

COVID-19 Stroke and Blood Clot Media Scan

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Is COVID-19 actually a disease of the blood vessels? New research could help explain odd symptoms from strokes to purple toes

<https://www.thestar.com/news/canada/2020/06/04/is-covid-19-actually-a-disease-of-the-blood-vessels-new-research-could-help-explain-odd-symptoms-from-strokes-to-purple-toes.html>

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Media Outlet: Toronto Star

Fifteen-year-old Jake Reymer was sitting at his computer one day this spring when he looked down at his toes to discover they'd turned a strange shade of purple.

"At first I thought, I don't know, maybe I bruised them somewhere," he remembers. But, after developing a cough and sore throat for about 36 hours, they started to "get more and more tender." For a few days it was "almost hard to walk."

His concerned parents began Googling. Half of their six-person family had recently fallen ill with flu-like symptoms after a March break trip to St. Lucia. Could it be some strange sign of the new disease causing the world to shut down?

"And that's when the first reports started coming out of Italy and France about how this virus was presenting in teenagers," remembers his dad, Jeff.

"That was the first time we even heard the term COVID toes."

They're just one of a growing constellation of symptoms — from strokes to blood clots to heart attacks — that have mystified doctors treating COVID-19 who originally thought of it as a respiratory condition affecting the lungs. At the beginning of the pandemic, health officials weren't even recognizing symptoms like COVID toes as part of the disease. Guidance from public health officials advised that cough, fever and shortness of breath were its hallmarks.

But a growing body of research suggests COVID-19 may be a vascular disease affecting the blood vessels, an important part of the puzzle that could change how it's treated.

This evolution in thinking "opens the chapter to understanding some of these odd complications that have been so vexing," said Dr. William Li, a physician and the president of the Angiogenesis Foundation. The non-profit based in Cambridge, Mass., tries to understand blood vessels and their role in health and disease.

Li is a co-author of a new paper published in the New England Journal of Medicine that examined seven lungs of patients who had died of COVID-19.

When people first started to get sick, the focus was on those organs, he said. But that started to shift as health workers saw first thousands and now millions of patients with COVID-19, including many whose symptoms didn't fit the typical profile of a respiratory disease.

Patients were showing up with blood clots, strokes, brain swelling and, on the more mild end of the spectrum, toe pain.

The authors approached their study “like a crime scene investigation,” trying to figure out why all these strange symptoms were happening, Li said.

“And looking at these tissues, what we found was that the respiratory virus had not only infected the lung, but the virus had also made a beeline for the cells lining blood vessels,” he said. When those endothelial cells are damaged by the virus, it makes the blood more likely to clot, he said.

The study’s authors saw from close-up pictures that the virus had moved from the air sacs of the lungs, “infecting directly into the blood vessel cells.”

The cells were being destroyed “from the inside out,” unlike when someone has high cholesterol and they’re damaged from the outside. There was “emergency blood vessel growth” as they divided to get more blood flow, which can lead to clots. The immune system trying to clear the virus can also cause inflammation and clotting.

“So this is sort of three strikes that we saw in our study to help explain this clotting,” Li said. The damage was found in “vast areas of the lungs” at the same time, he added, and not just “a few pockets.”

That’s “not something that we normally see with respiratory virus, and it seems to be unique to COVID-19.”

His study also looked at the lungs of people who had died from H1N1, and found they had nine times fewer blood clots in the lungs.

An April paper in *The Lancet* also showed damage to endothelial cells in several areas of the body including the lungs, heart, kidneys, liver and intestines of COVID-19 patients.

Isaac Bogoch, an infectious diseases specialist at the University of Toronto and University Health Network, said he hasn’t seen any COVID toes yet but has seen some vascular symptoms such as blood clots, in patients at Toronto General. It’s “not uncommon” for diseases to have “an inflammatory component,” he said.

Cat-scratch disease, a bacterial infection caused by cats who turn on their owners, is one example. But it’s important to remember that “most people don’t get a blood clot,” he said, adding that within hospitals doctors are “still seeing blood clots in some individuals but certainly not most individuals.” Li’s research might help explain, though, why older people and those with conditions like diabetes or heart disease tend to have worse outcomes. Their blood vessels are already more vulnerable.

And it does “open some new doors of thinking about treatments,” Li said.

Blood thinners could be one example. There are also ongoing clinical trials looking at dilating the blood vessels with nitric oxide, and stem cell treatments to regenerate the cells. It’s also important to remember that maintaining a nutritious diet can help keep blood vessels healthy, he added.

A New England Journal of Medicine paper from early May looked at outcomes of 8,910 patients across Asia, North America and Europe. It found that the use of either ACE inhibitors (medications that dilate blood vessels) or statins (drugs that help lower cholesterol) was associated with better survival. But the study could not prove a cause-and-effect relationship as it was not a randomized, controlled trial.

Researchers still don't know why COVID-19 is so much worse for some seemingly healthy people than for others, at what point the blood vessel damage starts to occur, and why blood vessels are affected in some parts of the body but not others.

"The unknowns of this disease still far outnumber the knowns, so it will take time to construct the full picture of how the SARS- COV2 virus actually causes COVID-19," Li said. But blood clotting could help explain COVID toes, as well as more serious symptoms like strokes.

Multisystem inflammatory syndrome, which has been diagnosed in a small number of kids and teens who test positive for COVID-19 or antibodies that suggest they had it, may also be connected to blood vessel damage, he added.

Luckily, Jake didn't experience any severe issues, but he did have an on-and-off fever. He's the only one in his family who had the COVID toes. His dad, Jeff, said he had "the heavy, heavy chest" and didn't feel like he had "a full set of lungs" but was lucky it didn't get more serious. His younger sister Ella had a low-grade fever for several days, but his mom and two other siblings didn't notice anything out of the ordinary. They were told by doctors, who diagnosed Jake's toes through virtual visits, to assume they all had it, said Jeff. And their family shows the wide range of effects the disease can have on different people.

"We've got four kids, so we have a larger sample size," he said with a laugh. "We've shared air amongst us and 50 per cent had issues and 50 per cent didn't."

The Reymer family was initially told not to go for testing and just to keep self-isolating. By the time Jake and his father did get tested weeks later, when it opened up to people with more unusual symptoms, they were both negative, possibly because the virus had already cleared from their systems. The province is now urging anyone with even one mild symptom, including loss of taste and smell, and COVID toes, to get a test, as well as asymptomatic people who work in front-line jobs or think they may have been exposed.

Jake is now back to playing basketball and walking around the neighbourhood. He's feeling good and his toes seem to be improving. But they're still purple.

"They haven't shown any real signs of resolving," he said.

"I'm 100 per cent, it's just my toes still aren't normal."

Coronavirus Update: Blood kits will be sent to 10,000 Canadians to estimate total spread of virus

<https://www.theglobeandmail.com/canada/article-coronavirus-update-blood-kits-will-be-sent-to-10000-canadians-to/>

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Media Outlet: The Globe and Mail

A doctor at St. Michael's Hospital in Toronto is leading one of the first large-scale surveys – with 10,000 blood kits – that will examine participants' blood for antibodies that are specific to the virus that causes COVID-19.

- The antibodies are a natural part of the body's immune response. Initial studies with COVID-19 patients show they appear about three weeks after an infection has occurred and persist for at least 60 days.
- Because the first wave of infections in Canada is thought to have peaked sometime in mid-April, Dr. Jha said now is the ideal time to try to obtain a snapshot of how widely the disease has spread across the population.

10,000 Canadians to be tested for COVID-19 antibodies in hopes of understanding immunity

<https://www.ctvnews.ca/health/coronavirus/10-000-canadians-to-be-tested-for-covid-19-antibodies-in-hopes-of-understanding-immunity-1.4961439>

Date Published: June 1st, 2020

Media Outlet: CTV News

TORONTO -- After a person has developed antibodies against COVID-19, how long does that immunity last?

That is one of the crucial questions that a new study led by Toronto researchers is hoping to answer. By testing the blood of more than 10,000 Canadians for antibodies, which are developed after a person is exposed to the virus to fight it off, the Action to Beat Coronavirus study is hoping to not only find out whether immunity fades with time, but also discover just what percentage of the Canadian population has been exposed to COVID-19 -- and how many of those people got the virus without displaying any symptoms at all.

