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Immunosuppression for hyperinflammation in COVID-19: a double-edged sword?

Mehta and colleagues¹ postulate that hyperinflammation in coronavirus disease 2019 (COVID-19) could be a driver of severity that is amenable to therapeutic targeting since retrospective data have shown that systemic inflammation is associated with adverse outcome. However, correlation does not equal causation, and it is equally plausible that increased virus burden (secondary to failure of the immune response to control infection) drives inflammation and consequent severity (as shown for other viruses2) rather than augmented inflammation being an inappropriate host response that requires correction.

The authors hypothesise that approaches such as corticosteroids or Janus kinase (JAK) inhibitors could be considered if hyperinflammation is present. Broad immunosuppression in patients with overwhelming viral illness might be inadvisable. Beneficial anti-inflammatory effects should be weighed up against the potentially

detrimental effects of inhibiting antiviral immunity, thereby delaying virus clearance and perpetuating illness. Accordingly, findings from multiple studies in humans and animals indicate that corticosteroid immunosuppression (both inhaled and systemic) impairs induction of anti-viral type-I interferon responses to a range of respiratory viruses,34 effects that are likely to also occur in the context of COVID-19. Selective therapies with JAK inhibitors could be expected to have similar effects. JAK-STAT signalling is a major component of the type-I interferon pathway.3 Tofacitinib has been shown to inhibit interferon-α production in vitro.5 Suppression of interferon or other mediators (eq. interleukin 6) could also promote secondary bacterial infection and further complicate the disease course.3

The decision to pharmacologically immunosuppress a critically unwell patient with COVID-19 remains a difficult one. Possible beneficial effects of reducing inflammation should be carefully weighed up against the potential for deleterious impairment of anti-microbial immunity.

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Authoritarianism and the threat of infectious diseases

Punitive social policy, encompassing the dismantling of the welfare state with the expansion of the penal state and its associated institutions, as nicely stated by Elias Nosrati and Michael Marmot in their Perspective, might indeed be considered an upstream social determinant of health. Nosrati and Marmot's analysis relates to the findings described by Navarro and colleagues, linking political ideology with policies aimed at reducing social inequalities such as welfare state and labour market policies.

The increasingly punitive policy environment in North America, Europe, and some South American countries (eg, Brazil and Argentina) is probably related to the spread of an authoritarian ideology that has xenophobia at its core.

However, a trait of those repulsion speeches that is often missed is how immigrants or strangers are referred to as parasites or contagious agents. Recent examples include the xenophobic and, in some cases violent, acts committed against Asiatic citizens in Western countries since the coronavirus disease 2019 outbreak began,3 or Donald Trump's statement that "tremendous" infectious disease is pouring across the Mexican border into the USA.4 Constant upheavals by the Trump and Orbán⁵ administrations about migrants, some of Brexit's collateral effects,6 and statements about refugees by the Italian politician Matteo Salvini⁷ and the Spanish far-right Vox party8 can be understood in this context.

It is not that foreigners cannot transmit threatening infectious





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