

## Coronavirus Clinical Report 11.4.20

This report summarizes key points and topics from web conferences, posts, podcasts, webinars, and interviews from the past days, and incorporates relevant information from physicians' COVID-19 social media updates, literature, and official updates.

\* Medint specializes in gathering medical information from a variety of sources around the world. The information presented is not a medical recommendation.

### The report is divided into the following subjects:

1. **General- relevant links**
2. **Relevant updates and studies**
3. **ICU/ Emergency medicine**
4. **Telemedicine**
5. **Gastroenterology**
6. **Neurology**
7. **Obstetrics/Gynecology**
8. **Immunology**
9. **Pediatrics**
10. **Hematoncology**
11. **Dermatology**

### Main Findings

#### **1- General**

##### 1.1 Relevant links:

- [Ottawa Hospital](#) published a **screening tool** to aim to reduce intubation rates and improve patient care in COVID-19 patients, according to the **late intubation** approach.
- [Ventilator sharing Protocol](#): **Dual-Patient ventilation with a single mechanical ventilator**, [published by](#) Columbia University Irving Medical Center.
- [Mechanical ventilation course](#) by Harvard University: the course includes general information regarding ventilation, machine problems solving, patient assessment before intubation, adapting ventilation mode, and more.
- Free **Lung POCUS** course, including COVID-19 patient case studies and demonstrations.

## 2- Relevant updates and studies

### 2.1 Treatment updates

- **Ridgeback Biotherapeutics** has developed an antiviral drug called **EIDD-2801** that **demonstrated promising results on drug tests and received FDA approval to begin clinical trials.**  
The researchers published [study results](#) on April 6<sup>th</sup> in Science Translational Medicine, and **the approval for conducting the clinical research was obtained on April 7<sup>th</sup>.**
- A [case series](#) describes IVIg treatment in the early stages of clinical deterioration with good results.
- [Research](#) describing **convalescent plasma therapy** in 10 severe condition patients:
  - The median age was 52.
  - All patients received antiviral therapy, 6 received methylprednisolone, and some received antibiotic treatment in case of co-infection.
  - The median time from onset of symptoms to plasma therapy was 16.5 days.
  - [Study results](#)- **improvements in symptoms were observed in 1-3 days, as well as CT improvement in all patients. The viral load decreased to undetectable levels within 6 days in 7 patients.**
- [Retrospective study](#) **evaluated Tocilizumab treatment in COVID-19 patients-**
  - 15 COVID-19 patients were included in the study, 2 of them were moderately ill, 6 were seriously ill, and 7 were critically ill.
  - 10 of them had at least one background disease.
  - 8 patients were treated with methylprednisolone.
  - All patients presented **elevated IL-6 levels before treatment.**
  - Study results- 3 critically ill patients died, 1 critically ill patient's CRP levels did not normalize. Among 11 patients, **CRP levels decreased to a normal range within a week.**

### 2.2 Relevant publications

- [Research](#) in Europe examined whether the occurrence of olfactory and gustatory dysfunction is one of the clinical symptoms in mild-moderate COVID-19 patients. A total of 417 COVID-19 patients were included in the study. **Face pain and nasal obstruction were the most disease-related otolaryngological symptoms.**
  - **85.6% of patients reported olfactory dysfunction.** Among them, 79.6% were anosmic. The olfactory dysfunction appeared before, after, or at the same time as the appearance of general or ENT symptoms.
  - **Among the patients without nasal obstruction or rhinorrhea, 79.7% were hyposmic or anosmic.**
- A viewpoint from Stanford University summarizes [key considerations for supporting the health care workforce](#), so health care professionals are equipped to provide care for their patients. The main issues raised among the staff members: what health care professionals were most **concerned** about, what

**messaging and behaviors** they needed from their leaders, and what other tangible **sources of support** they believed would be most helpful to them.

### **3- ICU/Emergency Medicine**

3.1 A retrospective study, conducted in Lombardy, Italy, examined 1591 patients admitted to intensive care units in approximately 72 hospitals across the province due to respiratory failure. All were RT-PCR virus-positive, their median age was 63, and approximately 82% were male.