This type of large-scale survey and testing has yet to be performed in Canada, according to Dr. Prabhat Jha, one of the study's lead researchers and director of the Centre for Global Health Research at St. Michael's Hospital of Unity Health Toronto.

"You want a true snapshot of the country," he told CTVNews.ca in a phone interview Friday. Those who get officially tested for COVID-19 are generally those who are showing clear symptoms. Because of this, the current testing alone doesn't provide the full picture of the virus's spread in Canada, Jha said.

This study, launching this month, is a collaboration between the University of Toronto, the Centre for Global Health Research at Unity Health Toronto and the Angus Reid Institute.

And all of the testing will be done without participants leaving their homes.

HOW IT WORKS

As Jha explained the study over the phone from the hospital, the sound of his team working away in the background was audible. They were putting together the home kits that will let participants collect their own blood samples, he explained.

The first phase of the study is an online questionnaire that will be sent out to more than 10,000 Canadians through the Angus Reid Forum, a nationally representative database consisting of Canadians from across the country who have signed up to help with studies and surveys.

Those who fill it out will be asked about their experience with COVID-19. Participants will be selected randomly from those who agreed to have their blood tested, and kits will be sent out, starting in the first week of June.

The kit itself is simple. It comes with a lancet to draw blood, gauze, an alcohol wipe, a bandage, an information sheet, an instruction manual and a consent form.

A lancet looks “just like a little green pen,” Jha said, but when you “push it against the finger ... it clicks and a small needle punctures the skin.

“When diabetics want to test their sugars at home, that's what they use to get a little finger prick of blood.”

Participants will place one droplet of blood onto five different circles on a special filter paper in the kit. The paper is then dried for two hours before participants mail it in the hospital to be analyzed for antibodies.

“It's a simple process that actually has been used in developing countries for quite a while, because doing blood-based studies [there] is really difficult,” Jha said. “So people have moved to this technology and interestingly, we're bringing it home to Canada.”

Jha said that home blood collection was the safest way to test in the time of COVID-19, when asking large groups of people to come into a hospital setting to give blood might not be a good idea. The blood samples will be sent by participants to the laboratory at St. Michael's Hospital of Unity Health Toronto.

There, researchers will use a combination of at least two different antibody tests to look at the samples, in order to minimize the risk of a faulty test skewing the results. Participants will be able to see their results if they choose, but Jha cautioned that “these aren't immunity passports.”

Even if a person learns that they have antibodies to fight the virus, “it doesn't mean that you can go out and start kissing people on the street,” Jha said.

After four to six months have passed, participants will be asked to fill out a second set of questions and send in another sample of blood to be tested. It's in this second round of results that researchers expect to get the most revealing data.

“Then we can see, [for] the people who were infected, did they keep the antibodies -- which is a sign of protection -- or did they lose them?” Jha said.

“And also are there new infections in people who weren't infected before? So that gives you some sense of ongoing transmission. Then finally we'll be able to say, well, by linking to the health records of testing, if someone had antibodies, did it protect them against getting infected in the followup period?”

“Very basic questions, but they have not been answered for the whole of Canada,” Jha pointed out.

WHAT RESEARCHERS HOPE TO FIND OUT

It's known that when a person is exposed to COVID-19, they develop antibodies that fight the disease, a natural reaction that most doctors agree provides immunity against the virus for some time after they've recovered. But there is still only preliminary data on this antibody response, and it's unknown how long this immunity lasts.

For some other viruses, the immune response wanes with time.

“People get repeat colds every year or even in one season, cause the protection to those goes down,” he said.

With many countries beginning to slowly re-open their economies, having a clearer picture of that immunity response is even more important, especially considering that there is no vaccine for COVID-19 yet.

This makes it all the more important to figure out what percentage of the population may have caught the virus but are asymptomatic.

“That's why we put an emphasis on trying to get a good random sample and encouraging even people who aren't infected -- or don't think they've been infected -- to participate,” Jha said.

“The point we make is this might or might not help you, the person taking the test, but it'll certainly help our seniors and give information that helps protect our seniors against COVID, cause that's the key kind of information that we need.

“So, you know, we're saying give your finger to help grandma, basically.”

Jha said that they will be looking at demographic info for the participants, and will be working to reach out to any groups that are underrepresented in the sample of the population that they end up testing. Because those who are older are more at risk of developing severe complications or dying as a result of COVID-19, researchers are aiming to get a larger sample of older adults than other age groups in their testing.

They hope to test around 6,000 adults from age 20 to 60, and 4,000 adults over the age of 60. Once researchers receive the results from the first round of tests, they'll be able to share some preliminary data by July or August, Jha said. Data related to the length of immunity will come later on after the second round of tests are performed in four to six months time.

This data could help policy-makers by providing a clearer look at the true rate of infection.

The results of the study could even assist with pinpointing the fatality of this virus in Canada, Jha said. If this study shows what percentage of Canada may have contracted the virus, that data can be compared to the existing data showing the hospitalization and death rate.

“By looking at the ratio of those, you can get a real indication of just how fatal this virus is and in what age groups,” Jha said. “And then that will be actually quite informative to thinking about strategies of what do you do in a second wave. Do you try to say, we'll not worry too much about young people or do you worry about young people?”

“All of those things that are currently guesswork will be much more informed.”

Learning how the coronavirus affects the body offers clues to fight COVID-19

<https://www.cbc.ca/news/health/covid-19-coronavirus-inflammation-immune-1.5591218>

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Media Outlet: CBC News

The devastating damage that the novel coronavirus inflicts on the human body can set off inflammatory havoc. As we learn more, doctors are gaining clues to hopefully prevent deaths and improve treatment.

Last December, COVID-19 entered the world stage as a flu-like illness causing fever, dry cough and a sore throat.

Since then, the list of how the illness can present has expanded, and expanded again, to include gastrointestinal symptoms like diarrhea, general aches, loss of taste and smell and serious blood-clotting problems, among others.

Of the more than five million infections globally so far, 2.4 million have recovered.

Most infected people have so few symptoms they are better off at home. The minority of serious infections in patients — mainly those over 65, though no age group is left unscathed — can confound health professionals caring for them.

The illness can worsen to a severe stage called Acute Respiratory Distress Syndrome, which includes severe lung inflammation and damage. These are often the patients who are admitted to intensive care units and need life support such as ventilation.

Dr. Lynora Saxinger, an infectious disease physician at the University of Alberta, co-chairs a provincial scientific advisory board reviewing how COVID-19 manifests and what it means for reducing transmission and extending treatment beyond current care measures.

"The landscape shifts really quickly," Saxinger said. "We just want to make sure that we're not missing [what] could be spreading, because that's where we're going to run into trouble."

Not typical clots

As initial anecdotes about inflammatory-like effects such as blood-clotting complications mounted into a clearer signal for caution, clinicians adapted their care while scientists worked to understand why it happens.

Now, Saxinger said there's more evidence of clotting damage in both large and small blood vessels. "This virus is doing different things in the body."

Experts say some of these inflammatory effects look to be unique to this particular coronavirus, which is known as SARS CoV-2.

Dr. Zain Chagla, an associate professor of infectious disease at McMaster University in Hamilton, Ont., said the wide extent of clotting with this virus differs from other infections, including from the deadly

SARS and MERS coronaviruses. With COVID-19, the clots occur in veins in the legs and lungs, as well as in arterial ones that cause strokes and can lead surgeons to resort to amputating a patient's limbs.

Medical researchers have also found tiny clots that damaged tissue throughout the body in hospitalized patients and in autopsies.

Chagla said this means that "from a therapeutic standpoint," it might be better to give patients a low dose of heparin, an anticoagulant or blood thinner. It's often used before surgery and in a variety of medical conditions to prevent and treat clots.

Clinical trial researchers are also exploring the use of high-dose anti-coagulants in carefully selected patients, Chagla said.

This week, Health Minister Patty Hajdu announced an accelerated path for clinical trials to help find answers to urgent COVID-19 diagnosis, treatment, mitigation or prevention questions while keeping patients safe.

On Friday, Montserrat Puig of the U.S. Food and Drug Administration and her team published what they called a road map for effective treatment of COVID-19, based on both repurposing existing approved drugs as well as those still under development.

