



China with the World: COVID-19 Experts Dialogues

The 4th Talk

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Prof. Zhiyong Peng

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As one of the leading professionals in Critical Care Medicine in China, Prof. Peng has extensive experience in clinical research, education and practices, with his particular focus on cellular metabolism, sepsis, clinical pharmacology and drug development.

Dr. Ming Zhong

Director of Department of Critical Care Medicine
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Dr. Zhong's current clinical research focus is the hemodynamic monitors in shocks, pathogenesis and treatment of ARDS, extracorporeal life support for severe cardiac and respiratory failure, clinical nutrition for critically ill, coagulopathy in sepsis. His groundbreaking utilization of protective ventilation in anesthesia for esophagectomy significantly attenuated postoperative inflammation of lungs.



Prof. Pierre Singer

Professor of Anesthesia and Intensive Care, Sackler School of Medicine
Director of the General Intensive Care Department
Rabin Medical Center, Beilinson Campus, Petach Tikva, Israel

Director of one of the main reference Intensive Care units in Israel and Chairman of the European Society for Clinical Nutrition and Metabolism, Prof. Singer is well recognised in Israel, Europe and globally for his impressive research and academic portfolio focus in Critical Care.

Dr. Enrico Storti

Head of Anesthesia & Intensive Care
Maggiore Hospital of Lodi , Lodi ASST, Italy

Postgraduate in Internal Medicine, Anesthesia and Intensive Care, Dr. Storti has very solid professional career with a special focus in Clinical Ultrasound. He was the president of the World Interactive Network Focused on Critical UltraSound (WINFOCUS). Now he is fighting the battle against Covid-19 in the frontline of Lombardy, Italy.



Prof. Jordi Rello

Intensivist
Leader of a sepsis and pneumonia research group at the Excellence Network for Biomedical Research Center in Respiratory Diseases (CIBERES)
Professor of Translational Medicine Vall d'Hebron Hospital Campus, Barcelona, Spain

As one of the globally well recognised professionals on his field and with intense research activity in infectious diseases and Critical Care, Prof. Rello is one of the first persons conducting, coordinating and publishing scientific articles in Europe regarding COVID-19 management.

Dr. Tomas Lamas

ICU Consultant
Egas Moniz Hospital, Lisbon, Portugal

Dr. Lamas is a restless professional with an extensive research portfolio and passion for Intensive Care and Emergency medicine. With a great reputation at national and European level and always looking for the next scientific challenge, he is currently based in one of the main public hospitals in the metropolitan area of Lisbon, Portugal.



Q (Prof. Singer): What do you think about the comorbidities and the age of the patients in the treatment of COVID-19? Is the mortality higher in elderly patients as it is reported from recent papers?

A (Prof. Peng): If the patient has comorbidities, they can be easily infected by COVID-19 and are likely to become severe cases. Regarding the treatment, I am not aware of any specific treatment for this kind of patients.

Q (Prof. Singer): Regarding the organization and protection of the teams, what are your recommendations?

A (Prof. Peng): For the personal protection, implementing “airborne precautions” is crucial: N95 face masks, protective shoes, goggles and face shields when working in the ICU. This right protection for clinical staff is crucial.

Q (Prof. Singer): How many professionals have been infected?

A (Prof. Peng): Most of the professionals were infected at the early stage because we didn’t realize the transmission was so high. Another issue was that we didn’t have enough Personal Protective Equipment (PPE) at the beginning, but the government ordered many companies’ quick production of equipment. Right now everything is ok. During the last month I didn’t even hear about any case of professionals infected by COVID-19.

A (Prof. Storti): Regarding the questions from Prof. Singer, yes, we have higher mortality among the elderly in Italy. Our experience is limited to only three weeks and I don't have clear figures, so please don't take this as truth. On the other hand, we are starting to see younger patients severely ill with ARDS that, unfortunately, have to be admitted in the ICU while, in the very beginning, we saw more elderly patients.

How to protect our team is an issue. To give you a rough idea, we have increased our ICU beds from 12 to 24. At the beginning, there was only 25% or less of our team members working because of a quite consistent number of professionals out of duty as they were found to be positive for COVID-19.

With smaller teams we are forced to cope with this situation by working very heavy long shifts. Also, it is an issue to do extra shifts and when you are deeply involved in a scenario which is totally unexpected and unknown. I have seen many experts, ICU physicians and professionals crying after their shifts.

