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RESEARCH ARTICLE

CELL IMMUNITY, AIR TRANSMISSION AND THERAPY APPROACH FOR COVID-19

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ABSTRACT

Betacoronaviruses cell immunity is taken on consideration as well as aerosol transmission and asymptomatic infectivity of COVID-19 carriers. The hydroxychloroquine and serotherapy are studied after identification and spreading of the virus. Its cell epitopes play a role on viral pathogenesis that influences morbility and mortality according to interstitial pneumonia, lymphokinestorms and thromboembolic happenings. Kawasaki syndrome and kidney involvement are discussed with other main pathologies before its prospectives from oral poliovaccine to more proper and specific vaccines.

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INTRODUCTION

T cells were studied for their response to structural (nucleocapsid, NP) and non-structural proteins (accessory NSP-7 and NSP-13 of ORF1) of the viral particles of SARS-CoV-2 in 24 subjects convalescent by COVID -19. CD4 and CD8 T cells were recognized in all convalescents which recognized multiple regions of the nucleocapsid protein (NP). 23 patients recovered from the first SARS, 17 years after the outbreak, still have a long-lasting memory of T cells with respect to the structural proteins of the nucleocapsid (NP), which demonstrates a cross-reaction towards the NP of the current SARS. The subjects without history of the primitive SARS, in 50% of cases (9/18) have T cells that react with the accessory proteins (non-structural NPS-7 and NSP-13 of ORF1). Epitopic characterization of NSP-7 specific T cells showed recognition of protein fragments with respect to animal betacoronaviruses, but very reduced for human common cold coronaviruses. Therefore infection with betacoronavirus induces a strong and long-lasting immunity of T cells with respect to NP structural proteins (Nina Le Bert *et al.*, 2020).

The issue of COVID-19 asymptomatics: Citing a study published in PubMed (Ming Gao *et al.*, 2020) I said that the asymptomatic are not infectious.

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An article was also written that would demonstrate that what I said in my last interview was not accurate, since the 455 people mentioned by the study were not infected because they were aware that the subject in question was positive for Sars CoV2, but asymptomatic; and therefore they had taken the right precautions. The study I cited stated precisely this: that the infectious load of Sars CoV2, in terms of the amount of the virus, of an asymptomatic positive buffer, is so small that it cannot infect people who come into contact with it . This is because to develop significant symptoms, you need a considerable amount of virus that the asymptomatic does not have. As for the issue of Sars CoV2 contagion, there are several scientific articles, some of which are being published (Luisetto *et al*, 2020), of which I am one of the authors, entitled: Covid-19 and other coronaviruses: transmission internal and external by air? State of evidence. In the International Journal of Current Research (Tarro, 2020), a careful examination is made between contagion by droplets or by air. We assume that Sars CoV2 is transmitted through the famous droplets, but the contagion and subsequent infection depend on the environment, the seasonal period and the viral load of the virus itself. In closed places, these droplets are more likely to spread. Outdoors it is very difficult. I could also report what Maria von Kerkhova, the WHO representative, said that talking about asymptomatic infectious is scientifically nonsense. And finally, I could cite an article published in Science last May 27, which reports data that refer to the presumed (far from scientific term) transmission of the virus by asymptomatics.

This is to clarify that the issue of contagion and subsequent infection by Sars CoV2 by an asymptomatic depends on many factors. A recent work (Prather *et al*., 2020) is based on the airborne transmission of aerosols produced by asymptomatic subjects (?) during breathing and speaking. We know that the (Flügge) drops establish direct or indirect contact (via surfaces), while the air aerosol leads to an inhalation by air, classic for the flu virus, less frequent for the coronavirus, see SARS before. Drops and aerosols are influenced by breeze and wind as on the other hand by the action of natural ultraviolet rays. Air pollution worsens the severity of COVID-19. On the other hand, aerosol infectivity depends on the weather, especially in closed rooms, already demonstrated for measles, first SARS and chickenpox. Control measures regarding viral load require a minimum titer to cause viral infection, especially for the permanence of the accumulated aerosol for hours. The "asymptomatic" and subjects with mild symptoms in exhaling the breath require a mask that reduces the number of viruses that are spread. It is reported that the virus would bypass the immune response in being introduced directly into the alveolar region of the lung and then be transferred (without replicating? There is no sense in this statement) to the pharynx and spread silently by asymptomatic "presumably" and therefore transmitted in the environment. According to South Korean scholars, the number of reported cases of COVID-19 patients who relapsed after the end of the disease is due to a false diagnosis because the South Korean CDC now states that reactivation in the human body is impossible for the virus. In fact, they found that the results of PCR tests of patients suspected of recurrence were of false positives, since the test is not able to distinguish between traces of living virus and dead samples, which remain after the patient's recovery without ability to cause injury (Tarro, 2020).

