Don’t have enough COVID-19 tests? No problem, we’ll make them!

It seems ages ago, the beginning of the coronavirus pandemic — remember? Or maybe you’d rather forget.

An invisible killer was on the loose, and the whole world was scared.

And we had only one tool — testing — to find out where that killer was, and figure out where it would strike next.

But there was one big problem. If tests were the key to tracking down the killer, where were the tests?

No one had enough.

The problem, as we all know, was the worldwide demand for chemicals and testing equipment skyrocketed when the pandemic broke. Companies ran out of everything, from reagents to nasal swabs and more.

Norway, as a relatively small country, often found itself way back in line when it came to supplies.

So what happened next might surprise you.

Vegar Ottesen: I find it kind of mind boggling that we were able to do this to the scale that we did. We went from a thousand tests in a small bottle to 10,000 tests fairly quickly. In a matter of weeks we went from concept scale to production scale.

CUE Podcast music

I’m Nancy Bazilchuk, and you’re listening to 63 Degrees North, an original podcast from NTNU, the Norwegian University of Science and Technology.

Today, I’m going to tell you the story of how Norway’s largest university, NTNU, tackled the shortage of coronavirus tests in a very unorthodox way.

It’s an unlikely story of how a bunch of lab geeks, some vanishingly small beads and two emails saved Norway’s bacon. And it’s even got a happy ending, in the faraway and beautiful land of Nepal.

I’ll give you an inside view of the very earliest days of the pandemic, to see how researchers were able to produce tens of thousands of tests for Norway to use in a matter of weeks. It was an incredible pressure cooker — everyone on the team was working to produce the tests, and at the same time trying to avoid getting COVID — which could have crippled the test production.

Nancy: So let’s begin at the beginning. In this story, that would be March 20, 2020.

Magnar: You know the way that happened was that my leader of the Department of Clinical and Molecular Biology got the request from St. Olavs Hospital. The whole medical faculty got the request, and the request was, do you have any kits for RNA extraction? And that was the simple question.

Nancy: That’s Magnar Bjørås.
Magnar: Professor in Molecular Medicine.

Nancy: Norway's first coronavirus infection was detected on February 26. Newspapers had already begun to warn of shortages of personal protective equipment and tests. On March 12th, the government essentially shut the country down. People were told to work from home whenever possible. Wherever you’re listening from, you can probably fill in the rest. Everything ground to a halt. People were afraid to go to grocery stores, no one got their hair cut. And yeah, toilet paper.

In Trondheim, doctors at St. Olavs Hospital began feeling the pinch almost immediately. St. Olavs is one of the four big regional hospitals in the country. So on March 20, they broadcast the urgent cry for help that Magnar Bjørås told us about earlier.

Magnar: When I saw that email, I thought immediately, of course we have kits, but we have kits maybe for two, three, 400 samples, it's nothing because we don't do large scale RNA extraction. We do small scale. So then I started to think there is no way we can provide them with anything that can support them in short run or long run.

Nancy: One thing you need to know about Magnar Bjørås is that he grew up on a farm. That’s part of how he got interested in biology.

Magnar: I grew up at the farm and I was very interested in the life on the farm and the animals and how living life was — what's behind it.

Nancy: It's not hard to imagine that his background on the farm, where you need to know how to fix things and make do with what you have, contributed to what happened after Magnar got that first email.

Magnar: So, when the request from St Olavs Hospital came because they were lacking reagents to do the extraction test, I thought that we can try to make an in-house test — and that's how it started. And I, we, thought that we'll do that now for the hospital for a few weeks, and so we can help them out of the crisis.

Nancy: At first Bjørås and his colleagues made a test that used alcohol to extract the viral RNA. It worked, but it would be tough to implement at the scale needed. No, they needed something that would be fast and easy to use.

Nancy: Enter another email. It turns out a researcher that Magnar worked with knew about this researcher over in chemical engineering who was doing some interesting work with nanoparticles.

Sulalit: So we actually received a more general email from Magnar's department addressed to the head of the group at our department. And then he forwarded the email to us because he had been knowing that I was working with such particles and the journey started.

Nancy: That's

Sulalit introduces himself.

Nancy: While Magnar grew up on a Norwegian farm, Sulalit grew up in India and came to NTNU to do his master's and then PhD in the chemical engineering department. He did a shared postdoc at TU Delft and NTNU, working with tiny iron oxide particles coated with silica. The particles were labelled with a little DNA barcode. By dropping these little harmless particles into a river, for example, they could trace the flow of the water along its journey, by sampling the water, plucking their little iron oxide particles up using a magnet and reading the barcode.

As it happened, they had already decided to try attaching RNA to the particles.

Nancy: And guess what: The SARS-CoV-2 virus , the virus that causes COVID-19, is an RNA virus!

Nancy: So before we go any further, we need to know how the NTNU test works, and why Sulalit's nanobeads — the ones he once used to study water flows — are important.