To protect our professionals, we used N95 masks, goggles, hats, double pairs of gloves and protective aprons. We, of course, also cover shoes.

We ask our ID doctors to supervise our procedures in the "filter zone" before the main entrance of the ICU. This "filter zone" was newly built as it was not present before, all thanks to our technical guys.

A (Prof. Zhong): I was shocked by the number of critically ill patients when I arrived in Jinyintan Hospital in Wuhan, the first designated hospital to receive COVID-19 patients. They present-

ed with severe hypoxemia and Multiple Organ Dysfunction Syndrome (MODS).

Also, there was a lack of medical staff and we didn't know whether our personal protection was enough to keep us safe. The situation got better when the physicians from all over China came to Wuhan to help local professionals.

 **Q (Prof. Singer): Did you protect your teams by doing shifts? If somebody was infected and quarantined, how did you manage?**

A (Prof. Peng): Of course anyone tested positive (abnormal chest CT or typical symptoms) should leave the team and have a rest, and we would recruit a new professional as other colleagues would be in risk to be infected, even though they did not fear of the infected patients.


A (Prof. Zhong): There is a rotation (shift): one team every four weeks and after that they have to leave and another new team will take over. The professionals need, at least, one-week rest as working under such pressure is exhausting. We needed more people for these shifts.

 **Q (Prof. Rello): What is the rotation of these shifts, 12 hours?**

A (Prof. Peng): Yes, for physicians one shift is 12 hours. Usually, in my team, we assign three physicians to each shift. In the morn-

ing they need to stay on duty for 4 hours, then they can go out to have lunch and some rest (even when not all of them will do it) and then they rotate so there is always, at least, one physician keeping an eye on the patients in the ICU.

A (Prof. Zhong): In the beginning, for the nurses one shift was eight hours, but later we found that eight hours was too exhausting because workload is much higher than standard, therefore they could not keep working so long. Then, we shortened their shifts to 6 or 5 hours with a higher rotation of shifts.


 **Q (Dr. Lamas): I have one question about the nurse shifts. After working for 5 or 6 hours, do they go back home and come next day, or they work 5 hours in the morning and then 5 hours in the evening? How do you manage these nursing shifts? We find very difficult to manage so many rotations.**

A (Prof. Zhong): In our ICU, if the nurses have a 5-hour shift in the day time on the first day, on the second day they will have a 5-hour shift in the afternoon, and on the third day they will work at night. After that, they get a whole day to rest.


 **Q (Dr. Lamas): During the 5-hour shift, do you use the complete protective dress and equipment?**

A (Prof. Zhong): To be honest, in the very beginning we were not very sure of what was the right protection working in such an isolation ICU, but we had the N95 masks, face shields and double gloves. For almost two months, no staff got infected.


A (Prof. Peng): I remember that the medical staff had to spend, at least, 4 hours in the ICU before going to the resting room to have some food or drink water. When they went back to the ICU, they must change and dress a whole new set of protective equipment. Therefore, in order not to waste protective equipment, they had to stay in the ICU for at least 4 hours before coming out.

 **Q (Dr. Lamas):** What is the nurse-bed ratio and doctor-bed ratio in your ICU?

A (Prof. Zhong): My ICU was a temporary ICU. The former ICU had only 16 beds which were not enough and the temporary one expanded to 26 beds. During the first month, we had 50 nurses and 12 physicians. Now, we have 80 nurses and 15 physicians.

 **Q (Prof. Singer):** About the equipment, having an increased number of patients who need mechanical ventilation, I guess you didn't only have sophisticated ventilators but maybe also some simple ventilators? Are you using them?

A (Prof. Zhong): In our temporary ICU, every bed has a medicalized ventilator. We did not use home-use ventilators such as BiPAP. No matter whether they are for non-invasive or invasive ventilation, we all use the same ventilators.



Q (Moderator): We have a question from the audience. When the doctors and nurses finish their shifts, do they go home or stay at hospitals or any places nearby?

A (Prof. Zhong): At the hospital I support now, most medical staff come from other parts of China and don't live in Wuhan, so the physicians and nurses will stay in hotels near the hospital between shifts. Even for the local professionals, most of them do not go back home after shifts. For those going home, they isolate themselves from their families.

