The War Against Chloroquine

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Dear Editor

We were very impressed by the two editorials in the British Medical Journal that begin to reveal the magnitude of the crisis associated with the COVID epidemic, the overshadowing of scientific approaches, and the revelation of behaviours and conflicts of interest that, to our knowledge have never before reached this level [Abassi, Godlee]. From this point of view, our recent personal experience seems to us to be of relevance.

Following initial evidence communicated by Chinese investigators, reporting that chloroquine and remdesivir were effective *in vitro* against SARS-CoV-2 [Wang], Chinese colleagues concluded that they would begin to use hydroxychloroquine, which was well known to be non-toxic and usable *per os* [Multicenter], rather than remdesivir (which was unavailable and an extremely expensive product, the actual toxicity of which had never been well evaluated), which can only be used by infusion (thus increasing complications by 5 to 10% of due to the infusion itself)). This appeared to be common sense. A communication was then issued by the Chinese authorities saying that, in the first 100 patients, they noticed that chloroquine led to a difference in terms of symptoms, radiological images and viral carriage [Gao]. Since these were the only elements were available, we immediately submitted an official research project to carry out an observational study comparing the duration of virus carriage under hydroxychloroquine compared to the historical series from China, which had reported that it was about 20 days [Zhou]. This study began and some patients received azithromycin in addition to hydroxychloroquine, for which we had preliminary results of its *in vitro* efficacy against SARS-CoV-2 (azithromycin is effective on more than one RNA virus), and which is recommended to avoid bacterial superinfections in pneumonia. At that time, we were surprised to see that the addition of azithromycin significantly shortened the virus shedding period despite the low number of patients [Gautret]. The reactions to this very simple paper,

the data of which were later confirmed in a meta-analysis [Million-1], were spectacular and so disproportionate that it led us to question ourselves as to the reason for such over-reactions.

I (DR) was first harassed by the publisher (Elsevier) of the journal in which we had published this article (International Journal of Antimicrobial Agents) due to the fact that one of the co-authors was a collaborator of ours and editor of the journal. Of course, the editor of our own paper was not this individual, but one of the best known specialists in the world in the field of infectious diseases, and the reviewer was one of the best known specialists in the world in the field of coronaviruses, as has since become clear.. Initially, the publisher asked me (DR) to retract the article, which I refused to do. I (DR) sent a letter from my lawyer explaining that I would sue the publisher if he retracted it without our agreement, because there was no fault or error in the study. The publisher then asked if we had any conflict of interest with Sanofi, because in France it is Sanofi that distributes generic hydroxychloroquine drugs. We replied that, of course, we have no link of interest with any pharmaceutical industry, which would be contrary to the ethical standards of our institute. The journal subsequently accepted ten letters of protest against our article, most of which appeared to be very far-fetched. Nevertheless, we answered each one politely and professionally.

In addition, I (DR) have suffered continuous harassment from various influence groups [Roussel]. First, from so-called “scientific” journalists from various major newspapers in France (Le Figaro, L'Express, etc.) who, after the publication of our first study on chloroquine, began a systematic war against me (DR) and against this treatment. Certain journalists have written more than 30 articles attacking me (DR) in less than 18 months. Fact-checking teams employed by major newspapers (Le Monde, Libération, etc.) accused me (DR) of spreading fake news as soon as I (DR) began to mention the potential interest of using chloroquine to treat COVID-19. I (DR) have been the target of trolls on social media, some of them identified as being involved in lobbying various industries in studies carried out

