Prepare small, think big in crisis management

Building resilience for the next pandemic will be addressed today by Lennie Derde, a consultant intensivist at the University Medical Centre Utrecht, the Netherlands. Dividing her time between clinical work and research into severe infections and sepsis in the critically ill, Dr. Derde is the current chair of the International Trial Steering Committee of REMAP-CAP, an adaptive platform trial investigating the best treatment for pneumonia, including COVID-19. Understanding how to deal with surges in patients is informed by her roles during the pandemic, as well as much of the thinking around resilience.

"I think resilience is more than dealing with surges," Dr. Derde explained. "Rather than preparing ourselves for one big crisis that may never happen – with a piece of paper that ends up in a drawer for 30 years and is then unusable – we should prepare ourselves for smaller crises." Preparing for surges (on which there is plenty of helpful literature) is then vital. She points to a particular series in the journal Chest, which was of great use during the pandemic.1

“You have to talk about triage now, because if you have to do it, you want to know you have discussed it at length, and not made a decision quickly or lightly without the proper ethical considerations.”

LENNIE DERDE

Continued on page 2

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Resilience is almost like determining preferable over triage. Safely (i.e., with monitoring), that is to the ward, or keep them at home preferable than others, but if you for example. Dr. Derde added that considered – reducing patients, other strategies may have to be standby territorial army. In reality, there’s a crisis, rather like a bring specialist staff in whenever intelligently managing scarcity, “If you don’t have people, you don’t have ICU beds.” Resilience then becomes about something like seasonal flu. It is certainly a trigger for surges, and therefore a kind of training ground for pandemic preparedness. “If you can manage the yearly surge in patients from a seasonal influenza outbreak, that’s positive,” said Dr. Derde. “If it then turns into a pandemic, it becomes easier to manage because your systems are in order.”

Resilience is increasingly difficult, of course, especially with an ongoing scarcity of personnel in ICUs that looks to stretch well into the future. “We are short of nurses,” she said. “If you don’t have people, you don’t have ICU beds.”

Resilience then becomes about intelligently managing scarcity, something which affects the school of thinking that a hospital can bring specialist staff in whenever there’s a crisis, rather like a standby territorial army. In reality, other strategies may have to be considered – reducing patients, for example. Dr. Derde added that there are options which are more preferable than others, but if you can safely discharge people sooner to the ward, or keep them at home safely (i.e., with monitoring), that is preferable over triage.

In other words, building resilience is almost like determining which knobs can be turned in the great ICU machine to manage a surge of patients. “And the resilience part is when you plan for that in advance, and practice so that you get better at it,” continued Dr. Derde.

One of the positive examples that tested the theory of reducing patient admissions during the pandemic was ensuring people could be at home on oxygen, with wearable monitors, noted Dr. Derde: “I think we poached ICU-style interventions from the ward, like OptiFLOW nasal high flow oxygen for example.”

Triaging in and of itself, however, can be very challenging, she admitted. Without it, bad care is given to everybody. But with it, there are moral decisions. It’s a tough decision to say who will not be admitted anymore. “There comes a certain point where the interest of society subsumes the interest of the individual,” said Dr. Derde.

Such decisions have an impact on staff, as well as patients. “The last thing any ICU nurse or doctor wants to do is to have to triage,” she said. “To say, you are not getting a bed, not because we don’t think we can help you, but because other people have more right to these beds is really, really, stressful. It promotes moral injury to people.”

Of course, there are different triaging strategies and different cultural answers. The answer in Israel may not be the same as the answer in the Netherlands, for example. “Luckily, we didn’t have to turn that knob, but we got really, really close,” said Dr. Derde.

That’s why it is critical to organize an ICU in advance. “We have the opportunity to talk about it in ‘peacetime’ so that it is less frustrating if crises really do happen,” said Dr. Derde. “So that’s also resilience. You have to talk about triage now, because if you have to do it, you want to know you have discussed it at length, and not made a decision quickly less frustrating if crises really do happen, “ said Dr. Derde. “So that’s also resilience. You have to talk about triage now, because if you have to do it, you want to know you have discussed it at length, and not made a decision quickly.”

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Crises are 80% the same. It doesn’t really matter whether you have a nuclear incident or a pandemic, at least not in the first couple of weeks. It’s a surge of patients, there’s all kinds of chaos, and you have to manage that.”

LENNIE DERDE
A fascinating new trial looking at applying an old drug to induce disease tolerance to infection was discussed on Wednesday by Sebastian Weis, Professor of the Jena University Hospital, Friedrich Schiller-University, and group leader at the Leibniz Institute for Natural Product Research and Infection Biology – the Hans Knöll Institute, Jena, Germany.