A (Dr. Storti): In Italy, there are a number of physicians and nurses who prefer being provided with some areas to stay rather than return with their families. Personally, I haven't seen my family for a long while because we are deeply involved in an environment which is highly infective.

We are dealing with two kinds of population. One group, of course, is the ICU patients who may have ARDS or are on invasive mechanical ventilation and we also take care of patients in a new Step-Down Unit (SDU) of about 20 beds.

We arrange separate areas for the emergency department, and we are weaning a large number of patients because we don't have enough ICU beds. We are trying to keep these patients alive and provide NIV for them, but this kind of CPAP ventilation creates a scenario which is not positive from the infection spread point of view.

Finally, we found another sort of worse scenarios with the huge disproportion between resources and number of patients in the

emergency department, some of them very sick and demanding ventilation and advanced monitoring and we can't ventilate them properly because most of the ICU ventilators are already on use.

Q (Dr. Lamas): I understand that using HFNC is very risky for the healthcare workers because there is a dissemination of virus in the air but, when you don't have any available ventilators, then HFNC may be the only option for these patients. Are you using it?

A (Dr. Storti): We do it. We try to ventilate and provide oxygen to all patients, but it is not easy. Just a rough idea, we have increased our oxygen consumption, in terms of source, too close to "oxygen crash", because the total amount of oxygen consumption is huge. All the ventilators in ICU, SDU, and a large portion of medical beds, every single patient, if not ventilated, is having any oxygen therapy. Considering that, we have asked our technical guys to install twenty 220V oxygen sockets in the ER because there are not enough oxygen points to connect to the patients.

To keep our patients alive, CPAP is useful in the ER while waiting for SDU or ICU admission. It is not a gold standard, but that is the only way to keep them alive and that is the reason why we are even more committed to protect our staff, because they are still working in an unsafe environment.

In the very beginning we tried to keep separate tracks for positive and negative patients for COVID-19, but because of the outbreak, it has become very difficult to achieve.

Q (Dr. Lamas): And how about in China, do you used high flow oxygen therapy?

A (Prof. Peng): Actually, we have similar issues. If most patients are on HFNC, the hospital will run off oxygen supply and we are also concerned about the airborne generated from the infected patients. Actually, we monitored the virus presence and concentration near patients in different environments of 2 ICUs: One ICU had its windows open, while the second ICU was equipped with negative pressure. We detected a higher virus concentration in the air on the first ICU, whereas on the ICU equipped with negative pressure, the virus concentration in the air was ok, so this ICU equipped with negative pressure was safer for professionals providing HFNC to their patients. Therefore I highly recommend that, if you want to use HFNC, do it in an ICU with negative pressure. This is better for healthcare professionals.

Q (Prof. Rello): Do you use any pharmacological prophylaxis to protect the healthcare workers?

A (Prof. Peng): There is no pharmacological prophylaxis. We just have PPE, hand hygiene and avoid cross-contact. These are all the important measurements for the professionals' protection.

Q (Prof. Rello): If the healthcare workers become infected and cured, will they get infected again by the same virus?

A (Prof. Zhong): A: We observed some patients who were discharged from the hospital having a negative test and some


weeks later, they came back to the hospital to be tested positive again. We don't know whether these patients got a second infection, reactivation or they just weren't completely cured after the first admission, but it is also important to mention that we have seen some false negative tests.

We took samples from the mouth and throat, which were not deep, so we were unsure whether it was because of the sample obtention that we had false negative tests.

 **Q (Prof. Rello): The Lancet just published a very nice paper on mortality, It indicated and association of high Procalcitonin (PCT) and mortality. Does it mean that a high PCT would be criteria for prognosis?**

A (Prof. Zhong): We are aware of the paper in the Lancet and, in my experience, we observed nearly 100 patients, and we did not observe the same association between the PCT and the outcomes. So, I don't know if there is a relationship between PCT and the mortality due to COVID-19.


A (Prof. Peng): We also found that a high count of neutrophils and low count of lymphocytes predicted poor outcomes. Increased PCT levels probably indicates the secondary infection of the patients from bacteria or fungus, especially in the late stage of the illness, because these patients are in immunocompromised situations and can easily develop secondary infections.




Q (Prof. Rello): Regarding ventilatory strategies, here in Spain, we identified two different phenotypes: Some patients show a high pulmonary compliance, because they have a viral pneumonia and a severe hypoxemia. In the second phenotype, many patients were managed with delayed intubation, some of them with a high PCT that probably means over-infection, and the others were treated with delayed intubation like NIV. Do you document these two phenotypes in China and Italy? What are the implications of ventilatory management in these two phenotypes?

