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and combined pharmacotherapy have been recommended for patients with early-stage steroid-induced ONFH.<sup>11</sup>

We declare no competing interests.

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- 1 WHO. Coronavirus disease (COVID-19) situation report - 119. May 18, 2020. [https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200518-covid-19-sitrep-119.pdf?sfvrsn=4bd9de25\\_4](https://www.who.int/docs/default-source/coronaviruse/situation-reports/20200518-covid-19-sitrep-119.pdf?sfvrsn=4bd9de25_4) (accessed May 19, 2020).
- 2 Huang C, Wang Y, Li X, et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. *Lancet* 2020; **395**: 497–506.
- 3 Chen N, Zhou M, Dong X, et al. Epidemiological and clinical characteristics of 99 cases of 2019 novel coronavirus pneumonia in Wuhan, China: a descriptive study. *Lancet* 2020; **395**: 507–13.
- 4 Chen RC, Tang XP, Tan SY, et al. Treatment of severe acute respiratory syndrome with glucocorticoids: the Guangzhou experience. *Chest* 2006; **129**: 1441–52.
- 5 Guo KJ, Zhao FC, Guo Y, Li FL, Zhu L, Zheng W. The influence of age, gender and treatment with steroids on the incidence of osteonecrosis of the femoral head during the management of severe acute respiratory syndrome: a retrospective study. *Bone Joint J* 2014; **96-B**: 259–62.
- 6 Russell CD, Millar JE, Baillie JK. Clinical evidence does not support corticosteroid treatment for 2019-nCoV lung injury. *Lancet* 2020; **395**: 473–75.
- 7 Shang L, Zhao J, Hu Y, Du R, Cao B. On the use of corticosteroids for 2019-nCoV pneumonia. *Lancet* 2020; **395**: 683–84.
- 8 Lai KA, Shen WJ, Yang CY, Shao CJ, Hsu JT, Lin RM. The use of alendronate to prevent early collapse of the femoral head in patients with nontraumatic osteonecrosis. A randomized clinical study. *J Bone Joint Surg Am* 2005; **87**: 2155–59.
- 9 Jia YB, Jiang DM, Ren YZ, Liang ZH, Zhao ZQ, Wang YX. Inhibitory effects of vitamin E on osteocyte apoptosis and DNA oxidative damage in bone marrow hemopoietic cells at early stage of steroid-induced femoral head necrosis. *Mol Med Rep* 2017; **15**: 1585–92.
- 10 Liu LH, Zhang QY, Sun W, Li ZR, Gao FQ. Corticosteroid-induced osteonecrosis of the femoral head: detection, diagnosis, and treatment in earlier stages. *Chin Med J (Engl)* 2017; **130**: 2601–07.
- 11 Wang W, Zhang N, Guo W, Gao F. Combined pharmacotherapy for osteonecrosis of the femoral head after severe acute respiratory syndrome and interstitial pneumonia: two and a half to fourteen year follow-up. *Int Orthop* 2018; **42**: 1551–56.

For the AP-HP COVID-19 website see <http://covid-documentation.aphp.fr/>

See Online for appendix

## Assistance Publique–Hôpitaux de Paris' response to the COVID-19 pandemic

Assistance Publique–Hôpitaux de Paris (AP-HP) is the largest teaching hospital trust in Europe, with 39 hospitals, 20 000 beds (10% of all public hospital beds), and an association with seven universities. AP-HP also hosts 40% of the French biomedical research. As a result of its size and location, AP-HP has been a major player in France's COVID-19 response, as it was in responding to terrorist attacks.<sup>1</sup> AP-HP has a reputation of being an institution with a size, cumbersome operations, and internal competition that prevent any nimble response. We are a group of health-care professionals at AP-HP who are directly involved in the management of the COVID-19 response by AP-HP. Having faced the COVID-19 pandemic, and remaining humble in facing the future, we describe how size and coordinated management might actually have helped the organisation, speed, and consistency of the response to the COVID-19 crisis.

