential proteolytic cleavage at two distinct sites. Journal 106:5871-6.
21. JK Millet and GR Whittaker. 2014. Host cell entry of Middle East respiratory syndrome coronavirus after two-step, furin-mediated activation of the spike protein. Journal 111:15214-9.
22. X Ou, Y LiuZ Qian. 2020 Characterization of spike glycoprotein of SARS-CoV-2 on virus entry and its immune cross-reactivity with SARS-CoV. Journal 11:1620.
23. M Hoffmann, H Kleine-Weber, S Schroeder, N Kruger, T Herrler, S Erichsen, TS Schiergens, G Herrler, NH Wu, A Nitsche, MA Muller, C Drosten and S Pohlmann. 2020. SARSCoV-2 Cell Entry Depends on ACE2 and TMPRSS2 and Is Blocked by a Clinically Proven Protease Inhibitor. Journal.
24.JK Millet and GR Whittaker. 2014. Host cell entry of Middle East respiratory syndrome coronavirus after two-step, furin-mediated activation of the spike protein. Journal 111:15214-9.
25. I Hamming, W Timens, ML Bulthuis, AT Lely, G Navis and H van Goor. 2004. Tissue. A first step in understanding SARS pathogenesis. Journal 203:631-7.
26. HP Jia, DC Look, L Shi, M Hickey, Jr. 2005. ACE2 receptor expression and severe acute respiratory syndrome coronavirus infection depend on differentiation of human airway epithelia. Journal 79:14614-21.
27. T Yoshikawa, T Hill, K Li, CJ Peters and CT Tseng. 2009 SARS by modulating intrinsic functions of monocyte-derived macrophages and dendritic cells. Journal 83:3039-48.
28. R Channappanavar, J Zhao and S Perlman. 2014. T cell-mediated immune response to respiratory coronaviruses. Journal 59:118-28.
29. FA Rabi, MS Al Zoubi, GA Kasasbeh, DM Salameh and AD Al-Nasser. 2020. SARS-CoV-2 and Coronavirus Disease 2019: What We Know So Far. Journal 9
30. BJ Bosch, R van der Zee, CA de Haan and PJ Rottier. 2003. The coronavirus spike protein Journal 77:8801-11.
31. Y Chen, Y Guo, Y Pan and ZJ Zhao. 2020. Structure analysis of the receptor binding of 2019-nCoV. Journal.
32. M.A. Shereen et al. / Journal of Advanced Research 24 (2020) 91–98
33. X Zou, K Chen, J Zou, P Han, J Hao and Z Han. 2020. Single-cell RNA-seq data analysis on the receptor ACE2 expression reveals the potential risk of different human organs vulnerable to 2019-nCoV infection. Journal.
34. WJ Guan, ZY Ni et al China Medical Treatment Expert Group for. 2020. Clinical Characteristics of Coronavirus Disease 2019 in China. Journal.
35. I Hamming, W Timens, ML Bulthuis, AT Lely, G Navis and H van Goor. 2004. Tissue distribution of ACE2 protein, the functional receptor for SARS coronavirus. A first step in understanding SARS pathogenesis. Journal 203:631-7
36.Coronaviridae—Positive Sense RNA Viruses—Positive Sense RNA Viruses. 2011. Availableonline:https://talk.ictvonline.org/ictv-reports/ictv_9th_report/positive-sense- rna-viruses-2011/w/posrna_viruses/222/.
37. T Yoshikawa, T Hill, K Li, CJ Peters and CT Tseng. 2009. SARS coronavirus- induced lung epithelial cytokines exacerbate SARS pathogenesis by modulating intrinsic functions of monocyte-derived macrophages and dendritic cells. Journal 83:3039-48.
38. Y Liu, LM Yan, L Wan, TX Xiang, A Le, JM Liu, M Peiris, LLM Poon and W Zhang. 2020. Viral dynamics in mild and severe cases of COVID-19. Journal.
39. P Saule, J Trauet et al 2006. Accumulation of memory T cells from childhood to old age: central and effector memory cells in CD4(+) versus effector memory and terminally differentiated memory cells in CD8(+) compartment. Journal 127:274-81.
40. HR Wong, RJ Freishtat, M Monaco, K Odoms and TP Shanley. 2010. Leukocyte subsetderived genomewide expression profiles in pediatric septic shock. Journal 11:349-55.
41. S Nickbakhsh, C Mairet al 2019. Virus -virus interactions impact the population dynamics of influenza and the common cold. Journal.
42. Gautret P, VE et al Dupont HT, Honoré S. Hydroxychloroquine and azithromycin as treatment of COVID-19: results of an open-label non-randomized clinical trial International Journal of Antimicrobial Agents. 2020 Mar 20:105949.
43. Garraud O, Heshmati F, Pozzetto B, Lefrere F, Girot R, Saillol A, Laperche S. Plasma therapy against infectious pathogens, as of yesterday, today and tomorrow Transfusion Clinique etBiologique. 2016 Feb 1;23(1):39-44.
44. Marano G, Vaglio S, Pupella S, Facco G, Catalano L, Liumbruno GM, Grazzini G. Convalescent plasma: new evidence for an old therapeutic tool?. Blood Transfusion. 2016 Mar;14(2):152.
45. Diken, M.; Kranz, L.M.; Kreiter, S.; Sahin, U. mRNA: A Versatile Molecule for Cancer Vaccines. Curr. Issues Mol. Biol. **2017**, 22,

113–128.
46. Safety and Immunogenicity Study of 2019-nCov Vaccine (mRNA-1273) to Treat Novel Coronavirus—Full Text View—ClinicalTrials.gov. Available online: https://clinicaltrials.gov/ct2/show/NCT04283461 .