

The Royal Society of Medicine

Sharing the international lessons of COVID-19



Royal Society of Medicine
27 July 2020

Foreword

The Kantor Charitable Foundation was delighted to support the Royal Society of Medicine's landmark event on sharing the international lessons of COVID-19.

We do not need reminding of the shocking impact of COVID-19 on health and healthcare globally, and yet clinicians everywhere, day after day, continue to put themselves and their families in harm's way. The dedication and commitment of health professionals to selflessly improve the lives of others is truly humbling.

Our world is like a bus with two wheels hanging off an abyss. All eight billion of us, including the major global players, are inside the cabin. Whether we fall into the abyss or stand on all four wheels and move to our future together depends on how well we coordinate and collaborate.

But the world is torn apart by contradictions, from nuclear arms to the economy. COVID-19 has sharply aggravated an already critical situation in the rise of extremism and the manifestation of multidirectional racism.

Combatting this pandemic has become an existential fight for our future. The world can progress much faster by collaboration, when national interests are set aside and commercial concerns are shelved for the greater good.

And that is the spirit in which this conference was convened. We drew together an international faculty of leading clinicians to distil the evidence and consider the lessons learned from the respiratory, cardiovascular, and neurological responses to COVID-19. We also considered the challenge of developing a new vaccine.

We were fortunate to be able to involve leading experts from North America, Europe, Asia and Africa, and a large number of participants from every corner of the world joined the RSM webinar on 27th July.

Our shared ambition was to learn the lessons of COVID-19 in order to minimise the impact of future waves and surges of the disease, and plan more effectively for other pandemics.

History has shown us that a pandemic and the chaos it creates can cause lasting damage, not just in terms of a global economic shock, mass unemployment or widespread uncertainty. It can also create fertile soil for the politics of despair and division. The last great pandemic, the Spanish Flu, was quickly followed by the Great Depression and a rise in extremism which seized power in Europe. The divisions that were created led to the tragedy of the Second World War.

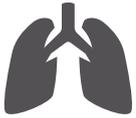
These lessons from the past require us to set aside our own agendas in the collaborative pursuit of lasting solutions. In this respect, the global medical and scientific community is leading the way. Now, as in the past, incredible feats can be achieved against seemingly impossible timelines but only when we are driven by a powerful and shared goal.

Despite all that has happened in the last six months, I remain optimistic. That optimism is grounded in the knowledge that we do indeed have a powerful and shared goal, to create a more equal and healthier world, and we are committed and dedicated to achieving it.

Dr Moshe Kantor
President, Kantor Charitable Foundation

Sharing the international lessons of COVID-19

This international COVID-19 conference took place on Monday 27 July 2020. We brought together thought leaders from around the world to share the key clinical lessons about COVID-19. We focused on four clinical themes:



**Respiratory effects:
critical care and
ventilation**



**Cardiovascular
complications and the
role of thrombosis**



**Impacts on the
brain and the
nervous system**

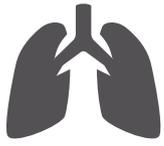


**Looking forward:
research, vaccines and
future management**



“The conference provided a unique platform for healthcare leaders across the world to come together and share their learning and understanding about Covid-19. The evidence presented by our expert faculty clearly demonstrated that international co-operation and interdisciplinary learning have already helped to significantly advance the care and treatment offered to patients. This spirit of collaboration must surely continue as the world prepares to manage future waves of the pandemic.”

Professor Roger Kirby
President, Royal Society of Medicine



Respiratory effects: critical care and ventilation

Respiratory disease is a prominent feature of COVID-19 and it remains a major management challenge for clinicians internationally. In February 2020, Dr Charles Powell from Mount Sinai in New York set up teleconferences with colleagues in Wuhan to understand the disease better as COVID-19 arrived in the USA. His immediate impressions were that proper use of protective equipment prevents infections in healthcare workers, and patients who had progressive respiratory failure seemed to respond to steroids.

Next, COVID-19 pneumonia has some unique aspects, specifically the nature of the adult respiratory distress syndrome (ARDS). Although patients universally have severe hypoxemia, COVID-19 has distinctive effects on lung compliance and microvascular regulation of blood flow with evidence of thrombosis. The roles of anticoagulation and non-invasive respiratory support are important considerations. Early tracheostomy can help mobilise patients quickly to improve rehabilitation and free up beds.