The review, published in *Frontiers in Immunology*, unravels factors leading to the "cytokine storm" that can rampage in people with severe COVID-19. Cytokines are small molecules released by the body's immune system to co-ordinate response against an infection or injury, ranging from a mild fever to suspected deaths in the 1918 flu pandemic.

Scientists are still working to understand the key events in cells, tissues and the body's immune system that tips the balance from a normal, protective, "hey, come help" call for reinforcements to an unnecessary, four-alarm call that leads to a life-threatening overreaction.

Puig wrote that potential drugs include those that could block the virus from entering our cells in the first place, antivirals to stop the virus from making copies of itself and therapies called monoclonal antibodies that dampen the haywire response from cytokines.

Inflammatory storm unleashed

People who develop symptoms of COVID-19 do so within 14 days, and it mostly occurs about five days after exposure.

Saxinger said when patients struggle with congested lungs and poor blood pressure control, it's often a manifestation of lung inflammation in response to the infection.

She said there's also an arc to the story of how the disease marches through the body from initial infection to damage to recovery or death.

"The initial infection triggers this body-wide response that is devastating," Saxinger said. "Then, when the infection itself might be coming under control, it's almost like you unleash this storm of immune reactivity and inflammation."

Once the storm is set off, doctors say treating the infection itself is unlikely to help much.

So, what could help? As physicians report more symptoms, scientists working in parallel are exploring why and how the virus replicates in some tissues and organs so well.

Matthew Miller, an associate professor of infectious disease and immunology at McMaster, is following the scientific advances.

The virus seems to use a receptor called ACE2 to enter human cells. Miller said many groups of researchers are working to understand what cells in our body have active proteins where the virus might be able to replicate and cause disease.

"Knowing what cells a virus is capable of infecting is really important, because it can help us anticipate what types of diseases or what types of symptoms it might cause," Miller said.

It's thought that the infectious dose a person is exposed to, as well as minute, genetic differences in the individual and whether they have underlying health conditions (like heart disease or diabetes) all play a role in how COVID-19 manifests.

Understand virus to guide reopening

For now, medical researchers are exploring how ramping up a beneficial aspect of the immune response that cells normally use to kill off a virus could be complemented with "immune modulators" to tamp down overreactions. It's a delicate balance and timing is key.

Miller said as we learn more about the unique features of SARS-CoV-2, governments and public health officials have been forced to "learn on the fly" and adapt pandemic plans built for a different respiratory infection: influenza, commonly called flu.

"One of the areas that this pandemic has really brought to light is that there's not enough focus on prevention control measures," he said.

Countries imposed and eased lockdowns without a firm grasp on what measures work best for this particular virus, leading to differences across the globe and shifting recommendations on wearing masks or physical distancing.

"I think we're all learning that we don't understand nearly as well as we should," Miller said.

Public health basics like staying home when sick, handwashing and cough etiquette apply to all respiratory pathogens. It's the specifics that are still a work in progress.

For Saxinger, these knowledge gaps mean that understanding COVID-19 will be a long-term effort.

"It's not just going to be a one, we're done," Saxinger said. "We are all going to have to figure out the best way to manage people and try to give them the best outcomes possible."

Could a simple gas produced by our bodies be used to treat COVID-19? Canadian trials underway

<https://www.ctvnews.ca/health/coronavirus/could-a-simple-gas-produced-by-our-bodies-be-used-to-treat-covid-19-canadian-trials-underway-1.4962611>

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Media Outlet: CTV News

TORONTO -- In the race to find an effective, low-cost treatment for COVID-19, a powerful molecule that has long captured the attention of medical researchers is gaining popularity.

Nitric oxide, a two-part nanomolecule made in the cells that line the blood vessels, is being examined as an experimental treatment for the disease caused by the novel coronavirus. Studies show it plays a role in helping to relax blood vessels and open the airways in the lung -- critical in treating those with advanced cases.

Among the companies vying to harness this naturally produced gas is a Canadian firm that is experimenting with using nitric oxide nasal spray or mouth gargles that may help those at a high risk of becoming infected from contracting COVID-19 in the first place.

SaNOTize Research has been given a \$400,000 grant from the National Research Council and is now conducting phase two of a clinical trial on people at high risk for contracting COVID-19, including front-line workers, and those with mild symptoms of the disease.

The trial, which started in British Columbia, is being expanded to participants in Quebec come June 1, with talk of an Ontario-based study in the near future.

"It's really important we get this trial done as soon as possible and then we can work with regulatory authority, then we can turn it around in three to four months," Chris Miller, SaNOTize Chief Scientific Officer, told CTV News.

Nitric Oxide has many properties -- it's produced by cells that line our blood vessels to help control blood pressure and open the airways in the lung, allowing more oxygen to be absorbed.

But researchers have also found nitric oxide has an antibacterial and antiviral effect.

SaNOTize's nasal spray is designed to "disinfect" your upper airway using nitric oxide. Initial tests of the company's product suggest that the spray inactivated more than 99.9 per cent of SARs-CoV-2, the virus that causes COVID-19, within two minutes during laboratory tests.

"You're using a hand sanitizer to disinfect your hands. It's a similar idea, but instead of a hand sanitizer, it's a nasal spray to disinfect your upper airway," SaNOTize CEO Gilly Regev told CTV Vancouver.

With no confirmed therapeutic treatment for COVID-19, researchers around the world have turned their attention to the molecule once dubbed "molecule of the year."

With its role in the human body discovered in the 1980s, nitric oxide is already approved for use in helping improve oxygen levels in premature babies and is used in some cardiac procedures and drugs for erectile dysfunction.

One of the studies suggesting it may have potential as a tool against COVID-19 is a report by Dr. Roham Zamanian, a pulmonologist at Stanford Health Care in California. His team gave nitric oxide to a woman suffering from pulmonary arterial hypertension who had also developed COVID-19.

Doctors treated her at home, adding the gas to her oxygen supply.

Over the course of 11 days, the patient improved and didn't need hospital care.

"We saw an improvement in her symptoms, we saw an improvement in her ability to walk distances over six minutes, which is our usual test of cardiopulmonary reserve," Zamanian told CTV News.

"We were able to document that she was feeling better and better as we provided her with the nitric oxide, until day 15, 16 where we want to begin to wean the medication off."

Her recovery encouraged Zamanian so much that his centre is now launching a study of inhaled nitric oxide in hospitalized patients and those recovering at home

Another study is underway at the University Health Network in Toronto to see whether high dose inhaled nitric oxide given in hospital can reduce levels of the virus and improve breathing in COVID-19 patients on ventilators.

Scientists in Boston and Louisiana are also giving several hundred severely ill patients nitric oxide, with preliminary results expected in the coming weeks. Several devices that produce nitric oxide have also been given the green light for testing in the U.S.

Researchers say side effects from the gas are minimal and they hope to have more data on the various approaches later this year, before the expected second wave of the disease.

Meanwhile, watching from the sidelines, is one of the three Nobel Prize winning scientists responsible for discovering the molecule some two decades ago.

"There's every reason to believe that the nitric oxide will work in the present coronavirus situation," American pharmacologist Lou Ignarro told CTV News.

"That's going to be worth much more than the Nobel Prize I will be so happy. You know I'm 79-years-old and this would just be the, the most fantastic thing I could hear."

Canadian Blood Services asks former COVID-19 patients to donate plasma

https://www.cbc.ca/news/canada/ottawa/ottawa-coronavirus-plasma-donations-1.5589501?_vfz

Date Published: May 29th, 2020

Media Outlet: CBC News

Canadian Blood Services needs more people who have recovered from COVID-19 to donate plasma for a project that could potentially help others suffering from the respiratory illness.

The project called CONCOR, is trying to figure out if plasma from previous COVID-19 patients could provide antibodies to help current patients fight the disease more effectively. Blood plasma is the straw-coloured liquid component left when blood cells are removed from whole blood.

Sixty Canadian hospitals are involved in the research, including The Ottawa Hospital.

About 1,200 Canadians have registered to donate their plasma and a few dozen have already made donations — but Canadian Blood Services says they always need more volunteers.

In order to determine if the treatment works, the trial eventually needs to inject 1,200 COVID-19 patients with the convalescent plasma, said Dana Devine, chief scientist at Canadian Blood Services.

"In order for us to provide the plasma to support all those trials, we figured that we really need about 1,800 people in our collection space," she said.