A (Prof. Peng): We observed that most of our patients had a low pulmonary compliance. If the compliance level is less than 10 or 15 ml/cm H₂O, it is not easy to wean them off the ventilators and it also correlates to poor outcomes. For this type of patients, the lower compliance, the poorer outcome.

I don't have any recommendations for ventilatory supports as any ventilatory support may not work for this type of patients with very low lung compliance.



Q (Prof. Rello): In Italy, did you see patients with high pulmonary compliance on viral pneumonia that require different ventilatory strategies? This is very important because, in the beginning, they are hypoxemic, and they get intubated very quickly but they don't behave like ARDS but like a viral pneumonia. In my opinion,

 **they need different ventilatory strategies like higher VT with lower PEEP and probably, prone position may not be required. What is your experience in Italy?**


A (Dr. Storti): Though question. We received very ill patients with hypoxemic blood gases that responded very well and quickly to protective ventilation, meaning lower Tidal Volume and higher PEEP. The PaO₂/FiO₂ improves quickly managing them with prone and supine strategies, but the problem comes when you try to start the weaning process. That is not so easy as they are still very weak, and present all the problems associated to early weaning. I don't know whether this is a matter of ventilatory strategy or, as some colleagues believe, during early ICU weaning after only one week, there is still a viral burden still active in the alveoli and it takes longer to trigger the inflammation response.

Sometimes, we also receive patients showing a clear ARDS pattern confirmed by CT scan and lung ultrasound that we use extensively in the ER and ICU as a bedside monitoring tool. Also sometimes we receive hypoxic patients with not such ARDS patterns and, you are right, we need to reshape a bit the ventilatory strategy according to this last different pattern.

It is important to clarify that I am not so sure about all the details of these patterns just because we have too many patients and it is tricky to provide the same constant standards of care to 24 ARDS patients together as it is an extremely time-consuming to focus on these many patients at the same time.

I have no examples of these two patterns you mention for chest compliance, lung compliance, but, obviously, the different pat-

terns may need to be ventilated in different ways. But again, in true ARDS, PEEP shouldn't be too high to protect them from pneumothorax. Anyhow when we have scenarios where we are less experienced, we managed these patients with the conventional protective ARDS strategy and maybe the compliance you mentioned better correlates with what the CT scan tells us.

 **Q (Prof. Rello): In these patients with isolated viral pneumonia, with high pulmonary compliance and severe hypoxemia, probably the main finding is hypoxic vasoconstriction. In these patients, the major issue is indeed related to perfusion, as the lung is ventilated and increased PEEP may not help. Are these patients taking benefits from nitric oxide (NO)?**

A (Prof. Peng): Actually, for this type of patients, if the lung compliance is less than 10 ml/cm H₂O, it is not good. If the compliance is around 20 ml/cm H₂O, we will try to help them by putting on prone position as soon as possible. Then we will proceed to very gentle lung recruitment manoeuvres that may improve lung compliance, just using a low PEEP, not higher than around 20 cm H₂O, otherwise we can induce lung injury and pneumothorax. For the general settings we set the PEEP below 10 cm H₂O for the lung-protective ventilation approach.

 **Q (Prof. Rello): Dr. Storti, any different comments on the use of NO to improve pulmonary perfusion?**

A (Dr. Storti): Yes, we use it. Since we have more than doubled our ICU beds, we also doubled the consumption of NO.

Sometimes we have a good clinical response, but sometimes they are non-responders. But this is my personal approach, meaning that, when I am not 90% or 100% sure, I always try to perform a NO trial and if I manage to reduce FiO₂, I'll try to keep the NO on.

I am aware of the fact that the Chinese colleagues do not use NO because we have discussed in the previous webinars but I have a quite positive experiences with NO; if the patient responds, I keep using it; if they do not respond, I suspend it.

Q (Moderator): We have a question from the audience about the NO use, since you are talking about it. What kind of patients do you think should be good responders to NO?

A (Dr. Storti): I don't have an answer to that, anyhow the physiological basics have been clearly described by Professor Rello and they seem reasonable.