1. Patients clinical characteristics -
  - **68% of subjects had at least one background disease**, and the most prevalent was hypertension (49%), followed by cardiovascular disease (21%), COPD accounted for a minority of cases (4%). The median length of hospitalization in the unit - 9 days.
  - **99% of patients needed respiratory assistance. In 88% of cases, invasive ventilation was required**, a significantly higher percentage than described in studies in China (ranging from 40-60%) and the US (19%).
2. Ventilation characteristics-
  - **The median PEEP - 14cm H2O.**
  - FiO2 was greater than 50% in 89% of patients.
  - The median Pao2 / Fio2 ratio was 160.
3. Research results:
  - **Ventilation:** The research compared ventilation data among older patients- aged  $\geq 64$  years and younger patients-aged  $\leq 63$  years:
    - **The median PEEP level was not significantly different, FiO2 values were higher in the older group, and the Pao2/Fio2 ratio was higher in the younger patients.**
    - The **high invasive ventilation rates are attributed to the severity of hypoxia** and the fact that the profile of patients admitted to the ICU included more severe respiratory conditions, and therefore moderate cases were not included.
  - **Mortality:** The mortality rate among all ICU subjects was 26%, with older patients having a higher mortality rate of 36% compared to 15% among younger people. It is important to note that at the time of writing this article, 58% of the subjects were still admitted to the ICU, but **the percentage of those released from the ICU was significantly higher among the young group- 21% compared to 11%.**
  - **Hypertension:** The incidence of hypertension was higher among the deceased versus those released from ICU- 63% versus 40%, respectively.
  - **The need for ICU capacity in COVID-19 patients is substantial**, with an estimation of **9% of all cases.**

3.2 [Webinar summary](#)- discussing **respiratory management for COVID-19 patients**, with specialist participants in the field of emergency medicine, ICU, and anesthesia (full names in [link](#). duration: 1.5h). The main key points:

- Late vs. early intubation- At the beginning of the outbreak, Italy, New York, and Washington supported an early intubation approach but realized the hard way it does not necessarily benefit patients, and therefore now support a late intubation approach and an oxygen-first strategy. From their experience, those who usually require early intubation are patients with comorbidities.
- By their definition, the deterioration looks like Progressive oxygen failure rather than Respiratory failure.
- **HFNC use is very common in the US, despite the risk of aerosolization.** To reduce the risk, they reduce the flow, but FiO<sub>2</sub> remains 100%. They emphasize that HFNC causes dehydration, therefore patients require volemic control.
- They **do not see an advantage to the use of an "aerosol box"** if there is full PPE. They even **warned of trying to use it with no previous experience.**
- **Intubation in "happy hypoxemic" patients**- discussed the fact that it is impossible to set a cut-off saturation value for intubation because patients look good (they mentioned patients with PaO<sub>2</sub> 30 who played on the cell phone) and recommend being flexible about it and **closely monitor the patients.**
- **Invasive ventilation**- They claim that in order to suppress respiratory drive and slow down RR (target below 20), high doses and combinations of many drugs are needed compared to what they were used to. Hence, they conclude that the respiratory center is not damaged.
- Lung tissue recruitment- The fear of low PEEP was that insufficient lung tissue would be recruited. However, this does not seem to be the problem, but rather **vascularization is the limiting factor.** They emphasize decoupling PEEP with FiO<sub>2</sub>.
- **Proning- They perform this in every patient who enters the ER and is capable of self-proning.** They emphasize it is related to any change of posture, including **lying on the side or sitting upright** could be helpful. Intubation was avoided in some patients due to proning. For ventilated patients- it is unclear how much that helps.