"The first two patients that were done in Ontario, my understanding from secondhand, is that those patients are doing well....I'm not sure what that means against anything else, but at least nothing bad has happened to the first two."

Ottawa man lends an arm

Ernie Cecchetto was the first person to donate plasma in Ottawa, according to Canadian Blood Services. He tested positive for COVID-19 after a trip to Mexico in March. He says the illness was like nothing he had experienced before.

"I liken it to a paralysis of the lungs," he said. "Like your lungs, [your] ability to oxygenate your blood, is just not there."

"What tears you up is seeing all the stories about the front-line workers, nurses and doctors, that get this COVID because they're exposed to so much virus, and their bodies can't fight it," he said

"When I heard about this program, understanding that I probably developed a certain amount of the antibodies, it's incumbent on me to do something."

Not everyone can donate plasma to the program. Donors must be younger than 67, have had a confirmed test for COVID-19 and be symptom free for at least 28 days.

For now, only men are able to donate because women may carry antibodies related to pregnancy which can react in a patient causing lung injury. Canadian Blood Services plans to screen for this soon, so women can still register to donate.

More hospitals part of plasma transfusion trial to treat COVID-19 with antibodies

<https://www.cp24.com/news/more-hospitals-part-of-plasma-transfusion-trial-to-treat-covid-19-with-antibodies-1.4958340>

Date Published: May 28th, 2020

Media Outlet: CP24 News

TORONTO -- The first two COVID-19 patients in Canada to receive plasma transfusions rich in antibodies are showing signs of improvement as the experimental treatment expands to trials in more than a dozen sites in Ontario and Quebec.

A senior media adviser for CHU Sainte-Justine hospital in Montreal says the outlook is "favourable" for a female patient who was the first to receive a transfusion May 15, noting she has been released from intensive care.

Meanwhile, a 78-year-old man who received the second transfusion May 22 at University Health Network's Toronto General Hospital was expected to make a full recovery, says his physician, Dr. David Hwang.

The patients are part of a controlled, randomized trial that is testing whether a transfusion of plasma donated by recovered COVID-19 patients can reduce deaths and speed up recovery.

The hope is that the influx of another person's antibodies will help an infected patient battle COVID-19 until their body can develop its own virus-fighting antibodies.

At least five patients had received transfusions by Wednesday, with more joining the trial daily. Researchers hope to study 1,200 participants in about 60 medical centres, 800 of whom will receive transfusions while 400 will be part of a control group that gets no transfusion.

A lead scientist for the CONCOR-1 study, Dr. Jeannie Callum of Toronto's Sunnybrook Health Sciences Centre, says the trial will be expanded to at least 20 hospitals by the weekend, most of them in Ontario but including a handful in Quebec, and three in New York City.

Callum, director of utilization for the department of laboratory medicine and molecular diagnostics, says researchers are targeting hospitals "with the highest activity" of COVID-19 cases.

"We're going to have one to two (trial participants) per day for the next two weeks. And then past that point we're going to be above our target which is to have three patients per day," says Callum, estimating it will take six months to study 1,200 patients.

Hwang says his patient was admitted two weeks ago for issues related to dementia but was tested and diagnosed with COVID-19.

The patient displayed no respiratory symptoms but breathing trouble emerged late last week, and he soon required an increasing amount of supplemental oxygen, says Hwang.

The need for oxygen also qualified the senior for the trial, says Hwang, and the man was quickly enrolled and randomly chosen for a transfusion the same day, a speedy progression Hwang chalks up to "a little bit of luck."

"We were preparing for things to worsen even further," says Hwang, a specialist in internal medicine.

"Some people plateau off, but there was no reason to believe that he was going to manage this himself. He's 78-years-old, he's a frail man."

Since then, the man's breathing has improved, although he still required some supplemental oxygen this week, says Hwang.

Dr. Christine Cserti, transfusion medicine specialist at University Health Network, outlined a massive coordinated effort to design and implement the trial in mere weeks as a global pandemic ravages many parts of the world, stifles economies and stretches health-care resources.

"What I saw on Friday, it just warmed me to no end," Cserti says of seeing the work culminate in Toronto's first COVID-19 plasma transfusion.

"People really just want this to work."

Of course, the use of convalescent plasma to treat an illness is not new. Among the ailments it has been used for is the 1918 influenza outbreak -- also known as the Spanish flu.

Callum says somewhere between five and eight per cent of people admitted to hospital get plasma for other reasons, and it's generally considered a safe procedure.

Cserti allows there's a "one to 10 per cent chance of a transfusion reaction," but that getting something like COVID-19, HIV, Hepatitis B or West Nile virus from a transfusion is "like being struck by lightning."

"These are things we all do sophisticated testing for," she says. "We feel really reassured about our blood supply."

A more serious complication is a lung injury called TRALI or transfusion-related acute lung injury, in which air sacs are flooded with fluid but Cserti pegs the chance of that happening at "one in 1,000 to one in 100,000."

If the trial is successful, there would be several challenges to employing plasma transfusions as a standard approach to treating COVID-19.

Callum notes it would require a significant increase in plasma donations, which must come from those younger than 67 who have fully recovered from COVID-19 and are symptom-free for at least 28 days.

"That would compete for slots for people to donate platelets that we need for people that have acute leukemia or cardiac surgery," says Callum. "So, we need to know it works."

Cserti notes there are cases where a plasma transfusion hasn't helped a COVID-19 patient, and although a much-touted U.S. COVID-19 trial involving 5,000 transfusion subjects suggested the approach was safe, it did not have a control group like this smaller Canadian-led study.

"There's always flash and pizzazz on early anecdotes, right?" says Cserti.

"Everybody says: 'Oh, this works so well,' and it's not until you get a control group chugging alongside that you say, 'OK, maybe this isn't that much better.'"

Hwang is optimistic there are benefits, noting the transfusion appears to reduce the time needed on supplemental oxygen and may allow a patient to get out of bed earlier.

But he doesn't expect it to be the treatment that will take down COVID-19.

"It's very resource-intensive. You need to get donors and go through this lengthy process just to get one unit of plasma. And, it's not even a preventive measure. It's just (something that is) modulating the disease or augmenting the trajectory of it," he says.

"I don't think this is going to be our answer to COVID, but it might be what will save some lives down the road."

This report by The Canadian Press was first published May 28, 2020.

At least 47 children in Canada investigated for inflammatory syndrome linked to COVID-19

<https://www.theglobeandmail.com/canada/article-at-least-47-children-in-canada-investigated-for-inflammatory-syndrome/>

Date Published: May 27th, 2020

Media Outlet: The Globe and Mail

Doctors in four provinces are now investigating cases of a mysterious syndrome in children that is believed to be linked to the coronavirus, but the suspected Canadian cases have not been as severe as those reported in New York and London, where a handful of children have died.

Alberta's Chief Medical Officer of Health announced Wednesday that doctors are looking into one suspected case in the Calgary health region, while British Columbia is investigating at least six cases.

The Hospital for Sick Children in Toronto and Sainte-Justine Hospital in Montreal are examining an estimated 20 possible cases each.

"It's still pretty rare," said Jeremy Friedman, the associate chief of pediatrics at SickKids. "The children, particularly the ones where I've been personally involved in their care, have actually not been that sick. That's a bit of a different message from when I first read the reports from New York and London."

Hundreds of children in New York and Europe have been sickened by the baffling new multisystem inflammatory syndrome, which features the overlapping symptoms of toxic shock, upset stomach and Kawasaki disease, a rare childhood illness that inflames blood vessels, most dangerously in the heart.

Pediatricians in London first alerted the world to the syndrome in late April. Not long after, New York, Italy, Spain and other places hit hard by the novel coronavirus began reporting similar cases, sometimes in children who tested positive through nasal swabs for active infections of COVID-19.

In other cases, blood tests found children had antibodies to the coronavirus, meaning they had been infected with the virus in the past.

In Canada, doctors are still trying to determine what connection the local cases might have to the coronavirus – a task that is proving difficult because antibody tests are not yet available, despite Health Canada having approved two such tests.

Dr. Friedman of SickKids said laboratories in Canada are working feverishly to verify the accuracy of the antibody tests, which have sometimes been unreliable in countries that rushed them into the field.

"I'd rather that we had a test we could rely on, even if it is a bit delayed, than jump to a test [where] we might be acting on faulty information," he said.

