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(U) Syria: Report Details 'Malicious' Plan by Hizballah, Iranian Militias To Spread COVID- 19 in Idlib

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(U) On 5 April, media sources revealed that Iranian militias were working on a malicious plan to spread the coronavirus [COVID-19] in the liberated areas in northwest Syria.

(U) The media office in the area south of Aleppo cited what it described as a private source as saying that a number of Iranian officers and Hizballah militia commanders held a meeting in the

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'Abtin area to discuss the possibility of transmitting COVID-19 to areas outside the control of the regime of [Syrian President Bashar] al-Asad.

(U) The source added that the meeting centered around the possibility of transmitting the virus through commerce or infected civilians. The significance of transmitting the virus to overpopulated [refugee] camp areas on the border with Turkey was also discussed, noting that the purpose of this was to create chaos in the area for military advantage.

(U) Shahm Makki, the physician in charge of the epidemiological surveillance laboratory, announced in media statements that there were no cases of COVID-19 in Idlib after tests conducted on 33 people believed to be infected with the virus all returned negative.

(U) The Syrian Salvation Government had earlier announced the closure of all main and secondary crossings in northern Aleppo countryside and in areas under the control of the [Syrian] regime and also that Friday prayers would be suspended and street markets closed within the framework of the preventative measures taken to combat the spread of COVID-19 in the governorate.

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(U) Bangladesh : Coronavirus: Suppression or Mitigation?

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(U) In 1898, two German bacteriologists Friedrich Loeffler and Paul Frosch found evidence that the cause of foot-and-mouth disease in livestock was an infectious particle smaller than any bacteria. This was the first clue to the nature of viruses and its genetic entities that lie somewhere in the grey area between living and non-living states. Coronavirus disease (COVID-19) has been identified as humanity's new foe, with the potential to prematurely end millions of lives. International Committee on Taxonomy of Viruses (ICTV) named the virus relevant to this disease as "severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)".

(U) There are different types of coronaviruses that cause illness ranging from the common cold to more severe diseases such as Middle East Respiratory Syndrome (MERS-CoV) and Severe Acute Respiratory Syndrome (SARS-CoV). The later one is a new strain that was discovered in 2019 and has not been previously identified in humans. Coronaviruses are zoonotic, meaning they are transmitted between animals and people. It is around 125 nanometres across and consists of 30 genes. It can be seen under an electron microscope. Several known coronaviruses are circulating in animals that have not yet infected humans. Common signs of infection include respiratory symptoms, fever, and cough, shortness of breath and breathing difficulties.

(U) In more severe cases, infection can cause pneumonia, severe acute respiratory syndrome, kidney failure and even death. It is now a major global health threat. As of 23 March 2020, there

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have been 350,076 cases and 15,927 deaths confirmed worldwide. Global spread has been rapid, with 198 countries now having reported that they are affected. However, 100,645 have also been recovered from the disease. Out of currently infected patients 95% are in mild condition and 5% are in critical condition. This article suggests some intervention strategies, which is based on the recent epidemiological modelling study carried out by Imperial College COVID 19 response team.

(U) On 18 March 2020, the Royal Society, an independent scientific academy of UK has shut down their building. The seriousness of the problem has then been realised. Some suggests that to understand the virus we need to compare it with the French emperor Napoleon Bonaparte. In the early 19th century, Bonaparte invaded much of Europe in order to establish French dominance over the continent.

(U) Viruses can only exert influence by invading a cell, because they're not cellular structures. They lack the ability to replicate on their own, so viruses are merely tiny packets of DNA or RNA genes enfolded in a protein coating, on the hunt for a cell they can dominate. Once a virus infects a cell, it tries to take over its host completely, much as Napoleon spread the French influence with every country he fought. Viruses themselves have no fossil record, but it is quite possible that they have left traces in the history of life. It has been hypothesized that viruses may be responsible for some of the extinctions of species seen in the fossil record.

