Immunity Debt and Immunity Theft

THE GLOBAL RESURGENCE OF RESPIRATORY INFECTIONS

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The recent resurgence of respiratory infections following the COVID-19 pandemic is a topic of great interest, with the prevalence of viral infections such as influenza and respiratory syncytial virus (RSV) on the rise around the globe.[1] With COVID-19 still spreading rapidly in many countries,[2] the collision of these viruses has been termed a 'tripledemic'.[3] The incidence of bacterial infections such as *Streptococcus pneumoniae* and group A *Streptococcus* have also been increasing.[4]

Whilst the mechanisms behind the rising incidence of these infections are unknown, current thought amongst experts are around the concepts of immunity debt versus immunity theft.[5] (See Box 1)

The innate and adaptive immune system

Both the innate and adaptive immune systems are crucial for the protection from illness.[6] The innate immune system is responsible for the initial immune response, responding rapidly against an invading pathogen.[6] While the adaptive immune system may take longer to respond, it compensates by forming immunologic memory and generating antibodies, thereby providing protection upon subsequent exposure to the same or similar pathogens.[6] The adaptive immune system relies on a tightly regulated interplay between T cells, antigen-presenting cells, and B cells.[6]

Box 1

IMMUNITY DEBT VS IMMUNITY THEFT

Immunity debt, or immunity gap, describes the consequences of decreased exposure to a variety of pathogens due to the non-pharmaceutical interventions (NPIs) taken to control COVID-19, such as lockdown periods and restricting public health measures.[5]

On the other hand, immunity theft suggests that severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) may compromise immunity, potentially making individuals who have had COVID-19 more vulnerable to other infections.[5]

IMMUNITY DEBT

Implications of COVID-19 lockdowns

The prevalence of infectious diseases such as influenza and RSV decreased significantly during lockdowns,[7] with a 93.4% reduction in RSV detection during winter 2020 in Australia.[4] Researchers accurately predicted there would be a rise in viral infections following the NPIs imposed during the COVID-19 pandemic,[8] with staggering surges in respiratory tract infections (RTIs) across the globe following the lifting of lockdowns in 2021.[4,9,10] In 2022, compared to 2019, Germany saw a four-fold increase in the number of RTIs,[9] with prevalence continuing to rise across Europe, with higher levels of fever and cough this past winter.[11] Interestingly, there also appears to be a seasonal shift, with statistical data showing that the number of infections and hospital admissions post-pandemic were similar or even greater outside of the typical winter peaks,[4] making immune health a consideration all year.

Experts state that due to the reduced exposure to microbial agents during this time, the increase in viral activity once the NPIs lifted was to be expected.[12] Although it has been stated that this has resulted in 'weaker' immune systems, it can be argued that lack of exposure does not weaken immunity, rather it simply does not enhance it.[12]

IMMUNITY THEFT

Immune system dysregulation

One of the most concerning long-term impacts of COVID-19 is the potential immune dysregulation that can persist after infection.[13] Multiple studies have identified protein and genetic material from SARS-CoV-2 persisting in the body for over one year following contraction of COVID-19.[13]

Viral persistence may occur following acute infection if a virus is not completely cleared allowing for the continued viral replication and viral protein production to persist in tissues.[13] These viral proteins are then released into circulation, interfering with immune responses, dysregulating the immune system, promoting inflammation, and activating latent viruses.[13] Viral persistence can damage tissues by altering the differentiation of virus-specific T and B cells over time.[13] A study demonstrated that immunological dysfunction persisted in patients with long COVID for 8 months after infection, with these patients demonstrating persistently highly activated innate immune cells and reduced naive T and B cells following infection.[14]