My questionable behaviour is very basic: when I see a high FiO₂ that already reached dangerous levels of pressure, I try to use NO in addition. And then I try not to use high FiO₂, but PEEP and driving pressure to adjust the tidal volume to protect the lung.

Q (Dr. Lamas): We don't have many ECMO machines, so how do you select patients for ECMO? And how do you manage the situation?

A (Dr. Storti): This is a tough question as in our hospital we don't perform ECMO, so we are forced to refer them to other hospitals. From the beginning of this epidemic outbreak in the north of Italy, we referred only a few patients for ECMO. Also, in some occasions we proposed patients but, unfortunately, it was too late to bring them to the ECMO network.

A (Prof. Rello): My personal opinion is that VA ECMO would be very useful in a few patients who develop myocarditis. They would benefit a lot. But we have a huge number of patients with hypoxemia and it is not realistic to consider ECMO for all of them.

A (Dr. Storti): I do agree. If you are able to administer NO and perform low-flow CO₂ removal with CVVH, there should be a reduction of patients in need for ECMO.

A (Prof. Peng): Actually, in my hospital we have already performed ECMO on 15 patients, and the mortality is around 50%.

When and how to initiate ECMO is a very important step as, from our experience, if a patient has a high CO₂, it probably means that there is also a severe lung injury and this kind of patients cannot be easily weaned from the ECMO. So, if a patient is on severe hypercapnia, they probably won't be easy to wean from the ECMO. Also, the elderly and those with several comorbidities will not be easy to be weaned from ECMO.

As our experience is limited to only 15 ECMO, I don't know if there are any differences with other virus-induced pneumonias or ARDS and maybe the mortality is similar or lower to other ARDS. Nowadays the survival ratio of H1N1-induced ARDS should be around 60%, but I'm not sure if we can extrapolate these results to COVID-19 as we only had 50% of survivors after ECMO.

A (Prof. Zhong): In our centres, in the beginning, we didn't have enough nurses/physicians-bed ratio so, for some patients it is possible that there was a delay to start ECMO. These patients had a long-time mechanical ventilation before the ECMO. Anyhow we managed to stabilize the vital signs but, as Prof. Peng mentioned, they were very hard to wean from ECMO. In some cases, even the inflammation and pneumonia were gone, but the lung compliance was still low, and these patients couldn't recover to a normal lung, even after more than one month on ECMO, and they died due to the consequence of the ECMO support.

In my opinion, if we have not enough medical resources, we must select patients for ECMO very cautiously avoiding those that have been on mechanical ventilation for too long as well as the ones with many comorbidities.

In conclusion, we have observed that ECMO effect is not as good for COVID-19 patients as we expected based on previous experiences.

 **Q (Prof. Rello): Two additional questions with regards to specific populations: Pregnant women and children. In pregnant, do you manage it differently during the third trimester?**

A (Prof. Peng): In my hospital, we admitted about 40 pregnant women infected with the COVID-19 and most of them had mild to no symptoms, even the chest CT showed just mild changes. From these, at least 10 women delivered the baby already, and we didn't find any evidence of vertical transmission from mother to foetus.

I also tried to understand what happens to pregnant women by comparing them to non-pregnant women of the same age but, unfortunately, it is difficult to find non-pregnant women on the same age who are ill from COVID-19, only a few and most of them are nurses.

I tried to collect some data from the community of infected patients and I couldn't find anything relevant, but I still think that pregnant women are vulnerable to the COVID-19, so I would recommend extra care even they don't show any symptoms.

 **Q (Prof. Rello): What about immunocompromised patients? And what about children? Because looking at the reports, initially the main target was elderly people, but later on younger people joined.**

A (Prof. Peng): Actually, I haven't seen any children infected with the COVID-19 in my hospital, but perhaps they are in the children's hospital.

For immunocompromised patients such as organ transplantation or under chemotherapy, radiotherapy, of course, they may be vulnerable to the COVID-19. I saw some of them and the evolution depends on their clinical story: if these patients are still at the early stage of the organ transplantation or chemotherapy, they can become severely ill. Other patients with an organ transplanted one or two years ago would be alright or show mild symptoms.

Q (Moderator): I would like to ask something from the audience. Did you observe if these patients are more likely to get a nosocomial infection in the hospital?

A (Prof. Peng): I didn't find any differences from other patients. Maybe the nosocomial infection is more likely to happen in a more advanced stage, not in an early stage, especially if the patient stays in the hospital for a long time.