Blood samples have been drawn from the approximately 20 children identified as possible cases at SickKids over the past three or four weeks, Dr. Friedman added. Despite none testing positive for an active coronavirus infection, he expects many will be positive for coronavirus antibodies.

Deena Hinshaw, Alberta's Chief Medical Officer of Health, said Wednesday that while little is known about the illness, it appears the inflammatory syndrome related to COVID-19 shows up several weeks to a

month after a child or adolescent is infected with the coronavirus. "Typically, a child who has this particular syndrome, would not be considered – again, for what we know right now – to be infectious or infected with COVID at that point.

"It seems to be more something that happens as a result of their immune system going into overdrive after an infection and causing this inflammatory response in multiple organs."

Dr. Hinshaw said the child being treated in Alberta is in stable condition in hospital.

On Monday, B.C. Provincial Health Officer Bonnie Henry said at least six cases of the syndrome were under investigation in her province.

In Montreal, Marie-Paule Morin, a pediatric rheumatologist at Sainte-Justine, agreed with Dr. Friedman that the cases she and her Canadian colleagues have seen so far have been less severe than the frightening reports in other countries. Only two of Sainte-Justine's suspected cases required treatment in the intensive-care unit, Dr. Morin said Wednesday, and none tested positive for an active coronavirus infection.

No Canadian children are known to have died of the illness.

Dangerous blood clots pose a perplexing coronavirus threat

<https://www.cbc.ca/news/health/covid19-clots-coronavirus-1.5585582>

<https://www.ctvnews.ca/health/coronavirus/dangerous-blood-clots-pose-a-perplexing-coronavirus-threat-1.4956038>

Date Published: May 26th, 2020

Media Outlet: CBC News, CTV News

First came a high fever, drenching sweats and muscle aches. Then, almost a month later, a weird numbness that spread down the right side of her body.

Darlene Gildersleeve thought she had recovered from COVID-19. Doctors said she just needed rest. And for several days, no one suspected her worsening symptoms were related -- until a May 4 video call, when her physician heard her slurred speech and consulted a specialist.

"You've had two strokes," a neurologist told her at the hospital. The Hopkinton, New Hampshire, mother of three is only 43.

Blood clots that can cause strokes, heart attacks and dangerous blockages in the legs and lungs are increasingly being found in COVID-19 patients, including some children. Even tiny clots that can damage tissue throughout the body have been seen in hospitalized patients and in autopsies, confounding doctors' understanding of what was once considered mainly a respiratory infection.

"I have to be humble and say I don't know what's going on there, but boy we need to find that out because unless you know what the pathogenic (disease-causing) mechanism is, it's going to be tough to do intervention," Dr. Anthony Fauci, the nation's top infectious disease expert, remarked during a medical journal interview last month.

Doctors and scientists at dozens of hospitals and universities around the globe are seeking answers while trying to measure virus patients' risks for clots and testing drugs to treat or prevent them.

Gildersleeve said health authorities "need to put out an urgent warning about strokes" and coronavirus. Not knowing the possible link "made me doubt myself" when symptoms appeared, she said.

Some conditions that make some COVID-19 patients vulnerable to severe complications, including obesity and diabetes, can increase clot risks. But many authorities believe how the virus attacks and the way the body responds both play a role.

"COVID-19 is the most thrombotic (clot-producing) disease we've ever seen in our lifetime," said Dr. Alex Spyropoulos, a clot specialist and professor at Feinstein Institutes for Medical Research in Manhasset, New York.

Clotting has been seen in other coronavirus infections, including SARS, but on a much smaller scale, he said.

Scientists believe the coronavirus enters the body through enzyme-receptors found throughout the body, including in cells lining the inside of blood vessels. Some theorize that it may promote clotting by somehow injuring those vessels as it spreads. That injury may cause a severe immune response as the

body tries to fight the infection, resulting in inflammation that may also damage vessels and promote clotting, said Dr. Valentin Fuster, director of Mount Sinai Heart hospital in New York.

It's unclear how many COVID-19 patients develop clots. Studies from China, Europe and the United States suggest rates ranging from 3% to 70% of hospitalized COVID-19 patients; more rigorous research is needed to determine the true prevalence, the National Institutes of Health says.

Prevalence in patients with mild disease is unknown and the agency says there isn't enough evidence to recommend routine clot screening for all virus patients without clotting symptoms, which may include swelling, pain or reddish discoloring in an arm or leg.

Some hospitals have found 40% of deaths in COVID-19 patients are from blood clots. Spyropoulos said that's been true at his 23-hospital system in the New York City area, Northwell Health, which has treated over 11,000 COVID-19 patients.

Cases there have dropped by almost half in the past month, allowing more time for research before an expected second and maybe third wave of infections, he said, adding: "We're racing against time to answer the key clinical questions."

Patients hospitalized with any severe illness face increased risks for clots, partly from being bedridden and inactive. They commonly receive blood-thinning drugs for prevention. Some doctors are trying higher-than-usual doses for prevention in hospitalized coronavirus patients.

A few have used powerful clot-busting medicines typically used to treat strokes, with mixed results. In guidance issued May 12, the NIH said more research is needed to show whether that approach has any benefits.

Fuster was involved in preliminary research on nearly 2,800 COVID-19 patients at five hospitals in the Mount Sinai system. A look at their outcomes suggests slightly better survival chances for virus patients on ventilators who received blood thinners than among those who didn't. Although the results are not conclusive, all COVID-19 patients at Mount Sinai receive blood thinners for clot prevention unless they are at risk for bleeding, a potential side effect, Fuster said.

Some COVID-19 patients, like Gildersleeve, develop dangerous clots when their infections seem to have subsided, Spyropoulos said. Patients treated at Northwell for severe disease are sent home with a once-a-day blood thinner and a soon to be published study will detail their experiences. Spyropoulos has been a paid consultant to Janssen Pharmaceuticals, makers of Xarelto, the drug's brand name.

In addition, Northwell is taking part in a multi-centre study that will test using blood thinners for clot prevention in COVID-19 patients not sick enough to require hospitalization.

In a small study published May 15, University of Colorado doctors found that combined scores on two tests measuring clotting markers in the blood can help determine which patients will develop large dangerous clots. One test measures a protein fragment called D-dimer, a remnant of dissolved clots. High levels sometimes indicate dangerous clots that form deep in leg veins and travel to the lungs or other organs.

Dr. Behnood Bikdeli of Columbia University's Irving Medical Center, said D-dimer levels in many of his COVID-19 patients have been alarmingly high, as much as 50 times higher than normal.

Concerns about blood clots in COVID-19 patients prompted a recent 30-page consensus statement from an international group of physicians and researchers. Bikdeli is the lead author.

It says that testing to find clots that require treatment includes X-rays or ultrasound exams, but poses a risk for health care workers because the virus is so contagious. Bikdeli said he fears when protective gear was more scarce, some dangerous clots were undiagnosed and untreated.

Social distancing may make people more sedentary and more vulnerable to clots, particularly older adults, so doctors should encourage activity or exercises that can be done in the home as a preventive measure, the statement says.

Warnell Vega got that advice after collapsing at home April 19 from a large clot blocking a lung artery. Doctors at Mount Sinai Morningside think it was coronavirus-related. Vega, 33, a lunch maker for New York City school children, spent a week in intensive care on oxygen and blood thinners, which he's been told to continue taking for three months.

"I just have to watch out for any bleeding, and have to be careful not to cut myself," Vega said.

Gildersleeve, the New Hampshire stroke patient, was also sent home with a blood thinner. She gets physical therapy to improve strength and balance. She still has some numbness and vision problems that mean driving is out, for now.

Doctors are unable to predict when or whether she'll regain all her abilities.

"I'm trying to remain positive about recovering," she said. "I just have to be patient and listen to my body and not push too hard."

Post mortem of elderly male who died of COVID-19 reveals appalling effects of coronavirus

<https://www.thestar.com/opinion/star-columnists/2020/05/15/post-mortem-of-elderly-male-who-died-of-covid-19-reveals-appalling-effects-of-coronavirus.html?>

Date Published: May 15th, 2020

Media Outlet: Toronto Star

The pathologist snaps a tissue sample under a microscope.

From the palette of samples, including heart, spleen, kidney, trachea, liver, he's chosen the lung for this demonstration. All of it comes from an elderly male who died of COVID-19, one of Ontario's first pandemic victims.