As the first surge began to subside it became clear that persistent lung injury and respiratory failure can follow recovery from the acute phase of COVID-19. The nature of lung injury after COVID-19, whether it is progressive or reversible for example, needs to be better understood to help people recover more quickly.

Modelling had predicted that the number of cases requiring hospitalisation would exceed capacity in New York, but Powell believes that planning measures to increase hospital bed capacity, staffing, and equipment, and enforcement of social distancing, helped the city cope with the demands COVID-19 placed on the health services.

Being situated in the middle of the USA bought some time for Dr Richard Oeckler and his colleagues at the Mayo Clinic in Minnesota. One of the biggest issues they struggled with was the definition of aerosol generating procedures and how to protect staff. They had some experience from Ebola and MERS epidemics, and opted for minimum personal protective equipment and precautions for airborne transmission. PPE spotters or champions made sure that everyone was following protocols.

Despite covering a predominantly white population, they noticed that 30-40% of patients were from ethnic minorities suggesting the unequal impact of social determinants of health. Another concern was the risk of isolation and moral injury for patients, families, and staff. Their response was to ramp up video conferencing and, unlike others, they allowed visitors for people at the end of life.

London experienced similar planning and resourcing challenges. In addition, Professor Anita Simonds from the Royal Brompton Hospital believes that the demands on the service were reduced by people with pre-existing conditions shielding at home.

The early front lines of COVID-19, such as Italy, may have faced the greatest challenge when least was known about the disease. Dr Eva Polverino, from Vall D'Hebron Hospital Barcelona, remembers the fear as news emerged of Italy's difficulties: "It was something really scary. People trying to invent new ventilators, trying to get protected. People dying everywhere, no beds. The first shock was really, really tremendous. Italian colleagues were desperate to receive five hundred ventilators. After about 10 days, we were looking for ventilators here in Spain."

The clinical lessons of respiratory illness are complex

International collaboration is an essential part of the response to COVID-19, thinks Powell. And then there is the experience of revisiting the sense of urgency clinicians feel as the surge subsides in their area but hits another place. The lessons learned in one region can be shared with colleagues in another.

The clinical lessons of respiratory illness are complex. Many hospital patients have severe hypoxemic respiratory failure, although the nature of ARDS is hotly debated. The lung disease may be of two varieties or a spectrum of the same illness. The virus affects ACE-2 receptors and increases angiotensin 2 levels, giving rise to some of the clinical features such as pulmonary vasoconstriction, pro-coagulation, and cytokine storm.



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**Dr Eva Polverino,
Vall D'Hebron Hospital Barcelona**

But the level of hypoxia seems out of proportion with the impact on the lungs, which poses a management challenge. Oeckler's approach is to view respiratory failure as a standard ARDS despite some unique features in pathophysiology.

Early on, the predominant thinking was that patients who had respiratory failure associated with COVID-19 should immediately move to invasive mechanical ventilation. But subsequent experience from multiple sites suggested a role for waiting when appropriate and using non-invasive strategies. The rationale of non-invasive strategies is to reduce the need for intubation, offload critical care units and step down patients early from critical care.

There is insufficient evidence on which non-invasive technique is best for which person, whether it is C-PAP or high flow nasal oxygen. Ongoing clinical trials will help answer this question, but there seems to be a role for reducing the need for intubation. A major lesson from the first wave of COVID-19 is that proper preparation for the next surge of COVID-19 is to ensure that adequate supplies of non-invasive ventilation equipment are available to avoid intubation and mechanical ventilation.

Powell identifies the importance of social distancing measures and handwashing, of appreciating the complexity of clinical features and presentations of COVID-19, of recognising the long-term health impacts, and of the spirit of international collaboration that is required for an effective response to this pandemic.

"There are certain aspects of coronavirus that are quite complex," he says. "The protean manifestations and the severity of manifestations is quite variable. And we don't understand why certain individuals have an asymptomatic course and some individuals develop fulminant respiratory and multi-system organ failure. Yes, there are some clues about differences in socioeconomic backgrounds, in genetics, perhaps, and in terms of obesity, but we don't understand fully the primary reasons associated with differences in outcomes."