in France before the COVID-19 epidemic [Foucart]. Other collectives, some of which pre-existed the crisis, attacked my work, such as the FakeMed collective, which was organised during debates on the state-funded reimbursement of homeopathic treatment in France. Interestingly, one of these collectives, Citizen4Science, which launched a petition to personally attack me (DR) and which gave interviews in numerous press articles criticising my work and that of my teams, was created by several employees or service providers within the pharmaceutical industry [Citizen4Science]. I have been the victim of personal attacks by other French infectious disease doctors, even during interviews given in the media [CNews], with one doctor, Professor F. Raffi, going so far as to telephone me in the middle of the night to threaten me if I did not withdraw my statements about chloroquine. This is an individual who has received the most money from the pharmaceutical industry over the past seven years, according to the French transparency register [Eurosfordocs]. He admitted this in court following my (DR) filing of a complaint [Valette]. Finally, my (DR) integrity has been attacked by a so-called "science-consultant" (Elisabeth Bik), who coordinated a group (most of whose members are anonymous) to find errors in the 3,500 articles I (DR) have co-authored during my career. This is despite the fact that on the Pubpeer site that hosts these comments, only eight of my (DR) articles had been brought into question between 2012 and 2019, and 200 of my articles were commented on Pubpeer between March and May 2021 (Figure 1). To my knowledge, only five errors have been found, which is far less than I might have imagined given the number of gels and Western blots I have published in my 40 year-career. The subject of most of the remarks was the interpretation of ethical process of sampling, which mostly involved stools and sometimes even lice! No cases of fraud were found.

I (DR) could have taken these relentlessness attacks as personal, but two things quickly came to light. First of all, there was what we refer to as "Lancet Gate" [Raoult], a quite

extraordinary situation where a group of five unknown people reported that they had had access to more than 80,000 patient's records and that hydroxychloroquine was the cause of nearly 10% of cardiac deaths [Mehra-1]. It has been reported that in the literature that, prior to 2020, and despite the fact that it has probably been prescribed to almost two billion people, only one occurrence of *torsade de pointes* has been reported [Verecki]. The same team published a paper in the New England Journal of Medicine [Mehra-2] that had later to be retracted, much as the Lancet paper. It is fascinating to see the extent to which this blinkered vision has allowed papers to be published which any reasonable reviewer would have stopped due to their absolute technical impossibility [Raoult].

The BMJ was not immune to this lack of objectivity, when it published an article in which the authors deliberately omitted to evaluate the effectiveness on mortality and critical care of the combination of hydroxychloroquine and azithromycin [Mahevas, https://www.mediterranee-infection.com/correction-scientifique/] and another published a pre-print of an article in which the authors were asked to change the elements that were favourable to hydroxychloroquine [Tang, https://www.mediterranee-infection.com/tang-et-al-bmj-donnees-favorables-a-lhydroxychloroquine-supprimees/]. At the same time, as criticism was raging about our article, which contained measurable, comparative data showing statistically significant differences, articles were published in the Lancet Infectious Diseases and in the New England Journal of Medicine on remdesivir, which were nothing more than advertising without any comparative studies [Grein, Beigel]. A study on plasmapheresis without the slightest comparative element was then published in Blood, which, to my knowledge, has not been the subject of the least criticism [Xia]. Although the mention of chloroquine had become taboo, we recently had the opportunity to do a meta-analysis study of all the identifiable, comparative publications on hydroxychloroquine (more than 200 are available on the c19study.com website) which revealed that their results were clearly dependent on the

existence of conflicts of interest, including with Gilead, the pharmaceutical company that developed remdesivir [Million-2]. We were able to show in a study that, in France, there was an almost perfect inverse correlation between the level of funding received by Gilead over the last six years (declared on the government transparency website) and the official positions taken towards hydroxychloroquine [Roussel]. On several occasions, we noted, particularly for French authors [Lescure], the absence of a declaration of conflicts of interest when studies on hydroxychloroquine or remdesivir were published. Throughout that time, the price of shares in Gilead has rose and fell, potentially resulting in stock exchanges in excess of 100 billion dollars [Chabriere]. Finally, Gilead succeeded in selling a considerable volume of remdesivir to the European Union at the very time when everyone was realising that the treatment had no significant value in the treatment of COVID-19 (Table). Even worse, while it was suspected that remdesivir had a mutagenic effect on Ebola virus and coronaviruses [Warren, Agostini], a recent study in the New England Journal of Medicine showed that remdesivir, when prescribed in a chronic SARS-CoV-2 carrier, was not effective, as viremia persisted (which really is proof of ineffectiveness, as in all chronic viral infections) and, furthermore, that it encouraged the appearance of resistant mutants [Choi] [Colson]. The treatment entailed a risk of generating mutants the outcome of which is unpredictable. In addition, the possible association of hyperimmune plasma by exerting selection pressure on the spike protein, the target of the vaccine, could lead to more specific selection of mutations at this site and make the entire vaccine strategy completely useless.

