HealthManagement
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`Molecular Tests are Pivotal in Combating the COVID-19 Pandemic`

The central laboratory of the Niels-Stensen-Kliniken group in Osnabrück wasted no time in setting up its own test facilities for the molecular detection of SARS-CoV-2. We spoke with Michael Erren, MD, Head of the Institute for Laboratory Medicine about his strategy and the importance of diagnostic molecular testing in fighting the pandemic.

Dr. Erren, the Niels-Stensen-Kliniken group comprises 15 medical facilities in and around Osnabrück, including nine clinics – you are the main healthcare provider for the city and its surrounding district. When did you first realize what kind of challenge you were facing?

I discussed the novel coronavirus with my colleagues back in mid-January, because a new pathogen is always a potential threat to the global health system. But it really hit me when we started to receive reports from China of the rapid spread of COVID-19 and the alarmingly high number of subacute deaths. And then, on 23 January 2020, the industrial city of Wuhan – a city with over a million inhabitants – was completely sealed off and remained so for weeks. That was a wake-up call. For me there was no question that a worldwide epidemic was imminent, one that would in all likelihood overshadow previous pandemics such as bird flu in 1997, SARS-CoV-1 in 2002, and swine flu in 2009.

Michael Erren, MD, head of the Institute for Laboratory Medicine, Transfusion Medicine, Microbiology, and Hygiene of the Niels-Stensen-Kliniken group in Osnabrück, Germany.

What was your initial reaction?

At that time our central laboratory had no testing facilities for Coronavirus, and we had to send samples to national test providers. I spoke with our management and immediately received the green light to set up our own facility. It was absolutely crucial for us to be self-sufficient in the important matter of virus diagnosis so that we could act quickly and independently – both in caring for our patients and in ensuring the safety of our staff. And with the rapidly escalating pandemic we quickly realized the advantage of being independent from external virus diagnostics providers for both test capacities and processing times. Our aim was to prioritize the care of critically ill patients and treat them without delay. Molecular diagnostic tests are pivotal in combating the COVID-19 pandemic owing to their excellent analytical sensitivity and specificity.

How has the situation developed in your catchment area?

So far, Germany has weathered the crisis relatively well – and the same applies to our catchment area. At present we are testing up to 600 people a day. These include suspected cases, patients who are sick and are prepared for surgery, staff who work closely and frequently with COVID-19 patients, and individuals who live or work in our elderly and nursing homes. We manage almost 400 time-critical tests in an early and a late shift and can process the results on the same day – or within 24 hours at the latest. For less time-critical cases we work with the MVZ Laborzentrum Weser headed by Professor Franz-Josef Schmitz.

When it came to selecting your own molecular diagnostic infrastructure you opted for the VERSANT® kPCR Molecular System1 from Siemens Healthineers. What were your reasons for this choice?

A number of factors were instrumental: For one, there was the massive demand for test systems that surged right from the outbreak of the pandemic, leading to huge supply bottlenecks that had not been anticipated. That's why we wanted to work with a provider whose supply chains we could trust and who we knew would provide fast and reliable support in dealing with technical problems. Then we were also looking for a

system with fast and streamlined workflows and easy IT integration. We wanted an automated system, requiring hardly any manual intervention, that would relieve the pressure on our laboratory staff even with high sample throughput. Finally, the solution also had to reliably protect our staff against possible infection.

Do you see any further advantages?

Well, there is also the benefit that molecular FTD PCR tests are carried out under the same thermal PCR conditions. This will be especially important in winter when we have to differentiate between different respiratory infections when reaching a diagnosis. SARS-CoV-22, influenza viruses (influenza A, B, H1N1) and RSV3 can all be processed simultaneously on the same PCR cycler. In addition to the high specificity, we were also impressed by the published data on the high sensitivity of the FTD-SARS-CoV-2 test2. We could confirm this high sensitivity in our laboratory, too. It reduces the risk that people infected with SARS-CoV-2 will be overlooked as a result of a low virus concentration or incorrectly collected nose or throat swabs. With the high sensitivity we are also achieving valid results in the pool tests that are being increasingly carried out, for example in the screening of staff or entire schools or in the testing of returning tourists. In terms of clinical care, a further benefit is that the course of the individual infection can be characterized on the basis of the PCR raw data (Ct values) – at least semi-quantitatively. On the one hand, it can be used to identify infected people with very high viral load (Ct value <20) who have the potential to become “superspreaders”. And on the other hand, with samples that still exhibit RNA ten days after the onset of symptoms and have a Ct value >30, we can conclude that the virus concentration is below the critical infection dose or that only RNA residues remain – that is, material that is no longer viable or culturable. High Ct values can therefore be used as a criterion in deciding whether to release patients from the clinic.

The automated VERSANT kPCR extraction module is being loaded with the pre-prepared patient samples.

How does the current situation impact your employees?

The workload is of course much higher than before the COVID-19 crisis and at the same time there is an increased risk of infection. Consequently, we attach great importance to protective measures in order to minimize the risk to our employees even when the number of tests is very high. And so far this strategy has been very successful. The high degree of test automation on the VERSANT kPCR platform has been a big help. Employees only have to handle the samples once at the beginning of the test when the samples are mixed with a small amount of lysis buffer at a sterile biological safety cabinet and transferred to the tubes. All further steps are processed automatically by the extraction module.

Do you believe that the COVID-19 pandemic can be brought under control with SARS-CoV-2 tests?

One thing is for sure, it won’t happen without testing. However, I would advocate a differentiated test strategy and not a mass screening without any reasonable stratification. A test always provides merely a situational snapshot of the time it was taken. Someone who has tested negative today may be infected by tomorrow, and a negative test result can easily lead to a false sense of security. In case of doubt, the test should be repeated after five days – this is the typical incubation time plus a safety margin. In addition, the throat swabs have to be taken correctly, which is not always easy. Furthermore, the virus can only be reliably detected in the throat in the first week and is often no longer present in the second week. I think it makes more sense to conduct testing in hotspots and on risk groups. Another argument against mass screening is that the diagnostic validity of a test, the so-called positive and negative predictive value, doesn’t depend on sensitivity and specificity alone, but also on prevalence – the infection rate in a defined group. The less frequent an infection occurs and the more random the testing, the more likely it is that there will be statistical “false-positive” results. Therefore, a test should only be carried out if the clinical symptoms and the individual circumstances suggest an increased probability that the group to be tested includes individuals infected with SARS-CoV-2. Indiscriminate mass screening of the general population is not very effective and would overstretch our limited testing facilities.

Michael Erren, MD, evaluates the analysis results for SARS-CoV-2 using the amplification and detection module of the PCR device.

Do you fear that Germany will be hit by a new wave in autumn or winter?
We have to assume that the rate of infection will increase in the cold season. Because from autumn onwards there are various phenomena at play. Virus-containing aerosols survive longer in colder air than in warm temperatures. Colder air reduces the dehydration and inactivation of the virus, which in turn increases its environmental stability. Indoor spaces are less well ventilated than outdoor spaces, which results in lower dilution effects. Then there are also more people indoors: They tend to sit and stand closer to each other. In addition, the mucous membranes are more susceptible to damage due to irritations caused by other respiratory pathogens. The immune system’s defense mechanism is reduced when mucous membranes have a lower temperature and blood supply is lower. And finally, temperature has a clear effect on the ability of respiratory viruses to replicate.
Let’s hope that it won’t come to that and that the epidemiological and laboratory diagnostic early warning systems can be optimized so that we identify these developments early enough to be able to take countermeasures.

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