(U) The human body does have some natural defences against a virus. But in this case, the virus can reproduce inside our body for days without triggering our immune responses. In case of COVID-19 symptom like fever and coughing are actually due to our immune system fighting back but virus delays this with extra genes it carries. Researchers thought that if they could understand the extra genes that COVID carries, then it would be useful to build antiviral medicine. However, development of a new vaccine requires at least 12-18 months. Because it needs to follow certain steps such as develop a prototype, animal trials, phase 1 human trials (to check side effect), phase 2 human trials (to check efficacy), phase 3 human trials (to evaluate efficacy and safety), regulatory approval, mass production and then public access.

(U) Two fundamental strategies have been suggested by the epidemiological modelling studies. One is mitigation and another is suppression. The aim of mitigation is to use non-pharmaceutical interventions and slowing the spread of epidemic diseases. This will reduce the healthcare demand while protecting those most at risk of severe disease from infection. Vaccines and drug can come under this strategy if available but where no such things available, then population immunity builds up through the epidemic, leading to an eventual decline in case numbers. Unfortunately for humans, some viral infections outpace the immune system. Viruses can evolve much more quickly than the immune system can and some viruses, such as HIV, work essentially by tricking the immune system.

(U) The aim of suppression is to reduce the reproduction number and hence to reduce the case number to low levels and gradually eliminate human to human transmission. Optimal non-pharmaceutical intervention policies include case isolation in the home, voluntary home quarantine, social distancing of those over 70 years of age, social distancing of entire population and closure of schools and universities. Juan Leon, an environmental health scientist at Emory

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University suggests that the studies show common household disinfectants, including soap or a diluted bleach solution, can deactivate coronaviruses on indoor surfaces.

(U) The main difference of the two strategies are that whether a country aims to reduce the reproduction number, R below 1, which is suppression or to merely slow spread by reducing R , but not below 1, which is mitigation. The main challenge suggested by the epidemiological study is that the non-pharmaceutical interventions need to be maintained for as long as the virus is circulating in the human population or until a vaccine become available. The research suggests that the population-wide social distancing applied to the population as a whole would have the largest impact and when combined with other interventions as mentioned above, there is a potential to suppress transmission below the threshold of $R=1$. The main problem of this approach is that these intervention policies will need to be maintained until large stocks of vaccine become available, otherwise transmission can rebound back to the wider population.

(U) The Imperial College research suggests that 'there are very large uncertainties around the transmission of the virus, the likely effectiveness of different policies and the extent to which the population spontaneously adopts risk reducing behaviour.' A word of caution about the transmission modelling based advice is that a measurable uncertainty or risk is different from an un-measurable one and that uncertainty has no effect on the conclusion drawn from the modelling output. Tolstoy, in his book 'War and Peace' mentioned that 'all we can know is that we know nothing. And that is the sum total of human wisdom.' Indeed this is the situation about coronavirus. So far we understood about the anatomy of a COVID-19 is that it has several features such as RNA enclosed in protein, spike protein and lipid membrane, which we may be able to target with drugs to break it down and stop it entering human cells.

(U) In the UK it was initially thought about the implementation of mitigation strategy but epidemiologists suggest that it could cost 250,000 deaths. Then it has been agreed that the epidemic suppression is the only viable strategy at the current time. In terms of intervention strategy, it has gone beyond this research and added the closer of all pubs, restaurant and cafes as well. An alternative opinion is that the suppression strategy will last many months and try to save everyone everywhere from this virus but it will kill many people by other means such as killing economy and also killing our future.

(U) A research published in the Science journal (16 March 2020) titled 'The substantial undocumented infection facilitates the rapid dissemination of novel coronavirus' suggests that the estimation of the prevalence and contagiousness of undocumented novel coronavirus infections is critical for understanding the overall prevalence and pandemic potential of this disease. Using reported infection within China in conjunction with mobility data and using Bayesian statistical techniques, they inferred that 86% of all infections were undocumented prior to 23 January 2020. These findings explain the rapid geographic spread of SARS-CoV2 and indicate that the containment of this virus will be particularly challenging.

