



# Enfermedades Infecciosas y Microbiología Clínica

www.elsevier.es/eimc



## Editorial

## Inflammation in HIV: A persistent challenge

## Inflamación en el VIH: Un reto persistente



Inflammation is intrinsic to HIV infection, much like how we were taught that type 2 diabetes is inevitably associated with an increased risk of cardiovascular disease. For reasons whose biological basis is not fully clarified, people living with HIV (PLHIV) who receive antiretroviral treatment (ART) that effectively suppresses viral replication continue to experience a state of low-grade chronic inflammation and immune activation.<sup>1</sup> Various causes have been suggested for this: translocation of bacterial products from a partially “permeable” intestine due to persistent and irreversible damage to the mucosal-associated immune tissue, persistent viral replication in a partially active reservoir, alterations in the gut microbiota, or the reactivation of latent infections like CMV, among others.<sup>2</sup> This persistent inflammation, unrelated to viremia, which is our best target for disease control, presents a challenge for clinicians who lack practical tools to monitor or treat this issue. Although common inflammatory biomarkers, such as plasma levels of CRP, IL-6, or D-dimer, have shown in numerous clinical studies an association with “hard” variables like mortality, they are not specific enough in clinical practice and can be influenced by many other factors, such as acute infections, autoimmune diseases, cancer, or even circumstances like age, higher body fat, lower physical activity, or smoking. Theoretically, these inflammatory biomarkers could each provide information on a facet of the problem or the origin of the inflammatory process, but their correlation is low, and their combined use offers little clinical value on a day-to-day basis.<sup>3</sup>

Moreover, even if we had a reliable biomarker, we currently have no means of intervening in it. All attempts to influence inflammation in PLHIV, beyond controlling viral replication, have proven ineffective in practice.<sup>4</sup> In this context, Serrano Villar et al.<sup>5</sup> have studied the attitudes of different specialists towards chronic inflammation in PLHIV. Internal medicine/Infectious disease specialists seem to have a better understanding of this problem than cardiologists or rheumatologists, to whom they were compared, but they are not the ones acting most proactively on this issue. It is the rheumatologists, used to managing diseases with a strong inflammatory component, who might adopt a more proactive approach, such as monitoring biomarkers or recommending anti-inflammatory drugs, whose rationale is still controversial in HIV but highly useful in the diseases they specialize in.

Another interesting finding from this study is the confirmation that years of clinical practice lead to pragmatism. Pragmatism emerged as a philosophical movement in the 19th century in the United States, proposing that only knowledge with practical utility

is valid and that, therefore, it is opposed to idealism. Pragmatism is utilitarianism or possibilism: only the useful is worthwhile. Pragmatism leads to skepticism, which is defined as doubt or distrust in the truth or effectiveness of something. In philosophy, skepticism is a theory of knowledge that asserts the nonexistence of truth, or that if it does exist, humans are incapable of knowing it. Trust in science prevents us from being skeptical: we must trust that advances in knowledge will allow us to understand the causes of persistent inflammation in PLHIV, and thus offer a solution. We must trust that not everything has been said about inflammation in HIV: Will there be any progress in the next years in the biology of the viral reservoir that will allow us to achieve a functional cure for HIV? Will we, in the future, be able to intervene at the very initial source of inflammation? We must believe that the answer to these questions is yes and continue to believe in science. The pragmatic attitude of physicians with more years of experience takes us back to the beginning: just as it is inevitable that there is inflammation in HIV or that there is a higher cardiovascular risk in diabetes, we must fight so that it is not inevitable that experienced physicians, in addition to being pragmatic, are also skeptical. In the meantime, let us continue researching inflammation in PLHIV.

## References

- Deeks SG, Tracy R, Douek DC. Systemic effects of inflammation on health during chronic HIV infection. *Immunity*. 2013;39:633–45.
- Mazzuti L, Turriziani O, Mezzaroma I. The many faces of immune activation in HIV-1 infection: a multifactorial interconnection. *Biomedicine*. 2023;11:159. <http://dx.doi.org/10.3390/biomedicine11010159>. PMID: 36672667; PMCID: PMC9856151.
- Watson J, Salisbury C, Whiting P, Banks J, Pyne Y, Hamilton W. Added value and cascade effects of inflammatory marker tests in UK primary care: a cohort study from the Clinical Practice Research Datalink. *Br J Gen Pract*. 2019;69:e470–8. <http://dx.doi.org/10.3399/bjgp19X704321>. Epub 2019 Jun 17; PMID: 31208976; PMCID: PMC6582446.
- Erlanson KM, Campbell TB. Inflammation in chronic HIV infection: what can we do? *J Infect Dis*. 2015;212:339–42. Epub 20150112.
- Serrano-Villar S, Moltó-Marhuenda J, Montero-Alonso M, Díaz-Torné C, López-Cavanillas M, Pérez de Isla L. Knowledge, attitudes and practices in HIV-related chronic inflammation and cardiovascular risk in Spain. *Enferm Infecc Microbiol Clin (Engl Ed)*. 2024;42:484–91.

Julia Barrado<sup>a</sup>, Vicente Estrada<sup>a,b,c,\*</sup>

<sup>a</sup> Unidad de Enfermedades Infecciosas, Hospital Clínico San Carlos, IdiSSC, Madrid, Spain

<sup>b</sup> Centro de Investigación en Red de Enfermedades Infecciosas (CIBERINFEC), Instituto de Salud Carlos III, Madrid, Spain

<sup>c</sup> Universidad Complutense, Madrid, Spain

\* Corresponding author.

E-mail address: [vicente.estrada@salud.madrid.org](mailto:vicente.estrada@salud.madrid.org), [vesda001@gmail.com](mailto:vesda001@gmail.com) (V. Estrada).

See related article: <https://doi.org/10.1016/j.eimc.2023.07.005>

<https://doi.org/10.1016/j.eimc.2024.09.007>

0213-005X/© 2024 Published by Elsevier España, S.L.U. on behalf of Sociedad Española de Enfermedades Infecciosas y Microbiología Clínica.