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[Commentary] Long COVID, linking etiopathogenic theories

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Abstract

In this letter we discuss the various theories involved in the pathogenesis of Long COVID and how they are closely interrelated, conditioning the full range of symptoms and signs presented by patients affected by this condition, as well as calling for the recognition of the disease by the health authorities that must begin to streamline their health processes to limit the burden of this disease, which tends to be chronic and degenerative.

Keywords: Long COVID, Viral persistence, Amyloid clots, Dysbiosis.

After four years of the pandemic, a syndrome has begun to emerge that is made up of an infinite number of symptoms and signs that survivors of acute COVID-19 begin to present, being classified as Long COVID and defined as the persistence of symptoms after 12 weeks of having suffered an acute picture.

Currently, many theories try to explain this chronic trend of COVID, highlighting the theory of viral persistence or viral particles, which mentions that the persistence of Sars Cov particles, mainly protein S and N, has been demonstrated in various tissues, excreta, and plasma up to 12 months after having suffered the acute infection. Another of the theories, and one that is gaining strength since the presence of these has been demonstrated in chronic COVID patients, is the presence of amyloid microthrombi, a characteristic that gives them greater hardness, little malleability, and greater capacity for occlusion of the microvasculature. which could ultimately lead to organ dysfunction. Another phenomenon has been demonstrated: the S protein of Sars Cov2 favors tissue amyloidogenesis, so this characteristic could support the amyloid characteristic of thrombi, which in turn are produced by the phenomenon of immunothrombosis, which is also favored by the persistence of thrombosis. these viral particles and the activation of platelets and lymphocytes (hyperactivity of platelets and the immune system will continue in chronic inflammation, nourishing the inflammasome and finally, activation of coagulation. [1][2][3][4]

Chronic and persistent inflammation can have positive or negative effects on the immune system; When there is positive feedback from the immune system, autoimmunity situations can be generated, due to hyperactivity of the immune system, conditioning risks of various autoimmune diseases. [5][6]

When negative feedback of the immune system occurs after an acute picture of COVID, it presents a kind of exhaustion of the cells, mainly CD4 and CD8 lymphocytes, which causes the system to weaken and sets the tone for other processes such as reactivation of latent viruses. and a dysbiosis process, in which the intestinal microbiota is affected, even by an imbalance between the pre-existing virome and the microbiota, where the pathogenic intestinal flora will have harmful effects on the human body, mainly affecting the brain-intestine axis, conditioning conditions various neuropsychiatric and gastrointestinal disorders; Another theory that would explain the diversity of symptoms manifested by these patients and related to dysbiosis is that of damage to the vagus nerve, the main cranial nerve that communicates the central nervous system with the parasympathetic nervous system, which may explain the various predominant symptoms: neuropsychiatric, digestive, respiratory and cardiovascular, this probably favored by the great neurotropism expressed by Sars Cov2 that culminates affecting the central nervous system and the vagus nerve, generating various dysautonomia, in addition to the fact that this great nerve serves as a means for the microbiota to send signals vagally to the central nervous system through the generation of neurotransmitters such as dopamine and serotonin. This dysfunction of the dysbiotic and vagal brain-gut axis is probably related to other processes such as neurodegenerative diseases in the longer term (Parkinson's, Alzheimer's, and other dementias).[7][8][9][10][11]

Finally, the chronic damage caused by Sars Cov2 is favored by alterations that occur in the acute setting of COVID-19 and which, if not stopped at this stage, will tend to become chronic with organic degenerative and probably irreversible affectation, which will increase the burden of disease inevitably. It is necessary to recognize this chronic disease caused by COVID and to generate adequate and efficient strategies for the control of acute COVID-19, preventing it from tending to its chronicity manifested in Long COVID.

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