Sulalit: The coronavirus test is basically done now taking swabs from the patient, mostly from the nose or sometimes from the throat. Once this swab is taken, it's mixed with some chemicals, which Magnar's group has made. And once these are exposed to the chemicals, the virus opens up. Then you get the viral genetic material, which in this case is RNA, and then we add our beads to the process.

Nancy: Then, you have to get the RNA from the virus out of the solution, and that's where the use of Sulalit's beads really shines.

Sulalit: So what the beads do is that they bind this viral genetic material onto their surface and using a magnet, we can then separate them out later on. We use a different solvent, a different solution where the beads then release this RNA back and then using some known technology, called a PCR polymerase chain reaction, we can find out whether this is the viral RNA or not.

Nancy: Those are the two places where the NTNU test cuts the need for chemicals.

The first is if there's RNA from any virus, it's attracted to the beads like bees to honey — no chemicals needed.

The second is that they can use a magnet to take the RNA coated nanobeads out of the solution. Again, no chemicals needed.

The last part of the test that you heard Sulalit describe involves a machine called a PCR — which is short for Polymerase Chain Reaction — to read the genetic code of the RNA. In our case, they did this work down at St Olavs. The PCR results allow the researchers to compare the code of the RNA they get from the patient to the code for the SARS-CoV-2 virus. If they get a match, that means the patient has COVID-19. That also means the test can be used to detect the new variants of the virus that are circulating around the globe now.

Sulalit: So with the addition of the beads, what it does is that it's specific to the COVID 19 RNA virus, as a result of which it gives us a very sensitive method of detection.

Nancy: The fact that they can create a coating that is specific to different genetic material is important, and not just because it makes their beads a very sensitive way to detect the coronavirus. I'll talk more about this later.

Nancy: OK, so back to late March. One day after the email goes out from St. Olavs, Magnar and Sulalit connect. Magnar again.

Magnar: We realized in one day that this is going to work. And then it just escalated.

Nancy: And one week after St Olavs sent its plea for help, the hospital got its new tests. The tests were double checked against the few remaining commercial tests the hospital had — and they worked! Not only that, but they were slightly more sensitive than the commercial tests.

Nancy: Once it was clear that the NTNU test worked, the Norwegian authorities got interested. Maybe… NTNU could make enough tests for the whole country?

Say… 5 million?

Because yes, that's what the authorities asked the university to deliver. Five point one million tests.

But it's one thing to make a small scale test. Making enough tests to really bail out Norway? Well, that's a whole other process. Sulalit again.

Sulalit: The initial days were very hard. To be honest, we were working 24 seven, the first two and a half weeks when we are trying to do tests more at a small scale level. And then when we started scaling up, we got in more people into the team. So that was a bit more easy let's say.

Sulalit: Initially we produced batches that were capable of producing kits for a thousand tests. And then within a week, we were producing in the range of 10,000 to 20,000 and grew.

Nancy: Right from the beginning, there was a core team with people like

Vegar: Vegar Ottesen. I'm a postdoctoral fellow at the Department of Chemical Engineering.

Nancy: It was Vegar we heard at the top of the podcast, marvelling at how fast the whole process went. His role was to inspect the nanoparticles after they had been made using a powerful microscope,

Vegar:characterizing the product to make sure that we got what we wanted to get and that the product quality was adequate for use.

Nancy: Then there was

Anuvansh :Anuvansh Sharma. I am a PhD candidate at the department of Material Sciences and Engineering at NTNU.

Nancy: Anuvansh had been working with Sulalit on the DNA-labeled nanoparticles that they were using to study water flows, but joined the team to make the nanoparticles for the COVID-19 test.

Anuvansh: With Sulalit, we were synthesizing the particles, the iron oxide particles and coating them with silica.

Nancy: At the peak of production, roughly 30 people were working in three independent groups. They had to make sure if someone caught COVID-19 in one group, the other groups could still keep producing tests. The pressure was intense. Norway needed tests. No one wanted to let the country down.

Vegar: So we had different production lines where we're separated in case of infection. So if one production line was infected, we could take that out of production and still maintain a certain volume that we could deliver to the country and to the world.

Nancy: To be able to make all these tests, the researchers essentially set up a factory at the university. It wasn't like any factory that you might imagine — it was a bunch of lab workers in a laboratory wearing white coats and goggles in front of lab benches fitted with fume hoods. Those are like big boxes with powerful fans in them to filter and vent potentially harmful gases or vapors from the work.

Nancy: I have tons of recordings from the labs at this time, but most of it is kind of boring. When Sulalit walked me down the line of fume hoods to describe the

production, it really didn't look like a massive factory churning out hundreds of thousands of nanobeads for the tests. In fact, if you have ever taken a chemistry class — that's kind of what it looked like. The only really cool sound I got was the sound of this machine, from the hospital, where they did the actual diagnostic part of the test — exploding the virus and then analysing the genetic material inside. Magnar is explaining to me what the machine is doing. You'll hear him say lysis buffer a bunch of times. (cut from magnar? 4:17 from Z24). That's the solution that pops open the viruses so they release their RNA.

