EXPRESSION OF CONCERN

Quousque tandem abutere, patientia nostra

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Address reprint requests to Pr. Didier Raoult, *Institut Hospitalo-Universitaire Méditerranée Infection*, 19-21 boulevard Jean Moulin, 13005 Marseille, France or at philippe.parola@univamu.fr Several of us in our institute, being professors of infectious diseases or microbiology, have for a long time referred to the NEJM as a reference journal. However, it appears that for the teaching of infectious diseases, in the context of covid-19, the NEJM no longer corresponds to the minimum standards that we teach students from the 3rd year of medicine onwards.

We consider that an infected patient can only be definitely categorized as such with the support of a diagnostic test confirming infection. For covid-19 therapeutic trials, several publications in the NEJM have reported analyses where patients were not tested but included in the analyses. We teach our students not to do that. In some cases, this reaches extraordinary levels. For example, about hydroxychloroquine as post-exposure prophylaxis, when 821 asymptomatic participants were enrolled through social media to receive hydroxychloroquine or placebo, the analysis was based on self-report of an illness that was "considered to be consistent with COVID" (13%), with less than 3% supported by PCR assays. ¹ In JAMA, other studies have been published in which the dosage and duration of the prescribed treatments are not indicated.²

Also, we teach students to differentiate between side effects that have direct consequences and require special care, such as kidney failure, and those that have no consequences or for which accountability is difficult to define, such as insomnia or constipation. We were surprised that in the very favorable study published on Remdesivir, the side effects of insomnia, constipation and renal failure were pooled. ³ The result was that the side effects were considered insignificant whereas acute kidney injury tested alone shows the renal toxicity of Remdesivir. Finally, the report of the use of dexamethazone in the RECOVERY trial can only leave one stunned. ⁴ Indeed, in basic reference textbooks or reliable sources, it is easy to see that glucocorticoids are recommended in the treatment of respiratory distress or severe respiratory infections together and/or after antiviral or antibacterial therapies. Under these conditions, it could be seen unethical not giving corticosteroids in the routine care in such circumstances and that such a trial should never have existed.

All in all, it appears that publications promoting Remdesivir or suggesting hydroxychloroquine with or without azithromycin failure ⁵ seem to be particularly favored, to the point of publishing studies that looked more like a Marx Brothers movie than Science, as was dramatically seen for the so-called LancetGate. ⁶ Cicero, in the dangerous circumstances of the evolution of the Republic and after Catilina's attempts to destabilize it, said to him "Quousque tandem abutere, patientia nostra?". We ask ourselves the same question to the NEJM, How long will you abuse of our patience? The biases shown in the studies on the COVID-19 have gone beyond, as in the Lancet for that matter, everything that has been seen so far. Please give us back a journal that we can use for medical education that does not contradict all principles we have used for so many years.

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