Professor Weis researches the molecular pathogenesis of severe systemic infections, including sepsis. As a post-doctoral fellow, he studied the genes that controlled iron metabolism during bacterial sepsis. Working with Miguel Soares (Instituto Gulbenkian de Ciência, Oeiras, Portugal) – one of the pioneers in the field of disease tolerance, he discovered the role of an appropriate metabolic adaptation in sepsis. "I used a knockout mouse strain that lacked the heavy chain of ferritin and found that they all succumb to bacterial infection," said Professor Weis.

He embarked on a seemingly fruitless search to find out why and to try stop these animals from dying. "Nothing worked, but that probably just meant we had actually found something exciting." In effect, they had discovered that mice exhibited a metabolic collapse that was controlled by ferritin, ergo identifying a mechanism of disease severity that was independent of the numbers of bacteria in the infected animal. He explained: "This is disease tolerance to infection."

"Disease tolerance is a defense strategy that lessens disease severity after infection."

SEBASTIAN WEIS

"We used to think about infectious disease as only about inflammation, the immune system, the microorganisms, and antibiotics ... people in intensive care units still die of organ failure even if there is sufficient antibiotic treatment and no extreme immune phenotypes."

SEBASTIAN WEIS

Professor Weis talked about ferritin’s effect on glucose metabolism during infection, and the effects of not having it: "If you delete this gene in the liver, then the mice cannot produce glucose anymore, and they die of hypoglycemia."

It’s a different view of infectious disease pathophysiology. "We used to think about infectious disease as only about inflammation, the immune system, the microorganisms, and antibiotics ... people in intensive care ..."
units still die of organ failure even if there is sufficient antibiotic treatment and no extreme immune phenotypes."

It turns out there are drugs already on the market which seems to target the same defense mechanism, epirubicin, a cancer drug that was coincidentally being researched by Dr. Luis Moita (now also at the Gulbenkian Institute). "With this, we have a drug that has been licensed for 30 years showing potential in a completely different indication, at a different dosage," he said.

Together with Professor Michael Bauer from the Department of Anesthesiology and Intensive Care Medicine at the Jena University Hospital they decided that testing to repurpose this drug in sepsis patients might be an option to prevent or decrease organ dysfunction in sepsis.

Professor Weis described his ongoing Phase II trial in Germany where low doses of epirubicin are given to sepsis patients. "This is new and exciting because now we have drugs that can target these kinds of mechanisms, no matter the pathogen," said Professor Weis. "It could be a multi drug-resistant bacteria. But if your organs don't fail, you don't die from the infection."

Should the drug reach Phase III trials and beyond, Professor Weis believes it could be ground-breaking. "We are dreaming just as researchers always do," he said. "If it works, it means we could give it to people very early after infection, even without pathogen or source identification preventing the deterioration from a mild infection, to life-threatening sepsis."

For patients in countries without ready access diagnostic departments, this might be a particular boon. "You could assume that even in resource-limited countries, this approach could still protect patients, to a certain degree, from a severe outcome," said Professor Weis.

There are many other benefits, which Professor Weis will outline. But what's important is that disease tolerance provides an alternative view of treating severe disease. Physician clinicians, he said, get excited since this might be a direct targeting of organ failure."

In other words, disease tolerance mechanisms as factors are often ignored in severe disease, but should be tested further. "Disease tolerance is a defense strategy that lessens disease severity after infection. If we can incorporate this concept into our perspective of how we understand and treat severe infections, we might be able to expand the horizon for future therapeutics in intensive care," concluded Professor Weis.

References
Conflict prevention for everyone

A fascinating discussion on conflict prevention will be given on Friday afternoon by Lewis J. Kaplan of the Perelman School of Medicine, University of Pennsylvania, and section chief, Surgical Critical Care at the Corporal Michael J. Crescenz VA Medical Center (Philadelphia, USA). He is also a past president of the Society of Critical Care Medicine. “There’s always some degree of conflict when people are critically ill,” Professor Kaplan told ISICEM News. “So regardless of whatever complex care environment you’re in, there’s always some tension.”

He characterizes the kinds of conflict as those between the care team and the patient or the patient’s family. “But you also see it within families,” he said. It can happen between different medical teams too. “It happens even when they are supposed to be collaborating – there are always individual goals and interests,” he said. “And understanding those drivers helps you navigate that conflict.”