It's a tiny piece of tissue, smaller than a pinkie nail. Shades of pink, mostly, with filaments of red and pinpricks of black.

The white circles are gossamer-like air sacs. Between them, the lungs have somewhere in the neighborhood of six hundred million alveoli. Oxygen travels through bronchial tubes through the spongy part of the lung — millions of alveoli — penetrating their walls.

"That's oxygenation," explains Dr. Michael Pollanen. "That's how the world works. Amazing huh?" There's evidence of inhaled dust, too.

And the black pattern of dots?

"Glad you asked. Oh boy, you're not going to like the answer! What's black in your lung? Smoking. This is what we call carbon pigment and it's present in all city dwellers, more so in smokers. If this man lived in the country, you wouldn't see it. But he lived in the city."

Noting some of the larger alveoli, Pollanen says: "This is emphysema. That's actually smoking-related lung disease. The lungs here are not entirely normal. This is a bit of a clue. His lungs were susceptible because of this."

Susceptible to the coronavirus, susceptible to the COVID-19 that killed him in a very short time.

Some of the air sacs, "you see there's debris in them. And you see what looks like spiderwebs. These are inflammatory cells. They're not supposed to be there."

More clues for what brought about mortality. But the real culprit, the gist of the disease that killed both this man and more than 302,000 people globally, as of this writing, are the Type 2 pneumocytes in the lining of the alveoli.

"In normal lungs, they should not be as prominent as this. They are prominent here, because this is the target of the virus: those cells, the pneumocytes. That's where the SARS-CoV-2 goes into and binds."

Plastering the surface of the cell. The phenomenon that leads to acute respiratory distress syndrome: an inability to breathe, which, at its most severe manifestation, lands patients on ventilators. Two-thirds of them will die anyway.

“This man has a whole bunch of them,” says Pollanen of the pneumocytes.

The spiky virus, with its crown of probes that attach (hence the moniker coronavirus), like suction cups, hijacking the cell, can’t be seen in this slide. But they can be identified under a more powerful electron microscope in the microbiology lab.

“It’s inside the nucleus of the cell. They’re all proliferating and reactive. Then notice over here, these are inflammatory cells. So there’s the inflammation. What’s really interesting — you have to tune your eye to it — is the pink material here. I’m tracing now the wall of the alveolus This pale pink stuff is more feathery. *That* is called a hyaline membrane. And *this* is a sign of severe lung damage.”

Many forms of serious lung damage will cause hyaline membrane. “You could have different viruses that cause the same appearance,” Pollanen points out. “That’s why you have to *demonstrate* the virus.”

He interrupts his non-linear dialogue, as scientist and reporter hunch over microscopes, to admire one particular wedge of the sample. “Ooh, look at that! Chunk of pink. That’s a really beautiful Type 2 right there.”

Beauty is in the eye of the scientific beholder.

For the reporter, Pollanen compresses the vast scientific concepts into a nut-graph: “Inside the alveoli, normally full of gas, we have what? Proliferating pneumocytes, inflammatory cells, hyaline membranes You have solid material inside those microscopic air sacs. That’s why, in an X-ray of the lungs, they would look white, because the X-ray can’t penetrate it. Also, very importantly, oxygen gas has got to go into those alveoli and then get into the blood vessels. That’s very difficult when the alveoli are filling up with this material.”

It’s an extraordinary inside look, literally, at COVID-19 disease.

The Star’s tour guide here at the coroner’s HQ on Morton Shulman Ave. Dr. Pollanen, is not just any ordinary pathologist; he’s Ontario’s chief forensic pathologist. “The brains of it all,” extols Dr. Dirk Huyer, Ontario’s chief coroner, the medico-legal yin to Pollanen’s forensic yang. (The pathology part of the coroner’s system is the Ontario Forensic Pathology Service.)

“I spend a lot of time trying to understand real content. Forensic pathology gives you an amazing perspective on medicine, too. One minute, you’re dealing with the cellular processes of COVID-19, and, the next minute, you’re dealing with skeletal remains from a clandestine grave.”

The men and women who respond to homicides and accidents, and, when deemed necessary, open up the victims from stem to stern.

But while the path of a bullet in the head can be easily traced visually, disease, COVID-19 specifically, is another kettle of fish entirely.

The disease may show itself under a microscope, prove the virus was present, but that doesn’t necessarily mean it actually killed that person.

Could be an underlying condition. Could be a secondary condition.

That's where "clinical pathological correlation" enters the picture — the observations of symptoms and manifestations from everyone who's cared for the patient: lung specialists, nephrologists, cardiologists, neurologists, all the doctors and nurses.

"Then, you look at autopsy and you put it all together," says Pollanen, with a *voilà* gesture.

He's conducted far fewer autopsies on COVID-19 victims than you might imagine. Autopsies have been performed on only a small fraction of bodies and none, apparently, by pathologists working in hospital morgues. (Hospital pathologists do autopsies purely for medical reasons.)

Families don't want their loved ones cut open and the coroner's office is quite considerate of that. There are also risks, although the autopsies are done in self-containment rooms, and those performing them wear protective equipment.

"When you're thinking about potential pathogens, aerosolized in the autopsy room, we will take a minimally invasive approach for health and safety considerations," notes Pollanen. "Because we have to balance what we need to know versus the health and safety of staff."

There's so much, frankly, that isn't known yet about risks.

When a person dies of COVID-19, is the virus dead, too?

"We don't know the details around that."

How long can the virus live inside a cadaver? "You need living cells for the virus to replicate. Once the person is dead, there's no more viral replication."

"But nobody has looked to see how long the virus persists, how long it can remain viable in the body."

Has a COVID-19 cadaver infected a pathologist?

"That's not been documented."

Can bodies still expel air with droplets that might be laden with the virus? "Not like that. But sometimes when you move bodies, you can get gas coming out. Usually from the stomach, gas bubbles moving up. That's not a serious risk."

The coroner's office only does COVID-19-related autopsies when there's a medico-legal issue, questions of causation such as whether there's been neglect in a nursing home.

"For us, it's not purely a medical research interest," says Pollanen.

Which is why, from these findings, we might see an inquest called in the future over the multitude of nursing home COVID deaths in recent months.

"I can't speak to that," says Pollanen, who is also on the faculty of medicine at the University of Toronto, which trains pathologists from around the world. "The factual basis of the matter will become hugely relevant when we analyze this retrospectively."

At the morgues, in Toronto and the regional offices, the autopsy, itself, follows classical protocols: internal examination, weighing of organs, taking samples for laboratory testing (the histology component). An adult lung that normally weighs 250 grams is so saturated with infection and pus in a COVID victim that it can weigh up to 1,000 grams.

The samples provide much broader insights than the swab sample the victim might have had while alive, which only confirms the virus is in the nose.

This is a clever and adventurous virus, biologically.

Its ability to infect and actively reproduce in the respiratory tract, thwarting the body's natural immune system, has stunned doctors.

Evidence suggests that after the virus attaches itself, the host cell snips the spike protein on the invader, triggering a chain of amino acids that help to pry open the host cell's membrane so that the virus's membrane can merge with it.

Once the invader's genetic material gets inside the cell, as described in a recent article in the journal *Nature*, the virus commandeers the host's molecular machinery to produce new viral particles.

Then, those "progeny" exit the cell to go and infect others.

Because, of course, the coronavirus doesn't confine itself to ravaging the lungs; it can push kidneys into renal failure; cause blood clots that impede circulation to the lungs, heart or brain, leading to multiple organ failure as the immune system is overwhelmed.

The classical autopsy has become more sophisticated, primarily through conducting CT-scanning, which sometimes removes the necessity of opening up the body.

But this has its limits.

"There's no substitute for going inside the body and examining tissue under a microscope," says Pollanen. "Taking a sample to determine if the virus is present."

The infection can be patchy or present throughout the lungs. "In other words, there may be areas that are involved and other areas that are not involved. Or it may be diffusely involved. That probably relates to the stage of progression."

Pollanen carefully returns his tissue specimens to their tray.

He knows why this poor man died. The mysteries of COVID-19 are profound. But for this victim, cause of death is not in doubt.

"It's the most fascinating part of medicine," says Pollanen of his specialty. "Because it is the branch of medicine that ultimately underpins everything. Not only disease, but violence, neglect, everything.