Cardiovascular complications and the role of thrombosis

A number of clinical questions about cardiovascular disease and COVID-19 need to be addressed, says Lord Ajay Kakkar. What is the significance of pre-existing cardiovascular and metabolic comorbidity in terms of COVID-19 outcomes? What do we understand about the problem of intravascular thrombosis? How might we prevent, in the future, the health system from becoming principally a pandemic treatment system? And what are the short, medium and long term consequences of COVID-19 on cardiovascular health?

Interestingly, once adjusted for variables, the increased risk in people with cardiovascular disease is much less than the risk associated with obesity, social deprivation, or male sex. But perhaps the bigger issue in relation to cardiovascular disease, explains Professor Barbara Casadei, is the indirect effect of COVID-19; how hospital admission for people with myocardial infarction has dropped by 20% to 60% depending on the type of myocardial infarction and the population. Any deaths will not be captured in the COVID-19 death statistics but they will be among the total excess deaths that have increased all around the world.

Death rates in India per head of population are low but that may be because only 10% of the population is over 60. Nonetheless, the burden of cardiovascular disease and obesity is high in people in their middle years, and a third of deaths are in those aged 45 years to 69 years. Noncommunicable diseases are an important risk factor.

“We do know that the middle-aged group have a high burden of cardiovascular disease risk factors, as well as cardiovascular disease and diabetes,” explains Professor Srinath Reddy from the Public Health Foundation of India. “If you look at the statistics before COVID the mean age of onset of myocardial infarction in Indians was about 52 years, whereas it’s about 62 years in Europe. There’s a very high prevalence of diabetes, hypertension, and cardiovascular disease in the 35 year plus age group. So it’s not surprising, therefore, that the COVID deaths are also associated considerably with comorbidities, especially cardiovascular and diabetes in younger than expected population.”

India has seen an impact on elective cardiac procedures but lacks data on out of hospital deaths. In the meantime, the Supreme Court has passed legislation to allow wider availability of telemedicine.

Reddy is intrigued that this may mean that people with cardiovascular disease are more likely to benefit from clinical oversight. The impact of this legislation will stay with India’s health system which has sought ways to deliver services to rural and remote populations, as well as overpopulated urban districts.

The hypercoagulable state is one of the more perplexing conundrums of COVID-19

Professor Samuel Goldhaber, from Harvard Medical School, explains that the inflammatory response to ARDS causes both endothelial dysfunction and superinfection. The subsequent pro-inflammatory state leads to myocardial infarction, stroke, pulmonary embolism, and deep venous thrombosis. The hypercoagulable state is one of the more perplexing conundrums of COVID-19. Autopsies show small pulmonary thrombi and these may arise inside the lungs rather than embolising from deep veins.

Standard doses of prophylaxis are not preventing deep venous thrombosis, for example, and it is clear that there is much that we do not understand about COVID-19 and thrombosis. Addressing this challenge is an opportunity for the health community to work together locally and internationally. Many clinical trials are in progress now, and health professionals can encourage patients to join these trials to get better data on anticoagulation regimes and particularly the intensity of anticoagulation.

“I think the real take home messages of the experience with regard to cardiovascular disease and COVID-19 is this: that cardiovascular comorbidities matter and should be recognized early,” concludes Kakkar. “And as we come to terms with having to live with a virus endemic in the human population now, we should be clear that targeting better cardiovascular health is an important general measure.”

The other key areas are determining whether anticoagulant therapy can impact on the natural history of COVID-19, and constructing well designed follow up studies to understand the long term effects of COVID-19 on the cardiovascular system - all of which requires international learning and collaboration.



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Lord Kakkar



Impacts on the brain and the nervous system

The neurological and mental health effects of COVID-19 may provide the greatest challenges to society. The delays and deferrals in care of patients with acute neurological conditions is a global phenomenon. The Cleveland Clinic saw a 30% drop in acute imaging and clinical presentations during the early pandemic, says Dr Andrew Russman: “I have had countless circumstances now with patients who have called my office talking about new stroke symptoms that they’re having and refusing to go to the emergency department, refusing to present to the hospital. And I think the harm that’s being done through this is really something that the individual patient can’t estimate.”

