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## Special Article

### COVID-19: Overview of rheumatology fellows<sup>☆</sup>

Andrea Garcia-Guillén,<sup>\*</sup> Sicylle Jeria, David Lobo-Prat, Luís Sainz

Servei de Reumatologia, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain



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#### ABSTRACT

SARS-COV-2 infection has spread worldwide since it originated in December 2019, in Wuhan, China. The pandemic has largely demonstrated the resilience of the world's health systems and is the greatest health emergency since World War II. There is no single therapeutic approach to the treatment of COVID-19 and the associated immune disorder. The lack of randomised clinical trials (RCTs) has led different countries to tackle the disease based on case series, or from results of observational studies with off-label drugs.

We as rheumatologists in general, and specifically rheumatology fellows, have been on the front line of the pandemic, modifying our activities and altering our training itinerary. We have attended patients, we have learned about the management of the disease and from our previous experience with drugs for arthritis and giant cell arteritis, we have used these drugs to treat COVID-19.

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### COVID-19: La visión del residente de reumatología

#### RESUMEN

La infección por SARS-COV-2 se ha extendido por todo el mundo desde diciembre de 2019, en Wuhan, China. La pandemia ha demostrado ampliamente la resistencia de los sistemas de salud mundiales, convirtiéndose en la mayor emergencia sanitaria desde la Segunda Guerra Mundial. No existe un enfoque terapéutico único para el tratamiento de COVID-19 y el trastorno inmunitario asociado. La falta de ensayos clínicos aleatorizados (ECA) ha llevado a diferentes países a enfrentar la enfermedad en base a series de casos, o a partir de resultados de estudios observacionales con fármacos fuera de ficha técnica.

Los reumatólogos en general, y específicamente los residentes, hemos vivido en primera línea la pandemia, modificando nuestras actividades y alterando nuestro itinerario formativo. Hemos atendido pacientes, hemos aprendido el manejo y gracias a nuestra experiencia previa en fármacos para la artritis o la arteritis de células gigantes, hemos utilizado estos fármacos para tratar la COVID-19.

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#### Introduction

The 2019 coronavirus disease pandemic (COVID-19) has created an unprecedented global health emergency and has rapidly led to a change in our professional and personal outlook.

COVID-19 is caused by the new SARS-CoV-2 betacoronavirus. It was initially detected in the city of Wuhan (Hubei, China) in December 2019 and has spread very quickly, with more than 4 million

confirmed cases worldwide as of May 11, 2020.<sup>1</sup> Spain has been one of the most affected countries, with more than 215,000 confirmed cases and more than 26,000 deaths, according to the most recent data from the Johns Hopkins Coronavirus Resource Center.<sup>2</sup>

The high transmission of the virus has led to a rapid spread of the infection, resulting in a high volume of patients requiring hospitalization or intensive care in a very short time. Simultaneously attending to the needs of so many patients, a significant number of them critical, has been a real stress test for the health system of developed countries, with an extremely high demand for resources, beyond those available. To tackle this global health crisis, countries have been forced to take extraordinary measures, including restrictive measures of social distancing and individual protection.

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<sup>\*</sup> Corresponding author.

E-mail address: [agarciagui@santpau.cat](mailto:agarciagui@santpau.cat) (A. Garcia-Guillén).

## The role of the rheumatologist in a “COVID” hospital

Rheumatologists have experienced this pandemic with particular intensity. Many of our patients are considered at risk of developing serious infections due to their immunosuppressed state, either because of their underlying disease or due to the use of immunosuppressive therapies. However, at present, there is insufficient data to indicate that rheumatology and autoimmune disease patients undergoing immunosuppressive therapy who are infected with SARS-COV-2 have a poorer outcome due to COVID-19.<sup>3</sup> Furthermore, some of these treatments are being investigated as potential therapies for the disease, including antimalarials, interleukin-6 receptor (IL) inhibitors (IL-6R), IL-1 inhibitors, or JAK kinase inhibitors. Confirmed data show that a subgroup of infected patients initially develop a phase of viral replication, but subsequently present a process of hyperinflammation as a response, by a severe activation of the immune system (cytokine release syndrome)<sup>4</sup> mediated by different cytokines (IL-1, IL-2, IL-6, IL-7, IL-10, IL-12, interferon- $\gamma$  and TNF- $\alpha$ ), resulting in clinical pictures with high morbidity and mortality.<sup>5</sup> In this sense, the design of selective cytokine (IL-1, IL-6R) blocking strategies or the use of JAK kinase inhibitors seems to play an important role in this cytokine release syndrome.<sup>4</sup> The extensive experience in rheumatology with these drugs in chronic inflammatory diseases allows us to suggest their potential beneficial effects in COVID-19 patients.<sup>6</sup>

This health emergency has taken us by surprise in a time of apparent well-being and calm and has been a challenge for the health system and for every one of us. Up until the beginning of May, our hospital had diagnosed more than 2093 positive cases by means of PCR or serology, with more than 1383 hospital admissions. Of these, 146 presented complications that required admission to the intensive care unit (ICU). With the incessant arrival of the first cases our hospital was forced to adapt quickly, drastically changing its organization and even its infrastructure, to become in a short time a COVID hospital, practically entirely occupied by infected patients. In addition to halting the rotations of our specialized health training, elective surgeries were cancelled, all non-essential care activity in outpatient clinics was cancelled, all non-urgent complementary tests were postponed and urgent surgical activity was moved to another centre. To absorb this high demand for care, ICU beds were created in the operating theatres or in the resuscitation area, and hospitalization beds were made available in areas usually devoted to waiting rooms or other purposes.