In the hospital environment, Professor Kaplan finds that much of the conflict centers around end-of-life decisions, or whether to or not to provide a particular kind of invasive therapy, especially those regarded as extreme.

People often have a very different expectation for how care should have unfolded. “They may not embrace it, they may not even want to hear it, or they may have a different reason for not wanting to hear it,” he explained.

“If you work in tertiary or coronary care, patients with difficult problems come with optimism bias too,” he added. “They think, ‘They will fix me and make this okay’. However, this is not always possible.”

Understanding those drivers, prior healthcare experience, access to care, healthcare literacy, and how they view a particular kind of physician or a particular hospital helps, said Professor Kaplan. “You need to recognize when there’s the potential for conflict before it arises,” he said.

Communication, or lack of it, is a driver of conflict. Physicians in particular, said Professor Kaplan, often use language that is laden with medical terms. “Sometimes people forget to translate it into understandable language,” he said. “And therefore, if you don’t do that, people don’t really know what the daily plan is, and what they can expect from it.”

That’s why since 1997 Professor Kaplan has put families on rounds. “They feel as if they are part of the team,” he said. “The pediatric ICU does this routinely. Adult ICUs are doing this much more commonly. But it wasn’t always something that was routinely done, and it does a lot to prevent conflict.”

The origins of this approach are a Yale bioethics program focusing on conflict mediation. “Those skills are deployable every day in the ICU, in clinic, and in every last committee that I’ve either served on or led, because there’s always some piece of this that is applicable,” he said. “I’ve used this on a routine basis. It’s changed the language that I use. It’s changed how I approach patients.”

“Everyone can benefit from this kind of education and training. And it’s not a physician-limited process.” In Professor Kaplan’s ICU at the VA, all the staff receive training. “We’ve taught the nurses, the food delivery people, the pharmacists, the people that manage the trash, the radiology technicians,” he said. “Everyone gets taught these things because everyone interfaces with the patient, the family and visitors.”

Conflict prevention teaching for fellows and residents is part of a yearly lecture series, and then reinforcement takes place in a ‘huddle’ in the ICU around change of shift. “Every third month I’ll show up at a different huddle and we’ll review a different aspect of it,” noted Professor Kaplan. “We may talk about a family that had a particularly difficult time, and a family that had a particularly good time. There is constant reinforcement.”

Previously, all end-of-life discussions occurred in the conference room, which was a glass room with a closed door. “It became known colloquially as the fishbowl, and everyone knew what kind of meeting was occurring,” recalled Professor Kaplan. Now, however, end-of-life discussions take place on rounds. “This is just as important as kidney function or your ventilator settings,” said Professor Kaplan. “Then the entire team gets to hear what words get used, what the cadence is like, the specific phraseology, how the family received that information, what they shared with us, and how vulnerable the person leading that discussion allowed themselves to be.”

There has been some pushback to having a family discussion on rounds, he acknowledged. “You can’t be buried behind the computer.
Continued from page 5 screen, just talking to the team; you have to engage with the family,” he said. “So therefore, rounds often take a little bit longer. But the trade off is you don’t have those afternoon meetings. You write your notes in the afternoon.”

Professor Kaplan recommends delegates interested in conflict prevention invite a specialist to their facilities, and send members of the team to learn how to do it. They will be able to return and teach everyone else. “This is regular information transfer. It needs to permeate into everything that you do,” said Professor Kaplan. “And then you have to practice. It doesn’t matter whether you use medical actors, people from other departments, or even record a simulated discussion to hear yourself. You have to understand how you are received, how you’re presenting yourself, and how you can make that better. Some of this will be uncomfortable when you do it.”

Physicians, in particular, find the learning quite challenging. “We are used to being the so-called captain of the ship, in charge of the team,” said Professor Kaplan, “Being put back into the position of the learner, acquiring a new skill, learning how to do things differently, can occasionally be uncomfortable, but the rewards for doing that are immense.”
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Emerging infectious diseases are a humanitarian concern

What might be coming next after COVID-19? This will be the topic of this morning’s talk by Janet Diaz (Geneva, Switzerland), a specialist in pulmonary and critical care medicine who leads a clinical unit at the World Health Organization (WHO) Health Emergencies Program in Geneva. She has been responsible for readiness and response to emerging infectious diseases, such as COVID-19 and Ebola. The clinical unit she leads develops norms and standards for clinical care for hazards, infectious and non-infectious hazards. It created the COVID-19 Living guidelines on Therapeutics and Clinical Management, for example. "I will touch on threats around respiratory viruses, which is pretty pertinent to the audience of this meeting," said Dr. Diaz. Along with seasonal flu, she will also talk about avian influenza, which is popping up again in different parts of the world.