Technology is critically important but for those who do not have access to the technology, they have been able to offer care safely in the office environment. Every patient, every visitor, every caregiver coming into hospital is screened, and every patient going into the hospital is tested for COVID-19.

In terms of neurology, thrombophilias associated with viral illness have increased. And given the complications with anticoagulation, care of patients with ischaemic strokes is made complex by the risk of intracerebral bleeding. Patients have presented with acute carotid or other vascular occlusions. As with other infectious diseases that cause systemic inflammation, COVID-19 is responsible for plaque disruption and endothelial dysfunction that leads to thromboembolism.

The epidemics of SARS and MERS hinted at the neurological effects of COVID-19, says Dr Hadi Manji, but the numbers were small. The first data from Wuhan suggested that 36% of patients had neurological symptoms, namely headache, dizziness, facial pain, and muscle pain. But it wasn’t clear whether these were effects of the virus on the nervous system, or whether these were the complications of hypoxia, a systemic illness and viraemia, or metabolic complications

Research from the National Hospital for Neurology in the UK shows no real correlation between the severity of COVID-19 respiratory illness and neurological presentations. Indeed, some patients present with a neurological problem first and then subsequently develop COVID-19 lung problems. Early diagnosis will have a better outcome, and COVID-19 is now a differential diagnosis for a wide range of neurological conditions.

Professor Emily Holmes emphasises the importance of taking mental health seriously in our response to the COVID-19 pandemic. A central point is that COVID-19 exacerbates mental health inequalities. Vulnerable groups are seeing a rise in mental health illness

internationally. Children may be isolated and at increased risk when kept away from school; isolating elderly people has consequences; and ethnic minorities are being affected disproportionately. There are other vulnerable groups that require attention, such as people recovering from intensive care and frontline health professionals.

That creates two issues, not only for an individual’s mental health, for example post traumatic stress, but also in their functioning. Delivering the kind of care that addresses both will mean society stands to benefit in the years to come. Hence, vulnerable people are a very important group to understand better and to find solutions for.

There is no health without mental health

Mental health illness is treatable but the scandal is that most people around the globe don’t receive adequate care. The pandemic is an opportunity to focus on and close this treatment gap, but we also need to look after mental health at a more social level. This is the first pandemic with 24/7 media reporting, and studies from the USA show that overconsumption of stressful content in media leads to mental health illness. Effective health messaging and understanding the psychological impacts are ways to fast track behaviour change in a pandemic to break the cycle of transmission, and get people acting on social distancing and healthy behaviours.

There is no health without mental health. The challenge ahead is to think about creative, innovative, interdisciplinary, multidisciplinary, ways of intervening and working on a more global scale.

Professor Sir Simon Wessely notes that although the Spanish Flu pandemic started to disappear in 1920, it “left behind a huge trail of neuropsychiatric complications” such as encephalitis lethargica which was linked to movement disorders and psychiatric disorders that stayed around for a generation. Society is facing an uphill struggle of rehabilitation for both the frail and also not so frail, and younger people are developing post-infectious fatigue syndromes again that will develop into major issues and provide therapeutic challenges.

“We have to stay together in this, use a broader definition of health, and remember that health is a much bigger concept than just the sum of our systems,” says Wessely. “The looming economic disaster may end up doing even more damage to our mental health and our physical health than the original virus itself. We have a choice: do we work together or do we work separately? And this is not just as disciplines, but as nations.”



“I have had countless circumstances now with patients who have called my office talking about new stroke symptoms that they’re having and refusing to go to the emergency department, refusing to present to the hospital”

Dr Andrew Russman, The Cleveland Clinic



Looking forward: research, vaccines and future management strategies

Making a comparison with the HIV epidemic, Dr Andrew Badley argues that while it took several years to get useful HIV therapies, the same stage was reached with COVID-19 in a few months. Clinical trial data are available on existing treatments with the prospect of future therapies such as IL6 receptor antagonists and recombinant antibodies.