Hydroxychloroquine: At the end of March in many newspapers I declared "antimalarial and serotherapy are working. A person who has contracted Sars CoV2 and has recovered can help others who contract it. " Well, I was right, as well as on other things. It is bad to be right while the world acts (or has acted) in the opposite direction: I would have liked to have heard similar statements from the entire scientific community and instead, in the aftermath of the declarations of President Donald Trump - " Against the coronavirus for ten days I have been taking hydroxychloroquine " (Rosenberg *et al*, 2020) the World Health Organization announced the decision to suspend tests on the use of hydroxychloroquine for the treatment of Covid-19, expressing concern for safety.

Well, after a few days, thanks to the investigation by the British newspaper Guardian, it is clear that "the study that sank the hydroxychloroquine is based on suspicious data". The WHO is forced to backtrack and with it all the governments that have given credit to the study published in The Lancet and New England Journal of Medicine, 2020. According to what emerges in these hours: "the origin of those studies is questioned. In particular, it emerged that the data to which the study refers, "was collected by a small Chicago-based company, Surgisphere, among the (very few) employees of whom there is a porn model and a science fiction author." Antimalarial is a product that, in the right dosages, helps fight Covid19, as happened for Sars. It is a drug and as such it can have side effects. Of course, the figure of the doctor is fundamental. It is not a therapy to experiment without resorting to a specialist. This is the truth.

Obviously like gammaglobulins for tetanus, the plasma antibodies of the healed subjects represent a logical use for the most serious patients. An efficient method of producing human monoclonal antibodies from memory B cells has demonstrated consistent neutralization of the SARS coronavirus. Human monoclonal antibodies as prophylaxis for SARS coronavirus infection have been used in ferrets (Tarro, 2020).

Identification and propagation of the virus: The recent success of identifying neutralizing human antibodies (mAbs versus MERS-CoV) suggests the possibility of using these methodologies for a rapid response against emerging viruses with the potential to cause pandemics. The ability to rapidly identify, propagate, and internationally share our SARS-CoV-2 isolate is an important step in collaborative scientific efforts to deal effectively with this international public health emergency by developing better diagnostic procedures, vaccine candidates, and antiviral agents. SARS-CoV-2 T-cell epitopes define heterologous and COVID-19-indiced T-cell recognition (Caly *et al*, 2020). Scientists determined earlier this year that there is a cleavage site in the SARS-CoV-2 spike protein for furin, a human protease, and that the spike protein is split into two subunits at that spot. This cleavage has been implicated in helping break the virus open so it can enter human cells (Neld *et al*., 2020).

Morbility and mortality: Large increases in mortality from heart disease, diabetes, and other diseases were observed. Further investigation is required to determine the extent to which these trends represent nonrespiratory manifestations of COVID-19 or secondary pandemic mortality caused by disruptions in society that diminished or delayed access to health care and the social determinants of health (eg, jobs, income, food security). Woolf *et al.* (2020) have provided an early count of these numbers by estimating excess deaths from COVID-19 and other causes. The goal is to update these counts in the fall of 2020 so that an accurate measure of the status of the pandemic and of efforts to mitigate the related morbidity and mortality are available to be debated.

Pathogenesis: In the case of a Covid-19 lung infection, the virus infects type II alveolar cells which consequently reduce the roduction of pulmonary surfactant. The surfactant has the function of reducing the surface tension of the alveoli (Bracco, 2020). The less pulmonary surfactant there is, the more the alveoli tend to collapse due to the increased surface tension of their surface. Consequently, the lung would tend to collapse, that is, to reduce its own volume, but collapse is prevented by the muscular movement of inspiration, which instead increases its volume. This means that a "low pressure area" is created in the interstitial space which attracts liquid and substances which are often inflammatory and which organize over time, giving rise to interstitial pneumonia. Similarly, the administration of surfactant during Covid-19 lung infection would allow the correct amount of surfactant to be maintained during the acute phase of the infection and would give time for type II alveolar cells to heal and independently resume surfactant production.

In its most severe form, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), the virus that causes coronavirus disease 2019 (COVID-19), leads to a life-threatening pneumonia and acute respiratory distress syndrome (ARDS). Although the mechanisms of COVID-19–induced lung injury are still being elucidated, the term cytokine storm

has become synonymous with its pathophysiology, both in scientific publications and the media. Drugs such as tocilizumab and sarilumab, which are monoclonal antibodies targeting interleukin (IL)-6 activity, are being used to treat patients; trials of these agents typically cite the cytokine storm as their rationale (NCT04306705, NCT04322773). Children are infected with the virus without suffering a serious disease and represent an important source of infection. It has been experimentally proven that young mice respond to lung tissue damage from viral infection through prostaglandins, while adult mice succumb. The angiotensin- converting enzyme (ACE) 2 receptor is particularly abundant on the cells of the lower lung pathways, whose situation explains the high incidence of bronchitis and pneumonia related to the severe infection of COVID-19. A fall in ACE2 activity in the elderly is partly responsible for the decreased ability to reduce the inflammatory response with old age. The reduction of ACE2 receptors in older adults puts them in a position where they are unable to cope with COVID-19 (Tarro, 2020). The novel coronavirus is a coagulative diseas with diffuse thrombosis of the vascular system: the fundamental role of anti-thrombotic drugs (Palma *et al*., 2020)