(U) There are other hypotheses also floating around such as the causal link between 5G network and corona virus spread around the globe. Though Public Health England has said that there is no "convincing evidence" that exposure below the International Commission on Non-Ionizing Radiation guidelines can cause adverse health effects. These guidelines go up to 300GHz, whereas

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the maximum for 5G will probably only be in the tens of GHz. Dean Koontz's fiction *The Eyes of Darkness* also generate some interest, where a character named Dombey narrates an account of a virus called 'Wuhan-400' which was developed at the RDNA lab outside the city of Wuhan, and 'it was the four-hundredth viable strain of man-made microorganisms created at that research centre'. The passage then gives intricate details about how the virus affects the human body. The chilling accuracy with which this 1981 book predicts the outbreak and the resemblance between 'Wuhan-400' and Coronavirus is a mystery for many and demonstrate how a science fiction become so powerful. However, the claims about coronavirus being a biological weapon are unsubstantiated.

(U) There are some good things also coming out from the coronavirus. A Stanford University study suggests that air pollution kills about 1.1 million people in China each year. The fall in pollution during the country's lockdown likely saved 20 times more lives than it has currently lost. In London, air pollution has also gone down. So, the current problem is pushing us to a green living. A good piece of news for Bangladesh and other humid region is that the high temperature and humidity cut the transmission of COVID-19. So summer and rainy season could damp down the pandemic.

(U) Victor Hugo once said, 'Where the telescope ends, the microscope begins. Which of the two has the grander view?' I think we need to understand the invisible organism better than what we know now in order to take a holistic view of our existence in this earth. We need more evidence in this area of research. We should know that the absence of evidence is not the evidence of absence. However, we all hope that virus will go its own way and humanity will survive, but if we don't think carefully about our present decision, then our decision about isolation on the one hand and global solidarity on the other hand will become incompatible. On the one hand, keeping our freedom for our survival and on the other hand giving up our freedom to safeguard our health - time will tell which is better. We should think with optimism about our world after coronavirus.

(U) The writer is a UK based academic, environmentalist, columnist and author

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(U) Pakistan: Scientists report
airborne coronavirus is probably
infectious

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(U) WASHINGTON: Scientists have known for several months the new coronavirus can become suspended in microdroplets expelled by patients when they speak and breathe, but until now there was no proof that these tiny particles are infectious.

(U) A new study by scientists at the University of Nebraska that was uploaded to a medical preprint site this week has shown for the first time that SARS-CoV-2 taken from microdroplets, defined as under five microns, can replicate in lab conditions.

(U) This boosts the hypothesis that normal speaking and breathing, not just coughing and sneezing, are responsible for spreading Covid-19 and that infectious doses of the virus can travel distances far greater than the six feet (two metres) urged by social distancing guidelines.

(U) The results are still considered preliminary and have not yet appeared in a peer-reviewed journal, which would lend more credibility to the methods devised by the scientists.

(U) The paper was posted to the medrxiv.org website, where most cutting-edge research during the pandemic has first been made public.

(U) The same team wrote a paper in March showing that the virus remains airborne in the rooms of hospitalized Covid-19 patients, and this study will soon be published in a journal, according to the lead author.

(U) "It is actually fairly difficult" to collect the samples, Joshua Santarpia, an associate professor at the University of Nebraska Medical Centre said.

(U) The team used a device the size of a cell phone for the purpose, but "the concentrations are typically very low, your chances of recovering material are small." The scientists took air samples from five rooms of bedridden patients, at a height of about a foot (30 centimetres) over the foot of their beds.

(U) The patients were talking, which produces microdroplets that become suspended in the air for several hours in what is referred to as an "aerosol," and some were coughing.

(U) The team managed to collect microdroplets as small as one micron in diameter.

(U) They then placed these samples into a culture to make them grow, finding that three of the 18 samples tested were able to replicate.

