Opinion

Coronavirus Disease 2019 (COVID-19) Crisis: Losing Our Immunity When We Need It the Most

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Simple Summary: With the current coronavirus disease 2019 (COVID-19) crisis, humans have developed new habits and adapted to a novel socioeconomic reality. Indeed, measures including confinement and lockdown have led to mental health problems, economic crisis, and social isolation, among other consequences. These consequences, along with hand washing, sanitization, and face masks, would reduce our immunity against infections, including COVID-19. Such reduced immunity could impact not only our vulnerability to diseases but also the efficacy of vaccines that carry the biggest hope to putting an end to this COVID-19 pandemic. Thus, there is a need to review these approaches and optimize measures taken to limit the spread of COVID-19 by taking into consideration the possible impact of these measures on our immunity to fight COVID-19.

Abstract: The ongoing coronavirus disease 2019 (COVID-19) crisis has led to a new socioeconomic reality with the acquisition of novel habits. Measures imposed by governments and health authorities such as confinement and lockdown have had important consequences, including mental health problems, economic crisis, and social isolation. Combined with newly acquired habits such as hand washing, sanitization, and face masks, these have all directly and indirectly led to reduced immunity. Such effects on the immune system not only impact the epidemiological profile with respect to COVID-19 and other infectious diseases but also limit the efficacy of the ongoing anti-COVID-19 vaccination campaign. Therefore, there is a need to review these approaches and optimize measures towards better population immunity, which is much needed during such an epidemic.

Keywords: coronavirus disease 2019 (COVID-19); immunity

The ongoing coronavirus disease 2019 (COVID-19) crisis [1], as well as the measures imposed by governments, public health recommendations, the emergence of new variants, and the delay in vaccination campaigns, has put a greater spotlight on the importance of population immunity during the critical phase of this rapidly evolving pandemic. In this paper, we focus on the hypothesis that the measures taken during the pandemic and the socioeconomic situation caused by this crisis are reducing immunity at a period when we need it the most.

One of the most important risk factors for immunity problems is obesity, which negatively impacts immunity [2,3]. We believe that the measures imposed to limit the spread of COVID-19, including home confinement, curfew, closed gymnasiums, and work from home recommendations, result in sedentary behaviors [4], which would lead to an obesity pandemic [5]. As we have previously suggested, obesity also increases the vulnerability of patients recovering from COVID-19 as it can lead to an impaired regeneration homeostasis [6] and impact the development of immune cells.

The other measures characterizing this crisis are the periodic hand washing and sanitizing along with physical distancing. Both of these reduce our contact with different infections and pathogenic agents. Contact with pathogens, in a similar way to vaccines,
stimulates the immune system [7,8] and increases its performance. However, with such
limited interaction with the environment compared to that before the start of the COVID-19
crisis, less pathogens are detected by the immune system. This could limit its functional
interaction as described by the hygiene hypothesis [9], especially within the context of
the COVID-19 crisis [10] and the impact on the microbiome [11]. This is also of particular
importance given the close link between the microbiome and immunity [12,13] as well
as the link between microbiota composition and mental health, including anxiety and
depression [14,15], during this COVID-19 outbreak as per the opinions of Venema et al.
and Janda et al. and supported by the research of Yeoh et al. [16–18].

The hard economic situation caused by this COVID-19 crisis [19] has also made a
contribution. For instance, many individuals have lost their jobs [20], and food insecurity
has worsened [21] due to price inflation in the markets [22]. Therefore, the grocery options
for individuals with limited income is more inclined towards unhealthy choices, including
high-fat, high-sugar, and high-salt foods, which are more affordable but have an impact on
immunity [23], including the microbiome [24,25], and further worsen obesity. In addition,
the poor nutritive value of such an unhealthy diet limits the intake of nutrients like
vitamins and therefore impacts the production of antibodies [26], among other immune
functions [27]. In addition, diets also impact the microbiota [28,29] and therefore mental
health and immunity.