Syndrome of Kawasaki: The pediatric inflammatory multisystem syndrome (PIMS) now described in association with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection has generated considerable interest, both for its severity and delayed emergence in an age group largely spared the complications of primary infection, but also for its overlapping clinical features with Kawasaki disease (KD), the leading cause of acquired heart disease in children in high-income countries. This has prompted considerable discussion that the 2 conditions could have different or shared etiologic and pathophysiologic pathways (McCrindle *et al*, 2020). This study suggests feasibility of ultra-rapid genomic testing in critically ill pediatric patients with suspected monogenic conditions in the Australian public health care system. However, further research is needed to understand the clinical value of such testing, and the generalizability of the findings to other health care settings.

DISCUSSION

The 2019 novel coronavirus disease, SARS-CoV-2, is now spreading globally and is characterized by person-to-person transmission. However, it has recently been found that individuals infected with SARS-CoV-2 can be asymptomatic, and simultaneously a source of infection in others. The viral load detected in nasopharyngeal swabs of asymptomatic carriers is relatively high, with a great potential for transmission. More attention should be paid to the insidious spread of disease and harm contributed by asymptomatic SARS-CoV-2 carriers (Tan *et al*., 2020). Early identification of asymptomatic COVID-19 carriers either in incubation phase or else convalescence period can be the key to prevent further spread of the deadly pandemic. Although rRT PCR (Real Time reverse transcription Polymerase Chain Reaction) is the gold standard of diagnosis but not mass screening friendly. Evaluation of salivary load of the SARS-CoV-2 virus which has a high affinity for ACE2 receptors of pulmonary and salivary gland tissues can be promising in detecting asymptomatic carriers well in time (in press). The World Health Organization's technical lead for coronavirus response, Maria Van Kerkhove, said at a press briefing on Monday (June 8) that asymptomatic transmission of the SARS-CoV-2 virus was "very rare."

On Tuesday, Van Kerkhove clarified at a follow-up Q&A session on COVID-19 transmission that she was referring only to patients who never show any symptoms at all, not those who have not yet begun to show symptoms—individuals who are classified as being presymptomatic—nor those cases that involve only mild symptoms. The WHO estimates that among truly asymptomatic patients, 16 percent can infect others. "We do know that some people who are asymptomatic can transmit the virus on". The New England Journal of Medicine of May 19, 2020 is reported with an article that mainly concerns kidney complications in the COVID-19 epidemic and recently published in Kidney International. Dr. Steven Fishbane and his colleagues looked in particular at the clinical results of 5,400 patients hospitalized for COVID-19 in a dozen hospitals in the Northwell Health metropolitan system of New York. Doctor Fishbane is the director of Nephrology at the aforementioned hospital and in March of this year he reported the experiences collected by his team on 5,400 patients from 15,000 hospitalized, describing in particular that 36.6% developed acute kidney lesions in particular representing an experience that after China and Italy shows an important and certainly high number of acute kidney lesions for the number of patients reported by this study, highlighting that the disease linked to the aforementioned epidemic is not only respiratory, but kidney represents an important problem that cannot be considered secondary.

In fact, 90% of patients with mechanical ventilation developed kidney lesions as opposed to 20% who are not intubated. It could therefore be thought that the concordance of respiratory and acute kidney failure is evident and represents an extremely serious problem. In fact, the patient with respiratory problems leads to neglect the kidney problem if it were not for the measurement in the hospital of the dosages of creatinine. Clinicians need to keep an eye on kidney function for COVID-19 patients and not just focus on respiratory disease. "We realize that patients need to be monitored very carefully in terms of the development of kidney disease and therefore the difficult decisions that go along with patient management in particular in doing a supportive dialysis etc." Since after Wuhan in China and subsequently in Italy, as now in New York, it is essential to be able to exercise a prompt diagnosis and therefore the need to have at hand the possibility of using the kidney dialysis services, whose presence becomes indispensable in hospitals for COVID-19 patients. All this underlines the importance of being able to treat the kidney together with the other aspects of the pathology.

Prospectives: According to Robert Gallo director of the Institute of Human Virology of the University of Maryland, when a carpet polio vaccination campaign was carried out in Russia in the seventies, in the following winter season there were almost no cases of flu and the same observation was made in Singapore with seasonal flu. COVID-19 exactly like polio and flu, are caused by viruses with an RNA-based genome, it is plausible that a vaccine stimulates the immune system to act not only on the one, but also on the other viruses More than 90 vaccines are being developed against SARS-CoV-2 by research teams in companies and universities across the world. Researchers are trialling different technologies, some of which haven't been used in a licensed vaccine before. At least six groups have already begun injecting formulations

into volunteers in safety trials; others have started testing in animals (Nature, 2020).

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