In practice, as pointed out in a BMJ editorial about Tamiflu [Godlee], the complete lack of scientific control observed in this situation, including by the world's most reputable journals, will leave lasting marks in terms of the entirely disproportionate attack on hydroxychloroquine. Although hydroxychloroquine is used in countries with populations of several billions, Western opinion leaders have fought a fundamental battle to promote an

ineffective and dangerous product, remdesivir, which has led to millions of euros being made by some opinion leaders and shareholders. They are continuing to try to neutralise all more economic therapeutic options which involve recycling old drugs (ivermectin, cyclosporine etc.) in favour of an extremely costly vaccine strategy whose results, given the rushed way in which it has been rolled out, could lead to another major strategic failure.

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Conflicts of interest

The authors have nothing to disclose.

Author contributions

Each author made substantial contributions to the conception, design, writing and review of this article

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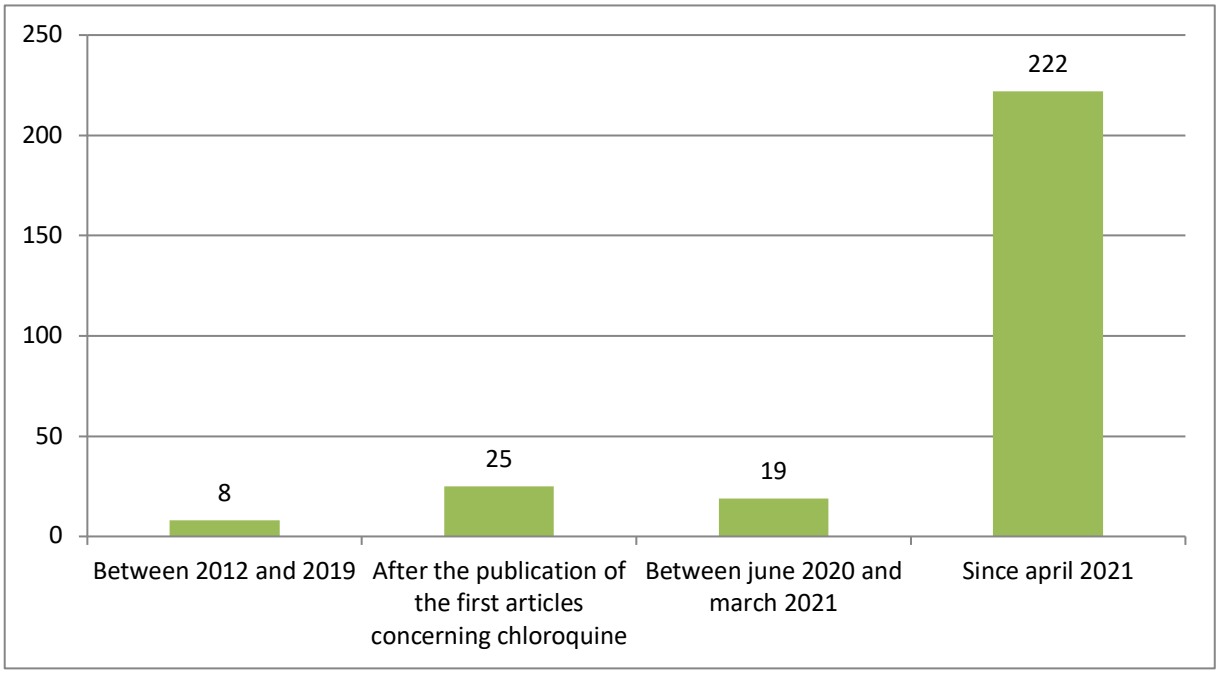
285 Figure 1: Number of Pubpeer comments on my (DR) articles over time.



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287 List available on the pubpeer.com website.

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289 Table 1. Comparison between remdesivir and hydroxychloroquine.

	Remdesivir	Hydroxychloroquine	Source
Treatment cost	>2000€	<10€	[AJMC]
Perfusion	YES	NO	
Efficacity on death	NO	YES	[Million]
Arrythmia	YES	NO	[Touafchia]
Authorised for use in EU?	YES	NO	[European Medicines Agency]
Bought by EU	YES	NO	[European Commission]

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