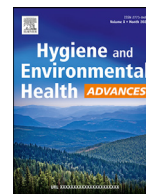




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### The effect of COVID-19 on our lifestyle and microbiome: What could long term imbalanced diet and germophobia mean for our immunity?



The COVID-19 pandemic has forced many countries into government-imposed lockdowns and social distancing. It is no surprise, especially following the COVID-19 pandemic, that we have changed our lifestyle, intensified our disinfection practices (which can affect both harmful and beneficial organisms), and are more conscious of diseases. (Finlay et al., 2021) We are currently seeing many countries going through a fifth wave of COVID-19 infections, with the use of preventative measures being reconsidered, and intense hygiene habits maintained. Can excessive hygiene practice and changes in our dietary lifestyle affect human susceptibility to infection?

In recent years we have seen growing numbers of non-communicable chronic as well as autoimmune diseases, including inflammatory bowel syndrome (IBD), cardiovascular diseases, asthma and eczema. (Organization, W. W. H. 2021; Miller, 2022) The increasing prevalence of these diseases shows a clear connection with the disruption of our microbiome. (Wilkins et al., 2019) The microbiome consists of trillions of microorganisms which are found on human skin and mucosal surfaces. The precise number of these organisms in the body has received much speculation, with values in the vicinity of  $10^{13}$ . (Sender et al., 2016) This diverse set of microorganisms includes bacteria, viruses, fungi and protozoa, which have evolved to coexist with and within us in symbiosis. (Dominguez-Bello et al., 2019) The development and function of many of our bodily systems, including the immune, digestive, endocrine and nervous systems depend on the normal functions of our microbiome. (Dominguez-Bello et al., 2019)

The ability of our microbiome to influence a diverse set of bodily systems is hypothesised via three routes connecting our various organs; the gut-lung, gut-brain and gut-skin axis. Consequently, disturbances to our microbiome (dysbiosis) have been linked as cause or catalyst to common disorders concerning these body axis. For instance, infants with eczema show decreased microbiome diversity, while feeding probiotics to mice leads to skin microbiome changes. (Abrahamsson et al., 2012; Levkovich et al., 2013) Additionally, studies have shown that respiratory diseases are frequently associated with gastrointestinal symptoms, while reports show dramatic improvement of hepatic encephalopathy with oral antibiotic administration due to the alteration of the intestinal bacterial flora. (Wang et al., 2014; Morgan, 1991)

Medications such as antibiotics can alter our microbiome, but diet and lifestyle also play a pivotal role. Western diets high in saturated fats increase bile acid production, which consequently alters the microbes able to survive this extreme environment. For instance, high bile acid cultivates *Bilophila wadsworthia* with evidence that this microbe promotes immune responses and increasing susceptibility to IBD (Devkota et al., 2012). These changes in the microbiome have been associated with irregular mucosal immune responses, such as the up-regulation of T-helper cells Th1, Th2 and Th17, the downregulation

of T regulatory cells (Tregs), and uncontrolled humoral immunity. This can exacerbate chronic intestinal inflammation and unavoidably cause tissue injury. (Zheng et al., 2020) The COVID-19 pandemic has undeniably been a catalyst to dietary changes, with economic constraints and virus spread impacting global trades, transportation services, workforce, and lockdowns decreasing physical activity and increasing snacking. (Finlay et al., 2021) These fluctuations in timing, quantity, quality and frequency of food consumption contribute to gut dysbiosis. Moreover, COVID-19 lockdowns and restrictions have changed our lifestyle dramatically and abruptly. Studies suggests that social interactions and behaviors also influence our microbiome, and so dysbiosis in these scenarios is not unexpected. (Finlay et al., 2021; Pasquaretta et al., 2018)

It is no surprise that the world is moving in the direction of increased germ-free conditions. These changes were necessary in the context of controlling COVID-19 transmission. However, we have to wonder what important microbiome support we are losing as a result? Is there a line after which these protective measures tip towards harm, and have we crossed it? What are the consequences to the future of disease control, are there any? Research is yet to answer these questions, nonetheless we currently know that (i) our current world continuously puts us at risk of dysbiosis and declining microbiome diversity, and (ii) this is linked to disease.

Researchers are slowly revealing the causes of diseases linked to the microbiome and dysbiosis. It is only very recently that we have seen evidence in pregnant women, where the response to viral or bacterial infections may change due to the alterations of the microbiome. (Fuhler, 2020) Other areas of research focus on the connection of the microbiome with our immune system in regards to critical care. Common medical procedures or treatments within an ICU environment, can aggravate the microenvironment of the host, by allowing pathogens to prevail over a healthy microbial population. Consequently, the breakdown of the host's microbial equilibrium, changes the microbiome to a pathobiome, which tampers with the regulation of inflammation and immunity. This can further worsen disease outcome. (Miniet et al., 2021) There is also evidence for the association of oral microbiome transmission with the duration of cohabitation between individuals. There was significant sharing of strains, which ranged between 12% and 32% for the gut and oral microbiomes respectively. Interestingly, the duration of cohabitation affected strain sharing more when compared with factors such as age or genetics. (Valles-Colomer et al., 2023)

Being able to demystify mechanistic processes such as microorganism transmission and altering of biome populations, will enable researchers to taxonomise findings around the microbiome, and elucidate more of its association with disease, especially non-infectious microbiome-associated diseases.

As we wait eagerly for research to further uncover the link between hygiene, dysbiosis and disease, we are left to wonder: If this trend in dysbiosis continues, are we at risk of introducing novel dysbiosis-diseases that would not have otherwise existed?

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## Declaration of Competing Interest

We declare no competing interests. SP is the senior author.

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