"It all starts with the observations made at post-mortem examination. That's the beginning of knowledge, of understanding."

Kids with suspected COVID-related syndrome need immediate attention, doctors say

<https://www.ctvnews.ca/health/kids-with-suspected-covid-related-syndrome-need-immediate-attention-doctors-say-1.4946229>

Date Published: May 20th, 2020

Media Outlet: CTV News

Kids who may have multisystem inflammatory syndrome in children, or MIS-C, a troubling complication of COVID-19 infection, need immediate attention and will probably need to be hospitalized, doctors said Tuesday.

Symptoms do not look like the classic symptoms of coronavirus and may mostly include stomach pain and vomiting, along with fever and perhaps a rash, the experts told other doctors during a meeting Tuesday organized by the U.S. Centers for Disease Control and Prevention.

It's becoming clear that many of the children with the new syndrome have damage to their hearts and need immediate treatment, they said at the Clinician Outreach and Communication Activity (COCA) briefing. And they believe it's increasingly clear that COVID-19 is involved, even though many of the children test negative for the virus at first and never seemed to have had symptoms of infection.

The syndrome appears to develop two to six weeks after infection with COVID-19 and affects mostly children who were perfectly healthy beforehand. The CDC issued a health alert last week warning pediatricians to be on the lookout, and at least 20 states plus Washington, DC have reported they are investigating possible cases.

"A striking finding here -- alarming -- is that in this group, about half the children already had coronary artery abnormalities," Dr. James Schneider, who heads pediatric critical care at Northwell Health in New York, told the briefing. Because the children were previously healthy, he thinks the abnormalities were caused by MIS-C, possibly as a result of a delayed immune response to the coronavirus.

"Any child at home who has fever, abdominal pain or symptoms such as rash and conjunctivitis should be seen by a pediatrician right away," he advised. "I think we need to have a low threshold for evaluation."

'Alarming' findings

More than half of the 33 children treated for MIS-C at Northwell in April and May had developed some sort of heart dysfunction, Schneider said. "They need good, old-fashioned critical care."

And most of the children had no underlying conditions that might make parents wary. "No definitive underlying conditions predispose children to this," he said.

Infectious disease specialist Dr. Nicholas Rister at Cook Children's Medical Center in Fort Worth, Texas, said he has examined several children with a range of symptoms.

"I feel very terrible -- some patients have said, you know, everything kind of hurts. And then swelling in various points of your body, especially your hands and your feet, and even your mouth," he said at a separate briefing.

"The biggest concern we have right now, especially in kids, is largely stemming from inflammation around the heart," he said. It's one reason doctors at first thought the syndrome was a rare condition known as Kawasaki disease. "And not just the heart but the major vessels around the heart," he added.

Dr. Michael Levin of Imperial College in London, who treated some of the first patients in Britain, said parents may hesitate to bring their children in, but they should.

Some of the children he and his colleagues have treated were already critically ill when they arrived at the hospital. "One of the reasons for this may have been the lockdown and fear of coming to hospital," he said. "The public health message in the UK was that patients should try and stay at home and not attend hospital," he added. So children were staying home with fevers ... and arriving in a seriously ill state."

Blood tests will quickly tell doctors if children might be experiencing MIS-C, Levin said. Tests for inflammation and heart damage can show if children are at risk and need to be hospitalized.

Quick treatment appears to work and most children go home after a few days in the hospital, both Schneider and Levin said.

Levin said most children tested negative for COVID-19 infection at first but later tests indicated they had probably had a past infection.

He said these young patients were showing symptoms of extreme inflammatory response. "There is a concern that we are seeing a dysregulated immune response," Levin told the briefing. "The timing of this illness does seem to coincide with when acquired immunity would be developing."

Many of the children in England who were diagnosed with MIS-C are from ethnic minorities, Levin said. "There seemed to be a predominance of children from black, African, Caribbean-British ancestry who accounted for about 46% of the cases," he said.

Twenty-seven percent of the children with the illness in a recent New York study were Hispanic, Northwell's Schneider said.

COVID-19: Here are the questions about the virus we still can't answer

<https://www.ctvnews.ca/health/coronavirus/covid-19-here-are-the-questions-about-the-virus-we-still-can-t-answer-1.4944990>

Date Published: May 19th, 2020

Media Outlet: CTV News

TORONTO -- As countries tentatively begin to relax lockdown restrictions in bids to revive their economies, many questions remain about the novel coronavirus and its effect on people.

Despite the tireless efforts of doctors, scientists, and researchers around the world, there are still lingering questions about the transmission of the virus, how it sickens individuals, and what will happen next.

Rob Kozak, a clinical microbiologist at Sunnybrook Hospital in Toronto who helped isolate the SARS-CoV-2 virus in March, said it's important to remember that people really only became aware of the virus five months ago.

"It hasn't been with us for long enough. We're just sort of starting to see now the follow-up on people who perhaps got infected in January and have recovered and what will happen with them," he told CTVNews.ca during a telephone interview on Thursday.

And, although quarantined individuals are eagerly anticipating a return to normalcy, researchers say the answers to questions about how that will happen could still be many months away.

Here are 10 important questions about the coronavirus from experts who are trying to answer them.

HOW MANY PEOPLE HAVE BEEN INFECTED?

Kozak said it's difficult to know how many people have truly been exposed to the virus because some of them may have been asymptomatic, meaning they had no symptoms. Others may have only experienced such mild symptoms that they weren't even aware they had COVID-19.

While the extent of exposure isn't clear now, Dr. Isaac Bogoch, an infectious diseases physician and scientist with the Toronto General Hospital, said it will be possible to answer that question eventually with the use of serology tests or blood tests.

"You don't have to do serology on every single Canadian, but you can certainly do serologic assays on a representative portion of Canadians and use mathematical modelling to estimate what the true burden of infection was," he explained.

Bogoch said he expects the number of cases will be "enormous" once the tally is conducted.

"The numbers that we have are clearly an under-reflection of what the true burden of illnesses is," he said.

HOW DO CHILDREN TRANSMIT THE VIRUS?

While children appear to be less affected by the coronavirus than older generations, Bogoch said it's still unclear what role they play in transmitting it to others. He also said they still don't know if children are being infected, but are affected differently than adults.

Jude Uzonna, an immunologist and infectious diseases researcher at the University of Manitoba, said there is now evidence that children are experiencing widespread and systemic inflammatory response syndrome, which is similar to an inflammatory illness called Kawasaki disease.

"It's still unanswered," he said. "If it is true, that young kids are really having this kind of condition, are you going to be sending your kids back to school?"

WHAT IS THE SEVERITY OF ILLNESS?

In addition to early evidence of a potentially dangerous inflammatory response in children, both Bogoch and Kozak said it's still too early to know what the spectrum of the illness is in different individuals.

Bogoch said they're still trying to understand how the virus affects blood clotting in some patients, for example, or why some people have reported a loss of smell or taste. He said they're also still in the process of studying how the virus binds to different parts of the body, such as brain cells and kidney cells.

While there has been a lot of attention given to the question of why some individuals are harder hit by the disease than others, Kozak said researchers still don't have concrete answers to that either.

"If you and I both got exposed to COVID-19, maybe I end up in the ICU (intensive care unit) with very severe disease and you get the sniffles and don't even go to get tested because you're not aware you're sick," he said. "We don't know what the reasons are for that discrepancy if we're both exposed to the same virus."

CAN PEOPLE DEVELOP IMMUNITY TO THE VIRUS?

Although there has been plenty of talk of concepts, such as "herd immunity" and "immunity passports," which are based on the premise that people who contract the virus won't be able to get it again, Uzonna said they still don't actually know if patients can develop a protective immunity to the virus and if they can, how long it would last.

"There are different types of immunity, for example, something like a smallpox will give you an immunity that is lifelong. Some immunities will just go away within a year or two," he explained.

Kozak said preliminary data suggests patients who contract the virus develop antibodies that will likely be protective against a second infection, but he said they still don't know enough about the disease's correlates of protection, which are markers that can be measured in a lab to determine whether someone is protected.

WHEN IS SOMEONE NO LONGER INFECTIOUS?