#### **4- Telemedicine**

- **Telemedicine updates-** The **American Medical Association- AMA** updated its [Digital Health Implementation Playbook Series](#) to include a new [telemedicine](#) guide for implementing real-time audio and visual visits between a clinician and a patient. The Playbook provides a 12-step process to guide the implementation of a digital health solution.
- **Adjusting the use of MoCA (assessment of cognitive function in the elderly) by telemedicine during the COVID-19 epidemic.** There are modified MoCA versions, including one adjusted for telephone use and some that omit visual or

auditory items with validated cut-off scores. Nevertheless it is important to evaluate several factors before performing the modified versions:

1. Interpreting test results requires a **full understanding of the examinee's vision and hearing abilities**- in the case of the use of an assistance device, the patient should be asked to use it.
  2. **Test administration will be non-standardized** due to difficulties correctly assessing the communication limitations.
  3. **One cannot alter subtest items or mode of administration** (that may result from misinterpretation of words, exchange of words with a similar sound, use of different means of communication in the same test) **and assume the same cognitive abilities are assessed.**
  4. In the absence of studies using standardized telemedicine MoCA versions, its results must be met with caution, and cut-off scores should not be the singular evaluating tool used for patient assessment.
- A tool developed in Switzerland to assist in decision-making regarding **ambulatory management and follow up of the general population, COVID-19 patients, and post-hospitalization patients**- the tool includes treatment algorithms, references to at-risk populations, home visits key points, and more.
  - A [link](#) to a convenient [framework](#) (4Ms) regarding **the use of telemedicine services with the elderly.**
  - **National Institute for Health and Care Excellence** published guidelines regarding the management of patients with [pneumonia](#) and [symptomatic treatment](#) in the community.

### **5- Gastroenterology**

Recommendations from gastroenterologists in Italy on using the following technique to reduce aerosol exposure as much as possible during gastroscopy:

(Attached images according to number)

1. Bite block set with O<sub>2</sub> tubing and nasal CO<sub>2</sub> sampling.
2. Anesthetic face mask applied over the bite block set and fixed with an elastic band system.
3. Rubber valve made with a glove-finger put on the endoscope port.
4. Vital signs monitoring during the procedure.



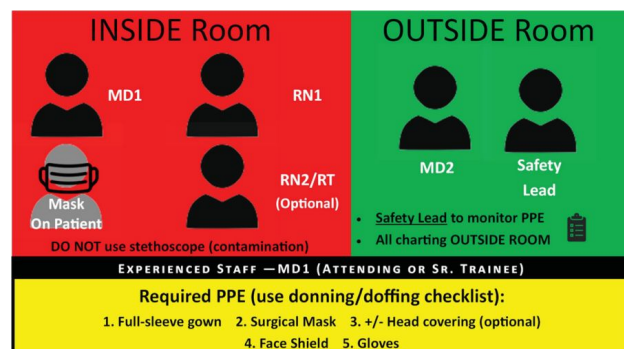
## 6- Neurology

### 6.1- Case reports:

- **The first report of meningitis associated with SARS-CoV-2 in Wuhan** - a 24-year-old man who experienced flu symptoms for several days (fever, general weakness, and headaches), was admitted on the 9th day of his complaints due to seizures and loss of consciousness. On examination, he had obvious neck stiffness. SARS-CoV-2 RNA was detected in CSF, although nasopharyngeal swab was negative. **A brain MRI showed changes in the lateral ventricles, hippocampus, and temporal lobes associated with the diagnosis of meningitis.**
- **The first report of a possible presentation of Guillian-Barre syndrome-** a 61-year-old woman was admitted due to symmetrical weakness in both legs, areflexia, and severe fatigue. Her symptoms worsened and progressed to her hands after 3 days. No respiratory or fever findings in the days prior to the weakness.
  - ❑ Laboratory results on admission were clinically significant for **lymphopenia and thrombocytopenia**. CSF testing showed normal cell counts and increased protein levels. Nerve conduction results supported **demyelinating neuropathy**.
  - ❑ 8 days after the initial presentation, COVID-19 related symptoms appeared, including cough and fever, and chest CT imaging demonstrated COVID-19 pulmonary findings.
  - ❑ **It is possible that the neurological manifestation appeared due to other unknown cause**, but it is unlikely the patient acquired the virus in the hospital area, as her relatives who cared for her during her stay were positive for SARS-CoV-2 RNA while the treating medical staff was found to be negative.
  - ❑ After 30 days of admission, she was discharged without any neurological or respiratory symptoms.