Another consequence of the ongoing COVID-19 crisis is the impact on mental health [30,31]
due to psychological stress, disturbed sleeping, and reduced social interaction, which can
lead to problems including depression, anxiety, distress, and panic disorder [32–34]. These
mental health issues during the COVID-19 crisis, along with the impact on immunity [35],
could also increase the usage/intake of products such as drugs, alcohol, and tobacco [36,37]
with consequent effect on immunity, as has been reported for alcohol consumption [38,39],
tobacco [40,41], and drugs [42]. Within this context, it is worth highlighting the importance
of pets as companions in reducing the discomfort caused by social isolation, with resulting
benefits for both mental health (depression, anxiety, and stress) and physical activity [43],
especially as they do not cause transmission of the COVID-19 virus [44].

Moreover, with the lockdown, some individuals may delay receiving the medical care
they need or reduce the frequency of visits to these services [45,46], especially given most
healthcare facilities would have reduced their regular services so that they could focus
their energy on treating COVID-19 cases. This also has a significant impact on general
health, including immunity.

Conclusions

The consequences of this multifactorial reduced immunity (Figure 1) can not only
increase the risk of developing a severe case of COVID-19 [47] and other infectious dis-
eases [48,49] but also limit the efficacy of vaccines [50].

However, to what extent the effects on immunity due to the issues discussed in this
paper (obesity, stress, mental health, hygiene hypothesis, etc.) impact the immune system
compared to primary and secondary immunodeficiencies would depend on many factors,
including the duration of exposure (which would be the period of the COVID-19 crisis),
the severity of these factors, and individual physiological and pathological profiles. Other
factors that could have an important influence include medication and the available medical
care, which could worsen or improve the immunological outcome. Within this context,
our theory indicates that these elements will have an immediate impact on immunity
and vaccine effectiveness (pertinent to the current outcomes in this pandemic) as well
as potential long-term effects that could persist in the future. Indeed, whereas factors
such as disturbed microbiota and mental health problems [51] can be reversed following
a healthy lifestyle and/or therapies, which will then improve immunity, other factors
such as obesity can turn into a chronic status [52] with long-lasting consequences [53],
including on immunity.
Therefore, it is urgent to find innovative solutions beyond home confinement and lockdown to get over this health crisis. Among the most efficient approaches would be to increase the physical activity of the population because exercise has been shown to improve immunity, including in the context of COVID-19 [54–56]. This could reduce the incidence of COVID-19 and improve vaccine efficacy. Importantly, the negative effects of this crisis on immunity described herein suggest the need to speed up the vaccination process before the effect of the vaccines is reduced, especially due to the emerging variants.

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Conflicts of Interest: The authors declare that there is no conflict of interest. This paper does not take any position for or against any decision of a political or economic nature.

Figure 1. COVID-19 crisis measures lead to reduced immunity via diverse factors that could impact both COVID-19 morbidities and vaccines efficacy.
References

1. Sohrabi, C.; Alsafi, Z.; O’Neill, N.; Khan, M.; Kerwan, A.; Al-Jabir, A.; Iosifidis, C.; Agha, R. World Health Organization declares global emergency: A review of the 2019 novel coronavirus (COVID-19). Int. J. Surg. 2020, 76, 71–76. [CrossRef] [PubMed]

2. Milner, J.J.; Beck, M.A. The impact of obesity on the immune response to infection. Proc. Nutr. Soc. 2012, 71, 298–306. [CrossRef] [PubMed]

3. Andersen, C.J.; Murphy, K.E.; Fernandez, M.L. Impact of Obesity and Metabolic Syndrome on Immunity. Adv. Nutr. 2016, 7, 66–75. [CrossRef] [PubMed]

4. McDowell, C.P.; Herring, M.P.; Lansing, J.; Brower, C.; Meyer, J.D. Working From Home and Job Loss Due to the COVID-19 Pandemic Are Associated With Greater Time in Sedentary Behaviors. Front. Public Health 2020, 8, 597619. [CrossRef] [PubMed]

5. Ghanemi, A.; Yoshioka, M.; St-Amand, J. Will an obesity pandemic replace the coronavirus disease-2019 (COVID-19) pandemic? Med. Hypotheses 2020, 144, 110042. [CrossRef] [PubMed]

6. Ghanemi, A.; Yoshioka, M.; St-Amand, J. Regeneration during Obesity: An Impaired Homeostasis. Animals 2020, 10, 2344. [CrossRef]