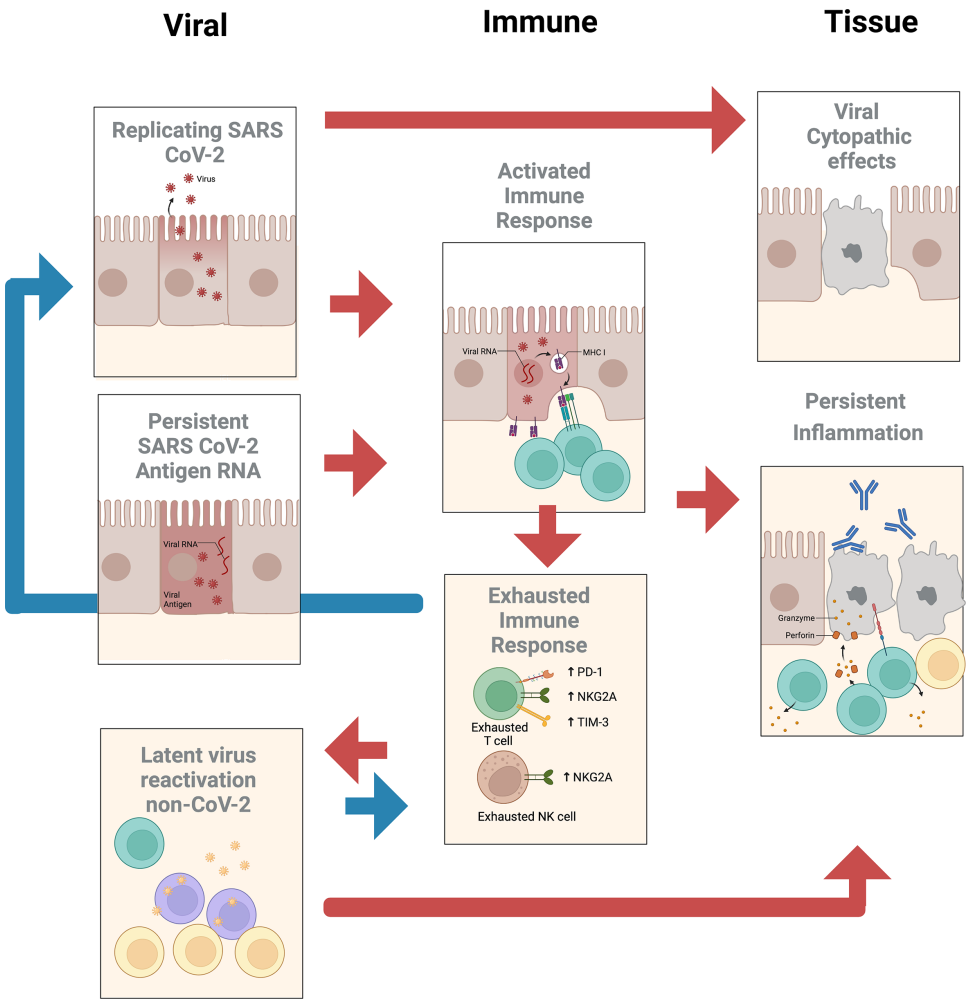
Remarkably, viral proteins have been found in tissues all over the body, including the reproductive system, cardiovascular system, brain, muscles, eyes, and lung tissue.[15] Viral persistence has also been demonstrated with other viruses, such as Ebola virus, which can linger in tissues and cause chronic symptoms and new outbreaks.[16]

HYPERACTIVE IMMUNE SYSTEM OR IMMUNE SYSTEM FAILURE?

Early on in the pandemic, two contradictory hypotheses existed for the pathophysiology of severe COVID-19.[17] The first hypothesis referred to an hyperactive immune system, or an overactive immune response caused by the excessive production of inflammatory cytokines.[17] The second hypothesis referred to immune system failure involving the collapse of protective immunity, with SARS-CoV-2 causing uncontrolled viral replication and dissemination.[17]

Recent research has demonstrated that it is possible that both hypotheses may be true, in that COVID-19 causes both an overexaggerated inflammatory response through excessive cytokine production, in addition to increased viral replication.[18] SARS-CoV-2 has also been found to cause increased T-cell activation and subsequent T-cell exhaustion.[19] This indicates that COVID-19 can lead to the dysregulation of both the innate and the adaptive immune systems (see Figure 1).[20]

Figure 1. Summary of potential viral, immune, and tissue roles in long COVID[16]



SUPPORTING IMMUNE SYSTEM HEALTH

Nutrients and herbal medicines

Certain nutrients and herbal medicines can support the regulation of immune activity, providing protection from infections, relief of common symptoms, and accelerate recovery.