As health professionals we have seen our usual routine change radically. The entire Rheumatology team was integrated into COVID-19 teams, made up of specialists from different specialties to provide care in hospital wards and in the emergency department. Routine outpatient care disappeared. When during a conventional year we would make more than 13,000 annual visits, more than 1500 ultrasound scans, and infiltrations and hospital processes during the day, overnight we went on to a telephone format. In parallel, we have maintained team care via email with the support of our nurse practitioner using a dedicated pandemic email address ([reumatologiacovid@santpau.cat](mailto:reumatologiacovid@santpau.cat)). Due to the knowledge and experience accumulated with our patients and biological therapies, such as IL-6R inhibitors, we rheumatologists have been able to collaborate in a global and integrated approach to the disease and its complications. We have played a key role in the development of the therapeutic protocols of our centre. The different treatment alternatives without a clear scientific basis, following studies carried out in China and Italy, have made it necessary to develop clinical treatment guidelines specific to each hospital. In our case, we opted initially for antiretroviral treatment (Symtuza) which was quickly replaced by a regimen of hydroxychloroquine 400 mg/12 h (one day) followed by 200 mg/12 (four days) + azithromycin 500 mg/d (three days). In refractory cases, we

chose to use biological therapy, specifically IL-6 receptor blockers (tocilizumab [TCZ] IV in our case) and in isolated cases SC Sarilumab. At the time of writing this editorial, about 120 patients in our centre have been treated with a single dose of IV TCZ, according to the recommendations of the Spanish National Agency of Medicines (AEMPS). To date, this strategy has proven highly effective, with mortality rates of less than 5.8% (unpublished data). In addition, a randomized study (TOCOVID NCT04332094) hydroxychloroquine + azithromycin 500 mg/day (three days) with an active arm of subcutaneous TCZ 162 mg x 2 repeated at 24 h has been initiated. The TOCOVID trial in recruitment phase has 70 patients randomized and results are expected to be published soon.

COVID-19 disease is multisystemic in nature and therefore requires a multidisciplinary approach. Collaboration between specialists from different settings has made it possible to offer comprehensive care to patients. In this sense, we have also started a study together with the pulmonologists of our centre to determine the role of the lung damage marker Krebs von den Lungen-6 (KL-6) in the stratification of the risk of respiratory complications in infected patients.

## The Rheumatology Fellow: a further “expert” in COVID-19

For rheumatology fellows, this unexpected situation has meant that our training itineraries have been set aside to devote ourselves exclusively to hospitalized COVID patients, accompanied by fellows and assistants from medical and surgical specialties. Being on the front line, we have contributed in every way possible, taking 12-h shifts every day for six weeks in the phase of maximum escalation, with the obvious consequent physical and psychological toll. We have been involved in situations that we would never have imagined, accompanying patients and families remotely, making ethically complex decisions and assuming a responsibility unthinkable in relation to our years of training. The uncertainty experienced in relation to a new disease, not only as professionals but also as patients in many cases, has meant we have experienced both sides of the pandemic. The lack of adequate means of protection, the protocols of action that change on a daily basis, the pressure of care due to casualties in the team, the fear of getting sick and the uncertainty about our immediate formative and professional future, have added to a situation of maximum tension with great physical and emotional impact.

Teamwork and comradeship are some of the positive aspects that this health crisis has brought us; definitely the two key elements in facing this challenge. The presence of doctors from different specialties working simultaneously, the joint effort with nursing, pharmacists, psychologists, assistants, hospital porters, administrative, cleaning and maintenance staff has enabled a multidisciplinary and global approach for the patient with COVID-19. Companionship, in this situation that is so complicated at both the professional and the personal level, has given us the strength to carry on day to day.

## Strengths of the health system and the future of specialist care

This pandemic has also shown that a strong health system and ensuring quality care requires both material and human resources. In this aspect, health professionals and in our case rheumatologists, have been on the front line struggling to care for patients in the best possible way, even without adequate protective equipment in many cases and placing our physical safety at risk.

The current healthcare model will undoubtedly require changes to make it more sustainable and minimize exposure risks. In this regard, enormous possibilities are opening up in the field of

telemedicine. This care model, using the new information and communication technologies (ICT), would allow waiting times to be optimised, unnecessary trips to be avoided, improve the flow of visits according to criteria of severity and encourage efficiency-based activity by practitioners. All of which will enable us to provide sustainable and quality care appropriate to the needs of our patients.

Implementing this new model of care effectively is not exempt from organizational, contextual, structural, and economic challenges. The type and percentage of patients that could benefit from this type of care, the infrastructure needed and the most appropriate technological tools to implement it in a cost-efficient way are some of the unknowns we face.

The COVID-19 pandemic has placed the rheumatology community in the spotlight, has given us the opportunity to contribute our experience in the treatment and development of new therapies for these patients and encouraged us to be pioneers in the care of the future, making fundamental changes that will form the basis for a new era of healthcare.

## Conflict of interests

The authors have no conflict of interests to declare.

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