Magnar:So you see the magnet, we use some combs that are outside the magnets and now it, actually, the magnet starts to go up and down in the solution with the patient sample and lysis buffer. (great background noise) So it's mixing the patient sample and the lysis buffer. So it will be a homogenous solution. And so what's happening now is that the lysis buffer is breaking up the virus and releasing the RNA into the, into the solution. So when we have done that, after that, we will actually turn on the magnet. So the magnet will attract the RNA.

Nancy: And they got good at it. Really good at it. And even though the work was exhausting, the feeling that what they were doing was bailing Norway out — helping the country track the virus — was a very powerful motivator. Sulalit again.

Sulalit: It feels really great to have helped society very directly. What, what amazes us, the whole team is that we were looking at producing some beads in a small lab scale, but within two and a half weeks, we were already testing live samples from patients and the system was working very robustly. So that's what we are very proud of in this whole project.

Nancy: By the autumn of 2020, when I sat down with Magnar, he and the other lab scientists were contemplating their next steps. Their laboratories had the capacity to make 1.2 million test kits per week.

Magnar:The first phase was to initiate production and to deliver to hospitals or to the health authorities in Norway. And the second step was in a way to look at, could we upscale this production so we can deliver abroad because as you know, there is also a huge shortage of reagents abroad.

Nancy: Pretty much every university has a technology transfer office, to help researchers with ideas that have commercial potential. This was clearly a natural.

Tonje:I'm Tonje Steigedal, I'm a business developer at NTNU technology transfer.

Nancy: Tonje Steigedal was involved with Magnar and Sulalit and the rest of the team in seeing if they could supply the tests internationally. It took a bit to figure out the logistics, but by the end of September last year, a million NTNU tests were shipped to Denmark and India. Other countries and customers would follow.

Nancy: The success of the test raised an important question for the researchers and the folks at Technology Transfer. Should they just go back to life as usual after the pandemic was over — or should they try something different? Tonje Steigedal again.

Tonje: It was a special situation and they, they were making the solutions for the hospitals and we had that in place before the summer, and then we were selling out of the university in the fall,

Tonje: But it's obviously not sustainable for a university to be a kind of manufacturer and selling this in the, in the market.

Tonje: So, uh, we have now we're now in the process of establishing a company, that will continue to bring this to customers nationally and internationally.

Nancy: The company, which will be called Lybe, from the first two letters of lysis … remember Magnar talking about that? And Be from beads. But the company won't just deliver coronavirus tests. Remember early on, when Sulalit was talking about how the coating on the beads could be tailored to attract different kinds of genetic material? The new company will expand on that.

Tonje: What's good about this is, uh, this technology can be utilized in in many ways, um, with minor adjustments, it can be used also for other respiratory diagnostics, like the normal flu and the other respiratory viruses. And then we also know that in the diagnostics, in the, in the clinic, there are many, many needs. Some, they do a lot of testing every day. So what we also then need is to come up with solutions that they need also for other microbes bacteria viruses and so on. So we will continue to develop the technology so that it can be used also for, for other diseases.

Nancy: Everyone was impressed with the speed of how people have responded — and of course, not just in Norway. Who would have guessed that there would be working vaccines roughly year after the pandemic broke? But when I asked people

what NTNU researchers learned from the COVID-19 pandemic, two things really stood out.

Nancy: One was the value of basic research — meaning research that doesn't necessarily have a real life application, but that just involves the pursuit of knowledge for its own sake. Vegar Ottesen.

Vegar: So how has this project inspired me or taught me about basic research? It wouldn't have been possible without a lot of basic research first. And I sincerely doubt that the basic researchers who were behind the chemistry, we used, the physics we used, could possibly have known how it would be used, how their knowledge would contribute to combating the pandemic in 2021 and 2020.

Vegar: Whenever a need arises a national, global scale, even like this, then it is very important to have the puzzle pieces ready to assemble the solution to the problem that we might face. We can't possibly assemble a puzzle without the puzzle pieces, that's basic research.

Nancy: The other was that it drove home the fact that an idea can become a reality in a hurry — especially if you have the adrenaline from a pandemic driving you forward. Sulalit again.

Sulalit: What we all keep on saying that we have excellent ideas, but we don't transform them into actions, in many cases in academics, but this was, this is what I'm going to look back, that this was a start for me to think that it's also possible in academics. It doesn't take such a long time.

OUTRO

Nancy: I'm Nancy Bazilchuk, and you've been listening to 63 Degrees North, an original podcast from NTNU, the Norwegian University of Science and Technology.

You'll find more information about NepaliMedNorway and more about the NTNU tests on our show notes page.

If you've enjoyed today's show, we hope you'll let your friends know and leave a rating on your podcast app. Editorial help and sound design by Randi Lillealtern from Historiebruket. Thanks for listening.