Key nutrients to enhance immune system health include zinc, vitamins C and D, probiotics, and quercetin, with specific therapeutic dosages recommended for protection against respiratory viruses (see Table 1).[21] Together, these nutrients play a key role in immune system defence and restoration (see Table 2).[21]

Table 1. Nutrient recommendations to protect against respiratory viruses[21]

NUTRIENT	DOSE
Zinc	25 mg/day **During infection:** 50-75 mg/day for 1-2 weeks
Vitamin D	1000-5000 IU/day, or higher if deficient
Vitamin C	500 mg-1 g/day **During infection:** Up to 6 g/day, in divided doses throughout the day
Quercetin	400-600 mg/day

Notable herbal medicines ideal for use in conjunction with the above nutrients to protect against respiratory viruses include andrographis, pelargonium, echinacea, and black seed oil.[21]

Lifestyle

Evidence clearly demonstrates the importance of regular physical activity, adequate sleep, and effective stress management for optimal immune system health. Lack of movement, poor sleep, and chronic stress can hinder immune function, promote inflammation, and increase the risk of infection from respiratory viruses.[22]

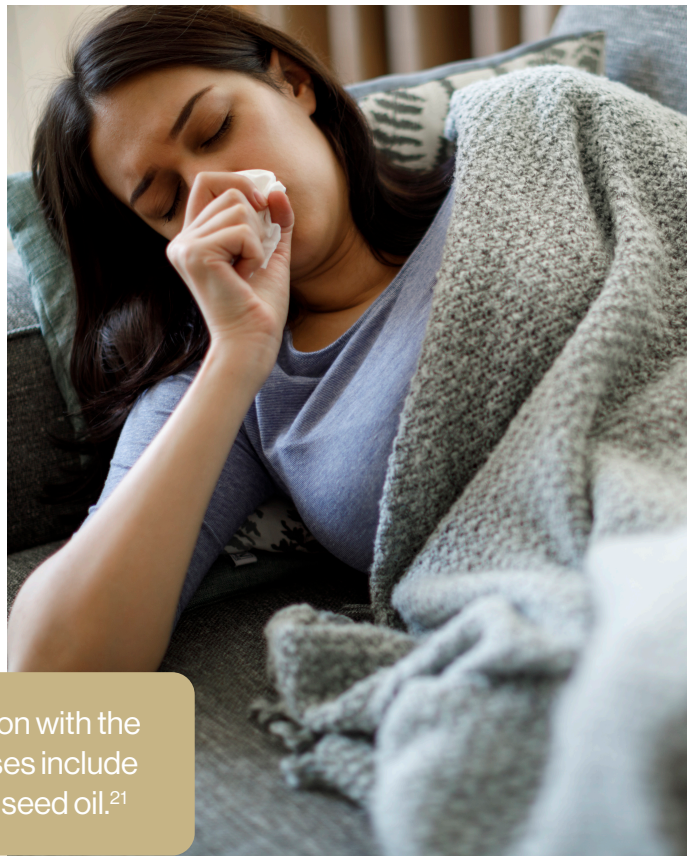


Table 2. Nutrients for respiratory viruses[21]

	SIX KEY CRITERIA					
	1 **Improves first line of defence against viral entry** (nose, throat, lung)	2 **Establishes immune-regulation activity**	3 **Exhibits antiviral activity of relevance to viral respiratory infections**	4 **Possesses antioxidant activity**	5 **Modulates inflammatory response to dampen hyper-inflammation**	6 **Low dietary intake and sub-optimal nutritional status is common**
Zinc	•	•	•	•	•	•
Vitamin C	•	•		•		•
Vitamin D	•	•	•		•	•
Quercetin			•	•	•	•

The pivotal role of the gut microbiome

With 70% of immune cells residing in the gut, supporting microbiome health is vital for a healthy immune system.[23] The microbiome plays a role in mounting immune responses, with a healthy microbiome exerting powerful immunomodulatory and anti-inflammatory activities,[24] however, in the presence of infection, these key responses can be disrupted.[25] Poor microbiome health is associated with an increased risk of respiratory infections and has been implicated in the prediction of COVID-19 severity, with microbial imbalance showing decreased levels of immune-modulating bacterial species and increased inflammatory markers in COVID-19 patients.[26]

CONCLUSION

The aftermath of the COVID-19 pandemic is still having a significant impact globally. The underlying mechanisms behind the rising rate of respiratory infections is not entirely understood, however, there may be multiple overlapping factors at play.

It is possible that immunity debt and immunity theft are not mutually exclusive, with decreased exposure to pathogens during COVID-19 NPIs, and immune system dysregulation following COVID-19 infection, both contributing to the resurgence of multiple infections worldwide. Building a vital and robust immune system is key not only to help prevent infections, but to also ensure the body has the resources available to recover efficiently and effectively from an infection when the challenge arises.

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