(U) For Santarpia, this represents proof that microdroplets, which also travel much greater distances than big droplets, are capable of infecting people. "It is replicated in cell culture and therefore infectious," he said.

(U) The potential for microdroplet transmission of the coronavirus was at one stage thought to be improbable by health authorities across the world.

(U) Later, scientists began to change their mind and acknowledge it may be a possibility, which is the rationale for universal masking.

(U) The World Health Organisation was among the last to shift its position, doing so on July 7.

(U) "I feel like the debate has become more political than scientific," said Santarpia.

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(U) "I think most scientists that work on infectious diseases agree that there's likely an airborne component, though we may quibble over how large." Linsey Marr, a professor at Virginia Tech who is a leading expert on aerial transmission of viruses and wasn't involved in the study, said it was rare to obtain measurements of the amount of virus present in air.

(U) "Based on what we know about other diseases and what we know so far about SARS-CoV-2, I think we can assume that if the virus is 'infectious in aerosols,' then we can become infected by breathing them in," she said.

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(U) Kyodo: FEATURE: Japanese Customs: A Guide In Brave New Coronavirus World?

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(U) TOKYO, April 18 Kyodo

(U) As the coronavirus pandemic rages unabated, nations around the world have started looking at each other to understand how they might impede the virus' spread.

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(U) Some experts say customs and social habits in Japan such as wearing face masks during seasonal flu outbreaks, bowing rather than handshaking, and removing shoes at home might play some role in hindering transmission of the virus, although to what extent is still unknown.

(U) But even as the scientific evidence remains pending, populations in Western countries have embraced at least one habit -- the donning of face masks in public -- that just months earlier they had seen as a quirk of Japanese or East Asian behavior.

(U) At the same time, Japan's apparently robust practices of social hygiene could have a downside, too -- the lack of urgency with which Japan is embracing social distancing, possibly due to overconfidence in the protection afforded by its hygiene habits.

(U) Wakaba Fukushima, a professor at the Osaka City University Graduate School of Medicine in the Department of Public Health, said in an email to Kyodo News that particular social customs found in Japan and other East Asian cultures are "potentially effective in fighting the spread of coronavirus."

(U) "However, results have not been reported, and we do not know at present to 'what extent' it might be valid based on proper epidemiological research, such as for example comparing the differences in infection rates and morbidity rates of people who practice these customs against those who do not," she said.

(U) Josh Santarpia, an associate professor of pathology and microbiology at the University of Nebraska Medical Center and research director of Countering Weapons of Mass Destruction at the University of Nebraska's National Strategic Research Institute, acknowledged such Japanese customs "probably didn't hurt."

(U) "Rigorous hygiene practices are very important to preventing the spread of disease, so anytime these practices are already ingrained it helps," said Santarpia.

(U) But he added that there were dangers in the adoption of mask-wearing by populations unaccustomed to it. In the United States, people frequently touch or adjust them, posing significant contamination risks. To have a "positive effect," people need to "wear them properly," he said.

(U) Experts have warned about how the coronavirus can cling to non-human surfaces, such as keyboards, doorknobs, countertops and even cardboard boxes, and some are now acknowledging what might seem obvious: it could last for days on the soles of your shoes.

(U) That said, Dr. Amira Roess, a professor of global health and epidemiology at George Mason University, says person-to-person transmission through "respiratory droplets" poses a much higher risk of infection than from contaminated surfaces.

(U) So what explains the discrepancies in confirmed infection and death rates among countries of similar socioeconomic levels? Is it an issue with cultural norms helping slow the spread of the disease, implementing proper testing protocols or other underlying factors?

(U) In Japan, the confirmed rate of infection has been low thus far -- about 72 confirmed cases per million people in a population of 126 million, according to data from the European Centre for Disease Prevention and Control and the United Nations as of April 17.