Q (Moderator): But you didn't notice a difference with other patients' populations, right?

A (Prof. Peng): No, I didn't find any differences from other populations. The lymphocyte level and severe lymphopenia depend on their situation, as ICU patients are very ill but in the wards, they are less ill.

Q (Moderator): That takes me to other question from the audience related to these "less ill" patients: Is there any experience of treating them at home or a different place other than hospitals?

A (Prof. Peng): Asymptomatic patients are requested to stay at home on quarantine but, unfortunately, in China now most of the apartments have only two bedrooms and it is difficult for them to maintain the quarantine and they easily infect other family members.

That was a big issue in early stage from Wuhan and that's why so many people were infected, because they got it from their family.

We opened a temporary hospital because we had not enough space to put those patients on quarantine, besides of the fact that I am not sure they would follow or obey the physicians' commands.

So, no treatment for the mild and asymptomatic patients, just stay at home, hotel or the temporary hospital.

 **Q (Moderator): Controversial question from the audience about the treatment. There is a new publication in NEJM about potential treatment with lopinavir and ritonavir. What is your experience with that? Do you think this is something that may work?**

A (Prof. Peng): Regarding the treatment, there's still not enough evidence to show which kind of medication would work against the COVID-19. I know the paper was just published yesterday for the lopinavir and ritonavir, and it didn't show enough evidence of benefit from RCT. Also, we need to be careful with lopinavir and ritonavir because it may easily induce cardiac injury and bradycardia.

A (Prof. Rello): My personal opinion is that we need to differentiate patients that show "influenza-like" illness, patients who develop pneumonia, and patients who develop ARDS, and we need to be very careful to avoid adverse events by doing things that are not based in solid evidence. Also, for instance, these drugs have plenty of interactions with drugs that we use in the ICU.

I fully understand that physicians want to try but we need to be vigilant to avoid adverse events and pharmacological interactions that make the patient's management more difficult and even can put healthcare workers in risk.

In line with other experts in Italy and the US, I believe that these patients should be left quiet: SARS is not influenza, and SARS is not ARDS! We need to avoid “doing too much” at any cost as it is of higher benefit than “only doing nothing”. This is just my personal opinion; do you support it after your experience in Italy?

A (Dr. Storti): First of all, I think that it is important to exactly define what is the lung involvement and I think that CT scan does the job as it is the gold standard. But also, lung ultrasounds are very useful, especially if you compare it with a chest X-ray instead of a CT scan. Ultrasounds can be useful in terms of looking at how the lungs are moving, how the lungs are interacting with the ventilator and how the lungs are changing with different PEEPs and ventilators’ set up.

Regarding the therapy, I personally have no figures as we are generating them now. We managed to be involved in in a trial which seems to be very promising, but by now we have only a few cases so, statistically, they don't mean anything.

I was asked to manage 45 patients, to date the largest population that might be tested in Italy, but I still didn't receive the drug, so my study is not feasible at the moment. Anyway, I think that to have clear figures about treatment and drug effectivity, it is too early as there isn't strong evidence about what drug/-s we should choose?

A (Dr. Lamas): Regarding the PCR test to diagnose COVID-19, we are having many false negatives even when we see some patients presenting the typical symptoms and are highly suspicious because of the CT scan images, their lymphopenia pattern and other evidences.

We had one patient that tested positive only on the 3rd PCR test when all the evidence was clear, and this is very stressful as we don't know if we can decrease the level of protection if this patient is on an ICU. Therefore, my first question is how many PCRs on the same patient are you performing to make sure about the correct result?

And the second question is if there is any useful blood test based in Immunoglobulin M and Immunoglobulin G as we see many companies offering them, but I am not any confident that using these tests is going to help us to manage these patients.

A (Prof. Rello): Regarding the PCR tests, I think that we need to adopt the same approach that we followed with influenza as this is a virus that has a special affinity for lower respiratory tract. For example, if you have a pregnant patient with a consistent presentation of influenza pneumonia and the nasal swab is negative, you will not change the approach and treat her for influenza pneumonia.

COVID-19 shows a very characteristic presentation with high C reactive protein, low PCT, lymphocytopenia and, in severe cases, intubation and mechanical ventilation. When you take a nasal or throat swab from this patient and the result is negative, that may happen because the viral burden is low, because there may be a problem with the test, or a problem when transferring the sample to the lab... and this is why I believe that we have to follow the same approach we adopt for influenza management and continue with the same management.