Clinicians are beginning to get a sense of which drugs are active but need to now understand at which stage of disease to use them. More information is required on therapies for people with mild to moderate disease, those who are already in intensive care, and the effects of combination therapies. Not all patients respond in the same way to the same therapy, and that's probably based upon where they are in the stage of the disease.

In Uganda, the development of COVID-19 was slow because lockdown was implemented early. "We benefited from the challenges of other countries," says Dr Monica Musenero. "We got all the knowledge. So most of our cases have been identified when they are mild." African countries took COVID-19 seriously, because they were expected to experience a devastating impact on weak health systems. Hence the approach was largely preventive and focused on public health measures.

Uganda has still embarked on vaccine research by trying to partner with people in a diverse range of countries because of the uncertainty about when an effective vaccine will reach there. With a small number of cases in some parts of Africa and limited involvement in research, the major impact of COVID-19 is economic.

According to Professor Robin Shattock, within six months of the pandemic starting 24 vaccines were in clinical evaluation with another 160 behind them in the pipeline. Developing a vaccine that prevents transmission is the ultimate goal but the first one may be a vaccine that prevents severe disease. The next challenge is for some of these vaccines to come through towards the end of this year and the beginning of 2021.

Another major issue is access, because rich countries are hedging their bets by trying to advance purchase as many different candidate vaccines as they can. In the short term, that means it is going to be tough for low and middle income countries to access vaccines.

The other challenge is the sheer volume of vaccine doses required and their delivery. If the ambition is to vaccinate the entire UK

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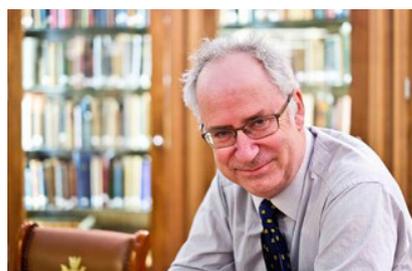
**Dr Monica Musenero,
Ministry of Health, Uganda**

population in the first half of 2021, for example, vaccination on that scale has never been done. Thinking globally, what is the realistic strategy for vaccinating 7-8 billion people? Currently, the largest number of vaccines that have been made in a year is half a billion doses of polio vaccine.

Whilst acknowledging the potential of vaccines and other advances, Professor Sian Griffiths stresses the simple messages about washing hands, wearing face masks, and physical distancing. It is the social and health inequalities that are making this disease much worse.

Also, this isn't just about preventing infectious diseases. Populations must be more robust with lower baseline risk from less diabetes, less heart disease, and more support for vulnerable communities. Politicians must think hard about the strategies they adopt. They need to prioritise prevention and keep populations healthy to help with future pandemics. The solutions lie in better basic public health and collaboration, such as making vaccines available to the world instead of allowing richer countries to buy them up.

In closing, Professor Simon Wessely remembered the words of Benjamin Franklin, one of the greatest politicians and scientists. Franklin once reminded his colleagues that "we had better hang together, or we will hang separately." The world needs to hang together now, warns Wessely, because the alternative is far worse.



"The world needs to hang together now, because the alternative is far worse"

**Professor Sir Simon Wessely,
Royal Society of Medicine**

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Panellists

Respiratory

Dr Charles Powell, Mount Sinai Hospital, New York
Professor Anita Simonds, Royal Brompton Hospital, London
Dr Richard Oeckler, Mayo Clinic, Minnesota
Dr Eva Polverino, Vall d'Hebron Hospital, Barcelona

Cardiovascular

Rt Hon Professor the Lord Ajay Kakkar, University College, London
Professor Barbara Casadei, University of Oxford
Professor K Srinath Reddy, Public Health Foundation of India
Professor Samuel Goldhaber, Harvard Medical School

Brain and nervous system

Professor Sir Simon Wessely, Royal Society of Medicine, London
Dr Hadi Manji, National Hospital for Neurology, London
Dr Andrew Russman, Comprehensive Stroke Center, Cleveland Clinic
Professor Emily Holmes, Uppsala University

Research, vaccines, and the future

Professor Roger Kirby, Royal Society of Medicine, London
Dr Andrew Badley, Mayo Clinic, Rochester
Professor Sian Griffiths, Imperial College, London
Professor Robin Shattock, Imperial College, London
Dr Monica Musenero, Ministry of Health, Uganda