AP-HP initially estimated that no more than 1000 patients with COVID-19 would be simultaneously admitted to intensive care units (ICUs) in the Île-de-France region; 400 of these patients would be admitted to ICUs in the AP-HP, close to the maximum capacity. However, the situation became worse than expected (appendix). At the height of the COVID-19 pandemic, 2677 patients with COVID-19 were admitted into ICUs in the region, 41% of whom were admitted to AP-HP. A few points deserve discussion.

A specific medical organisation was established, led by a central crisis medical director who was appointed by the CEO and supported by medical directors in each hospital. A clear chain of medical responsibilities enabled a

reactive operational decision making process throughout the whole institution.

Human resources for recruiting and training specialised staff were allocated from a single platform (appendix). We experienced shortage of various equipment and consumables made in Asia.<sup>2</sup> Centralised logistics made it possible to adjust quantities daily, in response to supply shortages. Universities called upon thousands of students in medicine, nursing, pharmacy, and dentistry who underwent specific training to work as paramedics, research assistants, or operators on a telemedicine platform.<sup>3</sup>

Management of available beds was crucial, so a central ICU bed-allocation system was organised at the regional level to optimise patient transfers across hospitals. This allocation unit was led by surgeons who were available as a result of the postponement of non-essential surgeries.

Using multidisciplinary working groups, practical guidelines were edited within 48–72 h, shared among all hospitals, and published on an AP-HP website. Examples of guidelines include the appropriate use of scarce equipment or drugs, optimal use of ventilators, and ethical issues. These guidelines were discussed during the central crisis team's twice-daily telephone meetings. Critical care response was coordinated through a daily meeting of ICU heads.

A COVID-19 research committee developed a global research strategy that was shared with the universities and INSERM. The top priorities were establishment of patient cohorts, biobanking, and clinical trials. More than 40 clinical studies enrolled more than 7000 patients. This fast initiation of research was possible because of a shared research support infrastructure and reallocation of all research personnel, supplemented by volunteers. The centralised pharmaceutical office made drugs and placebos available at each hospital. The value of this research effort will

be judged from the peer-reviewed scientific output in the near future.

The response to the crisis was data-driven, thanks to a single institutional data platform fed by a single information system, providing important decision making parameters (eg, length of stay, treatment, clinical pathway) in real time.

Large-scale initiatives were rapidly developed. Each day, a farm of 63 3D printers manufactured 1000 parts of various medical devices, bypassing a slow supply chain and avoiding disabled equipment. The Covidom telemedicine platform monitored more than 50 000 patients at home (appendix).<sup>3</sup>

A region-wide patient-tracing programme, COVISAN, was set up.<sup>4</sup> Devised by AP-HP under the umbrella of the regional health authority, the COVISAN programme brought together local authorities, general practitioners, non-governmental organisations, and private companies, which helped to secure the national lockdown exit plan.

All this was made possible because of extraordinary mobilisation and joint efforts of medical, paramedical, and administrative staff and with reinforcements from other regions (appendix). The COVID-19 crisis hit an institution that already had a shortage of nurses. A substantial number of health-care professionals became infected. We wish to acknowledge the tireless work of the highly motivated personnel at AP-HP. The COVID-19 crisis is not yet behind us; nevertheless, at a time when virtually every health system in the world is facing unprecedented challenges, we hope others will find our initial lessons helpful.

Members of the COVID19-APHP Group are listed in the appendix. We declare no competing interests.

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1 Hirsch M, Carli P, Nizard J, et al. The medical response to multisite terrorist attacks in Paris. *Lancet* 2015; **386**: 2535–38.