Also, and despite inconsistent test results, I wouldn't recommend to perform bronchoalveolar lavage (BAL) as we have to give priority to the healthcare workers safety.

A (Prof. Peng): I totally agree with you. The PCR sensitivity is only 40% to 50%, which is not good enough, anyhow you can try consecutive times.

On the other hand, just imagine that you could detect the antibodies in a blood test. That would be the best way to help you detect whether the patient is infected or not. If the patient's antibody levels are high then, definitely the patient is positive in the COVID-19, therefore you can combine these two tests.

If your patient shows the typical symptoms, the typical chest CT scan and also the elective flu tests, then we set the clinical diagnosis to COVID-19, even without the positive virus PCR test.

A (Prof. Zhong): I agree with Professor Peng and maybe the antibody test may help to diagnose these patients.

If we have a patient that was negative for PCR test, but positive for the antibody test as well as for the IgM and IgG, it gets very difficult to explain why the PCR is negative. Maybe its sensitivity is not enough for a relative low amount of virus? So, we must be very cautious with these negative results as we don't know whether these patients, upon hospital discharge, will spread the infection. Maybe the antibodies test would help.

A (Dr. Storti): We experienced that here, in the north of Italy, some hospitals ended up fully collapsed just because they were waiting for swab determination kits, which are showing a very poor sensitivity, especially with the "negative" results as they don't mean anything. I can support this idea because some of my physicians presented fever, coughing and the typical symptoms, and after two negative PCR tests and 10 hours, they got a highly "susceptible" positive CT scan.

It is an issue to adopt this as the determination test in Italy as there could be several problems when obtaining the sample, as for example, those associated to the operator management and sample manipulation. Also, in our ICU community in Italy, to confirm a negative test, we rely on sample aspiration from the lower respiratory track rather than just the nasal and throat swabs.

Also, following our Chinese colleagues' advice, we will start tomorrow the IgG and IgM determination in combination with the other tests. Anyhow, my opinion is not to combine but select a different system, but unfortunately, this is not easy because what our government and health care system are requesting is not to use IgG and IgM determinations to confirm tests.


A (Dr. Lamas): By combining IgM and IgG determinations, perhaps we can increase diagnosis' sensitivity together with CT scan and lymphopenia and then the picture would make more sense for us. It is quite difficult to manage low resources when trying to separate COVID-negative from COVID-positive patients to manage them, and that's why, as a doctor, I don't feel very confident about negative tests as we always keep some suspicion of having false negative results.

A (Moderator): It is great that we had discussed quite a lot about healthcare professionals' safety and protection during this meeting and, in line with that we have another question from the audience: are there already any available figures of COVID-19 mortality within the healthcare professionals?

A (Dr. Storti): I think that the mortality in Italy now is pretty high, but I'm not sure that an accurate calculation would be feasible now, as I do not fully rely on the swab tests and I am sure that we are

underestimating the positive population, therefore the mortality is difficult to be calculated.

Here, I heard that at least two healthcare professionals died: one was in the pre-hospital emergency services and the other one was a hospital nurse, but luckily, the number among professionals is very small.

 **Q (Moderator): I forward this question now to our Chinese participants, what is your experience regarding to mortality within the healthcare professionals?**

A (Prof. Peng): Currently we really don't know the mortality figures among medical professionals. I just know that some physicians and nurses died during this outbreak, but I don't know the official number. Also, I am not aware of the total number of healthcare professional infected.

A (Prof. Zhong): Neither am I aware of these figures. I think there should be some publications about the results and maybe we can see the mortality in these papers, but I am not sure.

In different kinds of population groups, they present different mortality rates. As said before and in my experience in the ICU, when the more ill patients progressed to a very severe situation, the mortality rate on this group is very high, even higher than ARDS patients from other cause.

Also, we know that the asymptomatic, mild and moderate populations are the larger proportion of the COVID-19 patients. Within this population I have treated colleagues and the outcomes were good.

A (Prof. Rello): Mortality figures typically show up 18 days after illness onset. So, in Europe we cannot still estimate that, at least from Spain we cannot provide any reliable information.



The webinar is initiated and organized by Mindray in the interest of the healthcare community to combat COVID-19. Thanks to the contribution of all the panelists who join in the discussion voluntarily with no conflict of interest.