Top of the list, however, will be viral hemorrhagic fevers, such as the threats from Ebola, Marburg virus disease, a rare but severe hemorrhagic fever, and Lassa fever. The latter is endemic in many parts of West Africa. Indeed, Dr. Diaz said many of the threats from respiratory diseases impact low and middle-income countries. "For those that are interested in the global health aspects, this is the bulk of our work," noted Dr. Diaz.

Dr. Diaz relayed that the focus of her work is not just on emerging, but re-emerging infectious diseases. That is why she will also talk about some, let’s say, older diseases. "People need to know the scale of the diseases that we never fixed, such as cholera," she said. "If you go around the world right now there’s a lot of cholera."

In a recent trip Malawi during a cholera outbreak she saw cases rise due to a vaccine shortage and lack of access to safe water. "It’s a real community problem, with lot of rains and floods and poor water systems," she said. "We can improve the care of patients, and I think it’s important for people to know the scale so we can get behind improving access to care."

For example, fluids are essential for resuscitation in those areas, noted Dr. Diaz. "But that package of care is unfortunately still very difficult to deliver, especially at some of the smaller health posts or health centers. Understanding the link between health and critical care infrastructure is so important."

There is, of course, an ever-present threat of an unknown ‘X’ – a future pandemic based on a future unknown pathogen. "I think that’s scary in itself," continued Dr. Diaz. But because of COVID-19, the world has been forced to build an architecture of pandemic readiness, response, and resilience. That is why COVID-19 will be discussed too. "COVID-19 is actually a relatively good example, even if at the beginning it was quite scary, and many sites were overwhelmed."

The community managed the acceleration of a clinical understanding in how to approach these patients, then it accelerated the research and development around treatment, recalled Dr. Diaz. As such, it succeeded in quickly putting together a package of tests, vaccines, and treatments. "Maybe it wasn’t coordinated or intended that way, but many people did many great things," she commented.

Yet, Dr. Diaz will emphasize that ongoing threats in low and middle-income countries should not be forgotten because of worries over the next big pandemic. "From a global perspective, we should be aware of what’s going on in the humanitarian side of medicine," she said. "If it can be packaged together, for us, it’s like the safe and scalable clinical work we do during emergencies."

The heterogeneity in ICU facilities is a crucial consideration, and Dr. Diaz has seen ICUs ranging from well-equipped, big-city centers, to non-existent infrastructures elsewhere in low and middle-income countries during the pandemic. "The structure can be..."
lacking, as can the access to oxygen, the number of existing specialists, and access to specialist training,” she said. “One of the biggest things that I don’t think people realized during COVID-19, for example, was how deficient oxygen systems were in many countries.”

That is why Dr. Diaz’s unit created WHO’s Oxygen Access Scale Up initiative. “It’s no surprise that countries without access to oxygen have been unable to build up their clinical critical care facilities,” she said. “The specialty is attached to a certain level of infrastructure, and it has to be built into the health systems.”

As well as infectious hazards, Dr. Diaz said it is also important to deal with non-infectious hazards, such as wars, natural disasters, and earthquakes too. “These put stress on a healthcare system, and require ICU services,” she said.

“I think everyone has a role to play in keeping the world safe, and responding to emergencies.”

JANET DIAZ

One of the most important issues to remember, however, is the interconnectivity of the health community. A lot of stress was put on primary clinical providers during the pandemic, and many physicians felt isolated, stressed Dr. Diaz. But they should know they were and are part of a global effort. “Clinicians can’t feel alone when they are really connected to the public health institutes, to the public health organizations, to diagnostics groups,” she said. “All these things have to be put into place, even though your role may be specifically taking care of a sick patient in ICU, which is what I used to do before I came to the WHO.

“What I’m saying is we’re actually part of a bigger framework. I think everyone has a role to play in keeping the world safe, and responding to emergencies.”
Predicting brain injury in critical care

Predicting cerebral complications using artificial intelligence (AI) was the topic of a talk yesterday by Soojin Park, an associate professor of neurology in biomedical informatics at Columbia University Vagelos College of Physicians and Surgeons, and an associate attending physician at NewYork-Presbyterian/Columbia University Irving Medical Center, NY, USA.

Speaking to ISICEM News, Dr. Park said that AI has found a place in the ICU in the absence of other kinds of diagnosis. “In the neuro ICU, a lot of our sickest patients who are at risk for secondary brain injury don’t have much of an exam to follow. Our mission is to derive actionable information from healthcare data to improve efficiency and quality of care in hospitalized or critically ill patients.”