7. Akira, S.; Uematsu, S.; Takeuchi, O. Pathogen recognition and innate immunity. Cell 2006, 124, 783–801. [CrossRef]

8. Medzhitov, R. Recognition of microorganisms and activation of the immune response. Nature 2007, 449, 819–826. [CrossRef] [PubMed]

9. Alexandre-Silva, G.M.; Brito-Souza, P.A.; Oliveira, A.C.S.; Cerni, F.A.; Zottich, U.; Pucca, M.B. The hygiene hypothesis at a glance: Early exposures, immune mechanism and novel therapies. Acta Trop. 2018, 188, 16–26. [CrossRef]

10. Sehrawat, S.; Rouse, B.T. Does the hygiene hypothesis apply to COVID-19 susceptibility? Microbes Infect. 2020, 22, 400–402. [CrossRef]

11. Thaiss, C.A.; Zmora, N.; Levy, M.; Elinav, E. The microbiome and innate immunity. Proc. Natl. Acad. Sci. USA 2021, 118. [CrossRef]

12. Thaiss, C.A.; Zmora, N.; Levy, M.; Elinav, E. The microbiome and innate immunity. Nature 2016, 535, 65–74. [CrossRef]

13. Sadler, R.; Singh, V.; Benakis, C.; Garzetti, D.; Brea, D.; Stecher, B.; Anrather, J.; Liesz, A. Microbiota differences between commercial breeders impacts the post-stroke immune response. Brain Behav. Immun. 2017, 66, 23–30. [CrossRef]

14. Rieder, R.; Wisniewski, P.J.; Alderman, B.L.; Campbell, S.C. Microbes and mental health: A review. Brain Behav. Immun. 2017, 66, 9–17. [CrossRef] [PubMed]

15. Dinan, T.G.; Cryan, J.F. The Microbiome-Gut-Brain Axis in Health and Disease. Gastroentero. Clin. N. Am. 2017, 46, 77–89. [CrossRef] [PubMed]

16. Venema, K. Foreword—The importance of a healthy microbiota in the era of COVID-19. Benef. Microbes 2021, 12, 1–3. [CrossRef] [PubMed]

17. Janda, L.; Mihalić, M.; Štastná, M. Is a healthy microbiome responsible for lower mortality in COVID-19? Biologia 2021, 76, 819–829. [CrossRef] [PubMed]

18. Yeoh, Y.K.; Zuo, T.; Lui, G.C.; Zhang, F.; Liu, Q.; Li, A.Y.; Chung, A.C.; Cheung, C.P.; Tso, E.Y.; Fung, K.S.; et al. Gut microbiota composition reflects disease severity and dysfunctional immune responses in patients with COVID-19. Gut 2021, 70, 698–706. [CrossRef]

19. Gupta, M.; Abdelmaksoud, A.; Jafferany, M.; Lotti, T.; Sadoughifar, R.; Goldust, M. COVID-19 and economy. Dermatol. Ther. 2020, 33, e13329. [CrossRef] [PubMed]

20. Crayne, M.P. The traumatic impact of job loss and job search in the aftermath of COVID-19. Psychol. Trauma 2020, 12, S180–S182. [CrossRef]

21. Niles, M.T.; Bertmann, F.; Belarmino, E.H.; Wentworth, T.; Biehl, E.; Neff, R. The Early Food Insecurity Impacts of COVID-19. Nutrients 2020, 12, 96. [CrossRef] [PubMed]

22. Singh, S.; Nourozi, S.; Acharya, L.; Thapa, S. Estimating the potential effects of COVID-19 pandemic on food commodity prices and nutrition security in Nepal. J. Nutr. Sci. 2020, 9, e51. [CrossRef] [PubMed]

23. Myles, I.A. Fast food fever: Reviewing the impacts of the Western diet on immunity. Nutr. J. 2014, 13, 61. [CrossRef]

24. Agus, A.; Denizot, J.; Thévenot, J.; Martinez-Medina, M.; Massier, S.; Sauvanet, P.; Bernaler-Donadille, A.; Denis, S.; Hofman, P.; Bonnet, R.; et al. Western diet induces a shift in microbiota composition enhancing susceptibility to Adherent-Invasive E. coli infection and intestinal inflammation. Sci. Rep. 2016, 6, 19032. [CrossRef]