6.2- Protected code stroke protocol- stroke patients management was written by the **American Stroke Association** to protect teams against possible exposure:

- Team members protection: A full personal protective equipment (PPE) and a face mask for the patient. In cases necessitating suction, intubation, ventilation, or CPR- **N95 should be used in addition to PPE.**
- Resource management:
  - Things to avoid- the use of a resuscitation room in order not to contaminate it, treatment in overcrowded rooms, contamination of other hospital environments en-route to imaging and back.
  - **Designate a safety team leader to monitor PPE** donning/doffing.



- The suggested team role distribution is shown in the picture.

## **7- Obstetrics/Gynecology**

- **Human Milk Banking Association of North America** calls to retract the *Journal of Human Lactation* publication regarding the disinfection of individual bags of raw breast milk and bottles of human donor milk in milk banking and clinical settings. The organization claims the publication violates FDA guidelines, which state that foodborne exposure is not a known transmission route, and the recommended bleach disinfection concentration is higher than the directives issued by the U.S. Environmental Protection Agency (EPA) and **could endanger vulnerable infants**.
- **A database study** collected data regarding **maternal and perinatal outcomes of pregnant women with COVID-19 from 18 different studies performed in several countries**. The study's main findings:
  - 108 pregnancies were reported in the studies, most of them present in the third trimester. Three maternal ICU admissions were noted with **no maternal death**, 2 of them had significantly high BMI, and **all 3 had comorbidities such as asthma and diabetes mellitus**.
  - Most women presented with fever (68%), coughing (34%), Lymphopenia (59%), and elevated C-reactive protein (70%).
  - 91% were delivered by cesarean section due to fetal distress, although the reasons for fetal distress were not specified in the various studies (whether it referred to abnormal cardiotocography findings or other factors like meconium-stained amniotic fluid etc.).
  - **7 cases of spontaneous vaginal delivery were not associated with poorer outcomes**.
  - In most cases, treatment included oxygen and antiviral therapy, in addition to antibiotics.
  - Neonates- **one neonatal death and one intrauterine death were reported**, as well as 6 cases of neonates ICU admissions due to respiratory distress, fever, thrombocytopenia, tachycardia, and impaired liver function.

## **8- Immunology**

- **Anti-Inflammatory Treatment-** to note, the treatment presented hereinafter is contradictory to the official organizations' guidelines regarding this topic. **Hospital Doctor Peset** in Valencia, Spain, utilizes a **prophylaxis protocol advising the administration of steroids prior to the development of respiratory distress**. According to the doctors, most hospitals reserve the anti-inflammatory treatment for severe cases, when, in fact, it is no longer effective for them.

- The doctors rely on the two main stages of the disease, the second one (the inflammatory stage) is mediated by macrophages and inflammatory mediators, which **they claim is the primary factor contributing to the mortality of the disease.**
- In patients that exhibit radiological changes, they initiate the administration of steroids on day 6 of the symptoms up until day 12 (methylprednisolone 80 mg/day), and in patients that improve, they add treatment with Tocilizumab or Anakinra. **They claim that the protocol has good results, fewer referrals to the ICU, shorter hospitalization duration, and significant improvement in the imaging results.**
- Two articles published in the last few days discussed the **MAS-macrophage activation syndrome** (also known as secondary hemophagocytic lymphohistiocytosis):
  - The [first](#) article presents a model for the **recognition of MAS-like presentation** in COVID-19 patients and describes **the potential of anti-cytokine therapy in the early stages of the disease.**
  - The [second](#) article describes the experience of one medical center that administered **low-volume plasma exchange with low dose steroids** for the treatment of patients with sHLH and liver failure caused by Dengue Fever and presents evidence proving that this therapy could be effective in COVID-19 patients as well.
- A [research](#) conducted in Shanghai evaluated titers of Nabs (neutralizing antibodies) in 175 recovered COVID-19 patients, which were admitted to hospitals with only mild symptoms. The antibodies were detected 10-15 days after the onset of the disease, and their levels remained stable thereafter. Nabs titers varied significantly between patients; 30% of patients exhibited low plasma Nab titers; in 6% of patients, the levels were undetectable. Furthermore, **a positive correlation was found between Nab titers and older age, as well as with elevated CRP levels taken at the time of admission, and a negative correlation was found between Nab titers and lymphocytic count.**