Dr. Park talked about the use of monitoring devices and digitized patient data to implement statistical and machine-learning decision support tools to detect physiologic state changes, and identify opportunities for early intervention. “Today, clinicians use a multitude of monitors to assess the function of the brain, and to measure oxygen, metabolism, or pressure, which together generate streams of data. Analyzing the streams and interpreting them over time, however, glean far more information. “Using data science would automate some of those tasks, as well as mine the data streams for patterns, connections and interactions that are not readily apparent to the human,” she said.

Essentially, her group takes a time series of physiologic signals, and then extracts what Dr. Park terms ‘features’. Take an electrocardiogram, which reads at perhaps 240 times a second. “You can look at the waveform peaks, or intervals between those peaks, and then you can look at the variability of those intervals,” she said. “We extract features from all of these physiological forms – we might even put heart rate variability with something else, like blood pressure changes.”

By combining data in different ways, researchers can test a hypothesis – say, the correlation between blood pressure and heart rate changes that are linked to certain outcomes. Using a machine learning algorithm and data from many, many other patients, they can then look for patterns within certain groups of patients. “I can say I know this group of patients within my population had this outcome,” she said. “So, what’s the pattern in those features that seems most pronounced in patients with that outcome?”

In doing so, Dr. Park said it’s possible to make a more precise prediction of a patient coming into the ICU. “Because while their signature of heart rate and blood pressure is going in a particular direction, we can say this patient is very much like those patients who happen to have this outcome,” she said.

Dr. Park described ongoing projects that demonstrate techniques to predict outcomes for patients. These include detecting delayed cerebral ischemia in subarachnoid hemorrhage patients, intracranial pressure waveform analysis to detect ventriculitis, automated time-varying measures to predict shunt dependency in acute hydrocephalus, and detecting subclinical neurogenic stunned myocardium using heart rate variability.

Dr. Park stressed the importance of detecting some of these conditions as they happen. Extracting such domain-driven features from physiologic data and building temporal risk scores, therefore, allows clinicians to more precisely direct invasive or aggressive diagnostic interventions with the intent to reduce cognitive dysfunction, and improve outcome, said Dr. Park. “The sooner you know, the more precisely you know, the better,” she said, terming it diagnostic intervention. “We are flying blind in certain scenarios, and secondary brain injury could be occurring without overt clinical signs.”

Dr. Park said these models are at the initial phases of a pipeline for AI use in critical care. The next step is validation. “You need lots of data, and you need to validate it by trying to see if it generalizes – in other words, does the model really perform as well on a totally unseen dataset?” explained Dr. Park. “We must take care to avoid introducing harm by implementing AI without rigorous adjudication of generalizability, accuracy, adoption, and unintended consequences on workflow.”

Unseen data from other centers and even other countries, is therefore, vital to validation. High impact events can be low frequency, so building datasets large enough to properly extract data signals can be challenging, said Dr. Park. But transferring and sharing large amounts of data for model building can raise logistical and privacy issues. “Federated learning offers an opportunity to decentralize model building and validation, while involving numerous collaborative investigators,” she said.

Dr. Park described decentralized projects between collaborative investigators in several centers, looking at hydrocephalus, ventriculitis, and shunt prediction. “Decentralization enables researchers from different places to work together on datasets, without breaching privacy or data sharing barriers. “It’s becoming a lot more popular to do this kind of decentralized model building when you hold a huge data set,” said
Dr. Park.

From July, another project will validate a delayed cerebral ischemia model across three centers, including her own. Dr. Park covered different methods to better test these models across different datasets and electronic medical records (EMR) using common open-source language, and other techniques.

"Models have to be validated and tested for safety and adoption, and should be designed to not disrupt workflow."

SOOJIN PARK

This work is innovative, said Dr. Park. "I am creating a 'situational monitor' that does not currently exist." This is opposed to a device alarm, or a typical clinical decision support tool embedded in an EMR for optimizing practice. "Situational monitors allow the clinician to become focused on impending clinical states in which early recognition can be of benefit," she added. "They would otherwise be missed without the aid of a computational tool."

In closing, Dr. Park said AI in critical care is complex, and about much more than model building. "Models have to be validated and tested for safety and adoption, and should be designed to not disrupt workflow," said Dr. Park. She hopes that in future, models will be universally available using shared platforms. "Technology and practices to enable interoperability are key to both validation and widespread adoption," she concluded.

References
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