25. Yang, W.; Cong, Y. Gut microbiota-derived metabolites in the regulation of host immune responses and immune-related inflammatory diseases. Cell Mol. Immunol. 2021. [CrossRef]

26. Axelrod, A.E.; Pruzansky, J. The Role of the Vitamins in Antibody Production. In Vitamins & Hormones; Harris, R.S., Marrian, G.F., Thimann, K.V., Eds.; Academic Press: Cambridge, MA, USA, 1955; Volume 13, pp. 1–27.

27. Wintergerst, E.S.; Maggini, S.; Hornig, D.H. Contribution of selected vitamins and trace elements to immune function. Ann. Nutr. Metab. 2007, 51, 301–325. [CrossRef]

28. Conlon, M.A.; Bird, A.R. The Impact of Diet and Lifestyle on Gut Microbiota and Human Health. Nutrients 2015, 7, 17–44. [CrossRef] [PubMed]

29. Chassaing, B.; Vijay-Kumar, M.; Gewirtz, A.T. How diet can impact gut microbiota to promote or endanger health. Curr. Opin. Gastroenterol. 2017, 33, 417–421. [CrossRef]
30. Li, S.; Wang, Y.; Xue, J.; Zhao, N.; Zhu, T. The Impact of COVID-19 Epidemic Declaration on Psychological Consequences: A Study on Active Weibo Users. *Int. J. Environ. Res. Public Health* **2020**, *17*, 2032. [CrossRef]

31. Shigemura, J.; Ursano, R.J.; Morganstein, J.C.; Kurosawa, M.; Benedek, D.M. Public responses to the novel 2019 coronavirus (2019-nCoV) in Japan: Mental health consequences and target populations. *Psychiatry Clin. Neurosci.* **2020**, *74*, 281–282. [CrossRef]

32. Ettman, C.K.; Abdalla, S.M.; Cohen, G.H.; Sampson, L.; Vivier, P.M.; Galea, S. Prevalence of Depression Symptoms in US Adults Before and During the COVID-19 Pandemic. *JAMA Netw. Open* **2020**, *3*, e2019686. [CrossRef]

33. Sher, L. COVID-19, anxiety, sleep disturbances and suicide. *Sleep Med.* **2020**, *70*, 124. [CrossRef]

34. Qiu, J.; Shen, B.; Zhao, M.; Wang, Z.; Xie, B.; Xu, Y. A nationwide survey of psychological distress among Chinese people in the COVID-19 epidemic: Implications and policy recommendations. *Gen. Psychiatr.* **2020**, *33*, e100213. [CrossRef] [PubMed]

35. Vasile, C. Mental health and immunity (Review). *Exp. Ther. Med.* **2020**, *20*, 211. [CrossRef] [PubMed]

36. Jane-Llopis, E.; Matytsina, I. Mental health and alcohol, drugs and tobacco: A review of the comorbidity between mental disorders and the use of alcohol, tobacco and illicit drugs. *Drug Alcohol Rev*. **2006**, *25*, 515–536. [CrossRef] [PubMed]

37. Tran, T.D.; Hammarberg, K.; Kirkman, M.; Nguyen, H.T.M.; Fisher, J. Alcohol use and mental health status during the first months of COVID-19 pandemic in Australia. *J. Affect. Disord.* **2020**, *277*, 810–813. [CrossRef] [PubMed]

38. Pasala, S.; Barr, T.; Messaoudi, I. Impact of Alcohol Abuse on the Adaptive Immune System. *Alcohol Res.* **2018**, *39*, 185–197.