## **9-Pediatrics**

- The CDC published a [report](#) concerning morbidity and mortality in pediatric COVID-19 cases. It stated that **the overall number of hospitalizations in wards and ICU is smaller than among adults**. Still, **children aged < 1 year accounted for the highest percentage of hospitalization** among pediatric patients with COVID-19. **Three deaths among pediatric cases** have been reported so far.
  - Among the 345 pediatric cases that were examined, 80 (23%) **had comorbidities** (specifically chronic lung diseases, cardiovascular diseases, and immunosuppression).
  - Among the 291 pediatric COVID-19 patients that were examined, **213 (73%) exhibited fever, cough, and dyspnea.**
  - Important to mention that many infected children experience only mild symptoms, which is why they are not tested. Therefore, **most tests are taken from patients with a more severe illness.**



- [JAMA](#) published a study that examined **the characteristics of COVID-19 in children in Madrid**. The study examined children that were hospitalized or were likely to be hospitalized and presented with typical symptoms of the disease or children that were in a risk group due to underlying diseases.
  - Among **365 children, only 41 had positive test results**, and they accounted for 0.8% of all the confirmed cases in the city.
  - **The median age of the pediatric positive COVID-19 cases was 1 year**, 25 of those patients were hospitalized, and 4 of them were admitted to a pediatric ICU.
  - **4 children required respiratory support beyond a nasal cannula**; of these, only one child had an underlying disease (recurrent wheezing).

## **10-Hemato-Oncology**

[Leukemia Research](#) journal published a review examining what is known regarding the possible impact of COVID-19 pandemic on patients with acute leukemia. Following are key points:

### 1. Delay in treatments:

- **Chemotherapy treatments and transfusion of blood products may be postponed** due to shortage or in order to prevent infection of immunosuppressed patients, however, this could negatively affect prognosis, especially of young patients with a moderate illness.
- **Hematopoietic stem cell transplantation could be delayed** since both the recipient and the donor need to be sufficiently healthy for the procedure to be successful. Allogeneic transplantations need to be postponed, even though there is no evidence of a transfer of the virus through blood products.
- The delay in treatments **interferes with long-lasting protocols**. For example, maintenance protocols for ALL, which could take up to two years. This delay has an unknown influence on disease recurrence or the survival of these patients.

### 2. Treatments:

- Due to the respiratory side effects of induction therapies, **the combination of chemotherapy with ATRA could be less dangerous than ATRA and ATO**. ATO can be used as consolidation therapy.
  - Important to mention that **ATO and Ivosidenib may prolong QTc**, as do Chloroquine and Remdesivir, hence the combination of treatments needs to be carefully evaluated.
  - Other drugs with side effects that could worsen the condition of COVID-19 patients such as Dasatinib and Venetoclax should be taken into consideration.

- ### 3. **Leukemia patients are immunocompromised and should postpone clinic visits as much as possible**, test for the virus according to the guidelines, and **make sure they have up-to-date vaccination status** in order to avoid secondary bacterial infection.

## **11- Dermatology**

The American Academy of Dermatology (AAD) **collects through [survey](#) reports regarding dermatological manifestations of COVID-19, and also information**



**concerning COVID-19 patients with underlying dermatological conditions.** All medical teams are welcome to enter cases. Entering cases takes 5-7 minutes to complete.

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