- 2 European University Hospital Alliance. University hospitals urgently call for more European collaboration to prevent drug shortages. March 31, 2020. <http://www.euhalliance.eu/2020/03/31/university-hospitals-urgently-call-for-more-european-collaboration-to-prevent-drug-shortages/> (accessed May 1, 2020).
- 3 Assistance Publique-Hôpitaux de Paris. COVIDOM: une solution de télésuivi à domicile pour les patients porteurs ou suspectés Covid-19 co-construite par l'AP-HP et Nouvel e-santé. March 12, 2020. <https://www.aphp.fr/contenu/covidom-une-solution-de-telesuivi-domicile-pour-les-patients-porteurs-ou-suspectes-covid-19> (accessed May 1, 2020).
- 4 Piarroux R, Riou B. Coronavirus: pour déconfiner sans provoquer une deuxième vague, une approche centrée sur le patient. April 27, 2020. [https://www.lemonde.fr/idees/article/2020/04/27/coronavirus-pour-deconfiner-sans-provoquer-une-deuxieme-vague-une-approche-centree-sur-le-patient\\_6037850\\_3232.html](https://www.lemonde.fr/idees/article/2020/04/27/coronavirus-pour-deconfiner-sans-provoquer-une-deuxieme-vague-une-approche-centree-sur-le-patient_6037850_3232.html) (accessed May 1, 2020).

## The COVID-19 MS Coalition—accelerating diagnostics, prognostics, and treatment

Rapid and comprehensive genetic sequencing has shed light on the origin of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and allowed timely implementation of PCR tests to determine the presence of viral RNA. PCR tests for SARS-CoV-2 are some way from being reliably qualitative and will never indicate how the disease might progress in an individual. As COVID-19 becomes endemic, there is a concomitant need for accurate serological assays to detect antibodies to SARS-CoV-2 antigens and ultimately tests for prognostic markers to target treatment options.<sup>1,2</sup> With this considerable genetic insight, and the emerging structural information, comes associated questions regarding the molecular descriptors that contribute to disease progression, especially when we consider spread across different populations. The power of mass spectrometry to generate rapid, precise, and reproducible diagnostic information that complements genomic information and accelerates our understanding of the disease, is now becoming a reality.<sup>3,4</sup>

Mass spectrometry-based analysis can answer questions broadly falling into two categories. The first concerns multi-omic profiling of the host response, correlating prognosis with disease severity. Robust biomarkers will further our understanding of disease mechanisms and the susceptibility of certain clinical groups. The most valuable of these prognostic markers will be those indicating the transition from a beneficial immune response to one that is harmful, ultimately resulting in respiratory distress. Such data will facilitate public health efforts for population screening, defining high-risk patients, tracking disease progression, and identifying sources of vulnerability that will permit treatment stratification and minimise or prevent future coronavirus pandemics.

The second category concerns the SARS-CoV-2 viral spike glycoprotein, which is not only key for host-cell attachment but is also a major target for neutralising antibodies elicited through vaccination. Although RNA sequencing is extraordinarily informative for viral mutation or adaptation via immune selective pressure, it cannot inform on a critical feature of enveloped viruses: viral spike glycosylation. The functional role of SARS-CoV-2 spike glycans, of which there are 66 per trimer,<sup>5</sup> is undetermined yet, along with associated conformational dynamics that shape receptor or antibody binding, a key factor for vaccine design. Investigating spike glycosylation and plasticity with advanced mass spectrometry methods on recombinant preparations and comparing this to wild type viral proteins is crucial to this effort.

The COVID-19 MS Coalition is a collective mass spectrometry effort that will provide molecular level information on SARS-CoV-2 in the human host and reveal pathophysiological and structural information to treat and minimise COVID-19 infection. Collaboration with colleagues at pace involves sharing of optimised methods for

For the Covidom application see <https://www.nouvel.com/covidom-le-suivi-des-patients-porteurs-du-covid-19/>

For the COVISAN programme see <https://www.aphp.fr/actualite/lancement-de-covisan-un-dispositif-de-suivi-renforce-des-personnes-covid>



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For the COVID-19 MS Coalition see <http://covid19-msc.org/>