Furthermore, in addition to not knowing how long someone may be immune to coronavirus, Kozak said they also don't know when a patient is no longer infectious. He said there is interesting data from Germany and the U.S. Centers for Disease Control (CDC) that suggests people may not be shedding the infectious virus about eight or nine days after they develop symptoms, but they still don't know for sure.

“We need to do lots of studies on lots of patients to truly see when a patient is no longer infectious, even though there may still be viral nucleic acid present in their nose or in their throat.” he said.

“That’s often a problem because you’ll be testing someone and they’ll still be positive, but maybe they’re not shedding virus anymore.”

HOW WILL MUTATIONS AFFECT THE VIRUS?

There have been studies claiming to show the coronavirus has mutated into more virulent strains; however, Kozak said that is still not certain.

“It is entirely possible that there are mutations that are associated with either worse disease or more mild disease,” he said. “So from a virology standpoint, that’s what we would want to look for. We want to know if there are any mutations where you’re more likely to get admitted to hospital and maybe the ICU or you’re more likely to be fine and just be able to go home.”

Kozak said that information will also be helpful in understanding why certain individuals become sicker than others and whether that’s related to an individual strain of the virus or their genetic predisposition, or a combination of both of those factors.

WILL THERE BE COMPLICATIONS AFTER RECOVERY?

With a lot of diseases, Kozak said patients will often develop complications from it months or even years after they have recovered.

For example, in the aftermath of the West African Ebola outbreak, Kozak said survivors experienced a lot of rheumatological or eye problems, even after they had recovered.

“So what we don’t know with patients, will there be a syndrome of like a viral syndrome, which occurs in patients after they’ve recovered from COVID?” he asked.

Kozak said it’s still too early to be able to answer those questions because they’re only starting to study the long-term effects on patients who recovered in January.

WHY ARE SOME AREAS HARDER HIT?

Uzonna said researchers are still unable to explain why some populations have been harder hit by the pandemic than others. He said many experts predicted that Africa would be devastated by the virus due to inadequate infrastructure and healthcare, but that hasn’t happened yet.

“Nobody has seen anything like that. So why is that? Why is Africa so far doing relatively OK compared to other countries?” he asked.

Uzonna said African nations aren’t taking more precautions than other countries so he wondered if there are other contributing factors.

“I don’t think it’s related to genetics because if you look in the U.S., the majority of the people who die are African Americans. I don’t think the African American have changed so significantly over time so there must be something that we don’t know yet,” he said.

HOW DO WARM TEMPERATURES AFFECT THE VIRUS?

Because the flu is considered a seasonal illness that affects more people in the colder months, some people have wondered if the coronavirus will follow the same trajectory and weaken in the summer.

Uzonna said they don't know how warmer temperatures will affect SARS-CoV-2 because it's different from the virus that causes the common flu.

Bogoch said they can't rely on data suggesting that warm temperatures and ultraviolet rays will decrease the spread of coronavirus because places such as Ecuador, El Salvador, and Bangladesh have all experienced intense outbreaks despite their warm climates.

WILL THE VIRUS DISAPPEAR COMPLETELY?

While Bogoch and Kozak said they're confident scientists will be able to develop a vaccine to protect against COVID-19, they said it's still not clear how protective it would be and how long the protection would last.

"Is the vaccine going to be 100 per cent protective? Or is it going to be like the flu vaccine where it significantly reduces your risk of getting this infection, but doesn't eliminate your risk of getting this infection?" Bogoch said.

"And if people get infected, is there the possibility that with the vaccine, they just might mitigate some of the severity of the infection that they'll have."

Although it may seem like there are still so many questions to be answered, Bogoch, Kozak, and Uzonna all agreed that most of them will have answers eventually.

"I'm cursed with a streak of optimism," Kozak said. "I think that people will find answers to these."

While he understands the public is eager for answers, Uzonna said they might have to be patient a while longer.

"Science is a rigorous process," he said. "I understand it. People want to get answers. People want them because of what is happening, but these things take time."

Could the blood of recovered COVID-19 patients be used to treat the virus? Canada is launching a trial to find out

<https://www.thestar.com/politics/federal/2020/05/02/could-the-blood-of-recovered-covid-19-patients-be-used-to-treat-the-virus-canada-is-launching-a-trial-to-find-out.html>

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OTTAWA –In late February Jerry Glubisz picked up a nasty bug going around in his Vancouver office. High fever, brutal cough and unrelenting fatigue.

“Worst flu I ever had,” said the 63-year-old. By the time a lab test confirmed COVID-19 on Mar. 19, Glubisz was already feeling “80 per cent better.” He didn’t have to be hospitalized or put on a ventilator. Now, more than a month after his symptoms eased, Glubisz feels “on top of the world.”

And his blood plasma just might be key to keeping someone else off a ventilator or preventing them from needing intubation.

It’s called “convalescent plasma” — using a survivor’s blood that has antibodies to rev up the immune system of a sick patient — an old idea once used in the Spanish flu being applied to the novel coronavirus sweeping the world.

Canada’s first national clinical trial to test that theory is about to get underway after Health Canada rushed to approve research that was co-ordinated by scientists and researchers on Zoom and late-night calls.

On Wednesday Glubisz became the first COVID-19 survivor to donate his “hopefully” antibody-rich plasma to the Canadian Blood Services’ new national COVID-19 convalescent plasma collection program.

It will be screened for any other viruses like Hepatitis B or HIV.

And within a week to 10 days, as the trial launches, potentially life-saving plasma could be used to jump-start the immune systems of patients in downtown Toronto and Montreal hospitals.

It’s a national collaborative clinical trial, one of the largest — and swiftest to be mounted — in Canada, co-ordinated with the two public blood agencies. So far 50 hospitals have registered to participate, though they are at various stages of their own internal approvals. The CANCOR trial, as it’s called, was approved by the federal regulator on April 16.

Led by Dr. Donald Arnold, director of the McMaster Centre for Transfusion Research who teaches at McMaster’s medical school, the trial will enrol 1,200 patients, 800 of whom will receive antibody-rich plasma, while the other 400 will receive the standard of care now used in intensive-care units.

The plan is to focus on areas that have the highest demand immediately — the hardest-hit hospitals are in downtown Toronto and Montreal — and to roll it out across the country as soon as possible. With luck, he says, it will be able to hit its intended target of 1,200 patients over the next four months.

There is a contingency plan to look at the data halfway through the trial to examine whether “there is an overwhelming effect here that’s good enough for us to say, ‘this works we should just open it up,’” Arnold said in an interview.

“It’s important to do this fast,” he said. “But it’s important to do it right, because if you don’t do it right then we still never get to an answer of whether or not this works.”

In the U.S. scientists and researchers are also mounting clinical trials, including one in New York with a planned enrolment of 500 hospitalized patients.

Arnold said as far as he knows, “none of them as big and none in the same population or at least not as big in the population we’re doing.” That is, hospitalized COVID-19 patients with respiratory illness, needing oxygen. “They’re not yet that sick,” he said.

“The point is for us to try to prevent them from getting that sick, and not needing the ICU or not needing the ventilator.”

The Food and Drug Administration says “although promising, convalescent plasma has not yet been shown to be safe and effective as a treatment for COVID-19.”

However the FDA has approved ways for doctors to use it in individual cases before the results of scientifically rigorous clinical trials are available. And early observations of about 2,600 patients who’ve received convalescent plasma outside clinical trials are encouraging, the Milwaukee Journal-Sentinel reported earlier this week. It quoted Mayo Clinic researchers who are trying to keep tabs on those case-by-case treatments.

A report Thursday in the Journal of American Medicine cautioned, however, that globally there is a dearth of randomized controlled trials on the value of convalescent plasma for COVID-19 patients. The only reports in medical literature are from a handful of cases in China.

Canada’s chief public health officer Dr. Theresa Tam refused to discuss any positive signals coming from the American efforts, or say when the treatment might be made more widely available in Canada, saying only that there are “many treatments currently in trial and convalescent plasma is one.”

Canadian Blood Services chief scientist Dr. Dana Devine says the public blood authority and its Quebec counterpart Héma-Quebec are now recruiting donors from among the more than 20,000 recovered patients in Canada.

The blood agencies are seeking male donors under 67, who’ve had a positive lab test for the coronavirus and have been symptom-free for four weeks. (Women’s blood, especially if they’ve been pregnant, often contains antibodies that complicate transfusions, she explained.)