39. Szabo, G.; Saha, B. Alcohol’s Effect on Host Defense. *Alcohol Res.* **2015**, *37*, 159–170.

40. Johnson, J.D.; Houchens, D.P.; Kluwe, W.M.; Craig, D.K.; Fisher, G.L. Effects of Mainstream and Environmental Tobacco Smoke on the Immune System in Animals and Humans: A Review. *Crit. Rev. Toxicol.* **1990**, *20*, 369–395. [CrossRef]

41. Aronson, Y.; Shoenfeld, Y.; Amital, H. Effects of tobacco smoke on immunity, inflammation and autoimmunity. *J. Autoimmun.* **2010**, *34*, J258–J265. [CrossRef]

42. Cabral, G.A.; Dove Pettit, D.A. Drugs and immunity: Cannabinoids and their role in decreased resistance to infectious disease. *J. Neuroimmunol.* **1998**, *83*, 116–123. [CrossRef]

43. Morgan, L.; Protopopova, A.; Birker, R.I.D.; Itin-Shwartz, B.; Sutton, G.A.; Gamliel, A.; Yakobson, B.; Raz, T. Human–dog relationships during the COVID-19 pandemic: Booming dog adoption during social isolation. *Humimat. Soc. Sci. Commun.* **2020**, *7*, 155. [CrossRef]

44. Costagliola, A.; Liguori, G.; d’Angelo, D.; Costa, C.; Ciani, F.; Giordano, A. Do Animals Play a Role in the Transmission of Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2)? A Commentary. *Animals* **2020**, *11*, 16. [CrossRef]

45. Ahmed, S.; Ajisola, M.; Azeem, K.; Bakibinga, P.; Chen, Y.F.; Choudhury, N.N.; Fayehun, O.; Griffiths, F.; Harris, B.; Kibe, P.; et al. Impact of the societal response to COVID-19 on access to healthcare for non-COVID-19 health issues in slum communities of Bangladesh, Kenya, Nigeria and Pakistan: Results of pre-COVID and COVID-19 lockdown stakeholder engagements. *BMJ Glob. Health* **2020**, *5*. [CrossRef] [PubMed]

46. Murewanhema, G.; Makurumidze, R. Essential health services delivery in Zimbabwe during the COVID-19 pandemic: Perspectives and recommendations. *Pan Afr. Med. J.* **2020**, *35*, 143. [CrossRef]

47. Shields, A.M.; Burns, S.O.; Savic, S.; Richter, A.G. COVID-19 in patients with primary and secondary immunodeficiency: The United Kingdom experience. *J. Allergy Clin. Immunol.* **2021**, *147*, 870–875.e871. [CrossRef]

48. Cohen, J.I. Primary Immunodeficiencies Associated with EBV Disease. *Curr. Top. Microbiol. Immunol.* **2015**, *390*, 241–265. [PubMed]

49. Chinen, J.; Shearer, W.T. Secondary immunodeficiencies, including HIV infection. *J. Allergy Clin. Immunol.* **2010**, *125*, S195–S203. [PubMed]

50. Bonilla, F.A. Update: Vaccines in primary immunodeficiency. *J. Allergy Clin. Immunol.* **2018**, *141*, 474–481. [CrossRef] [PubMed]

51. Minihan, E.; Gavin, B.; Kelly, B.D.; McNicholas, F. COVID-19, mental health and psychological first aid. *Ir. J. Psychol. Med.* **2020**, *37*, 259–263. [CrossRef]

52. Ghanemi, A.; St-Amand, J. Redefining obesity toward classifying as a disease. *Eur. J. Intern. Med.* **2018**, *55*, 20–22. [CrossRef] [PubMed]

53. Ghanemi, A.; Yoshioka, M.; St-Amand, J. Broken Energy Homeostasis and Obesity Pathogenesis: The Surrounding Concepts. *J. Clin. Med.* **2018**, *7*, 453. [CrossRef] [PubMed]

54. Abdelbasset, W.K. Stay Home: Role of Physical Exercise Training in Elderly Individuals’ Ability to Face the COVID-19 Infection. *J. Intern. Med.* **2020**, *2020*, 837596. [CrossRef]

55. Ranasinghe, C.; Ozemek, C.; Arena, R. Exercise and well-being during COVID 19—Time to boost your immunity. *Expert Rev. Anti-Infect. Ther.* **2020**, *18*, 1195–1200. [CrossRef] [PubMed]

56. Shahrbanian, S.; Alikhani, S.; Ahmadi Kakavandi, M.; Hackney, A.C. Physical Activity for Improving the Immune System of Older Adults During the COVID-19 Pandemic. *Altern Ther. Health Med.* **2020**, *26*, 117–125.