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(U) One factor that may be keeping the figure low is Japan's modest testing rate compared with other countries. As of Thursday, Japan had tested about 100,000 people, or a rate of 0.8 tests per 1,000 people, compared with over 540,000 tests (10.46/1,000) in South Korea, according to Our World in Data.

(U) But even taking that into account, the comparison with infection cases in other developed countries -- over 2,000 per million people in the United States and 3,900/million in Spain -- is stark, especially considering Japan's huge population of elderly people, who are seen as more susceptible to the virus.

(U) When celebrities in Japan call on fans on social media to take precautions against the virus with protective measures, they generally appeal for people to just do more of what they are already used to.

(U) "Let's strive to practice our everyday customs of gargling and handwashing, especially when we go into large crowds. Protection starts with small things. I don't doubt this," actor Koji Matoba wrote on his official blog on Jan. 30.

(U) Renna Kato, a member of the female idol group AKB48, posted on Twitter the same day, "It pains me that our New Year handshaking fan event had to be canceled. Everyone, please take care of your health. Wash your hands and gargle! And don't forget your masks!"

(U) The question of why Japan remains one of the least impacted countries by COVID-19 has also been a talking point on social media.

(U) Some posters have pointed to a list of personal hygiene norms, such as face masks worn zealously during the flu season, the use of toilet bidets, and baths taken almost daily.

(U) The frequent washing of hands, use of oshibori (hot towels) for cleansing the hands and face at restaurants, and the custom of bowing, instead of handshaking, cheek-kissing or other forms of physical contact, were brought up as a type of baked-in "social distancing" pervasive in society long before COVID-19 started making headlines.

(U) Although people may squeeze onto rush-hour trains, there is very little talking among many of the masked commuters, who are told in repeated public announcements to refrain from chatting on their cellphones, which is considered rude.

(U) Even so, skepticism was also in evidence on social media about Japan's relatively low coronavirus numbers, with about 10,000 confirmed cases and around 200 confirmed deaths reported by Japan's health ministry as of April 17.

(U) Experts point out that cases of COVID-19 in all countries have been undercounted to some degree because of limited testing.

(U) "One of the biggest challenges with comparing countries, and even cities, is that testing protocols and test kit availability are different everywhere," said Roess.

(U) But while testing protocols affect official government tallies, the culture around trusting the government and following its recommendations and the infrastructure of the health care system likely play key roles, too, she said.

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(U) On Thursday, Tasuku Honjo, a distinguished professor at Kyoto University who shared the 2018 Nobel Prize in Medicine or Physiology, said on a television program that Japan needs to ramp up PCR tests to detect virus infections to more than 10,000 per day, compared with the current peak of about 7,000 in mid-April -- dividing cases up into people with serious, mild and no symptoms.

(U) As part of his emergency proposals, he also urged residents of the three cities of Tokyo, Osaka and Nagoya to impose "complete self-restraint from outings" for one month.

(U) "This is a fight against an invisible ninja. The battlefield is at home and abroad, and it is necessary to know where and to what degree the enemy exists around us," Honjo said.

(U) Fukushima, a representative of the Japan Epidemiological Association based in Tokyo, said that predictions could be made about the effectiveness of practices such as handwashing and bowing instead of handshakes and hugs, since "the virus when attached to fingers can use the mucous membranes of the eyes, mouth and nose as portals of entry for potential infection."

(U) Masks, she stresses, are believed to control infection transmissions by reducing the dispersion of droplets discharged from the mouths of infected persons.

(U) She noted that a preliminary study published in early March in the Japan Medical Association on the dispersal of viral traces at an outbreak center in Singapore found positive samples of COVID-19 from a symptomatic patient beyond just personal protective equipment of medical staff.

(U) "The virus was detected from the floor of the patient's room, and for PPE the front surface of shoes. That does not immediately suggest a harmful effect from outdoor shoes, but it also suggests that we cannot rule out the virus clinging to shoes and being transported by them, either," Fukushima said.

(U) Santarpia also found viral contamination in air samples, surfaces such as toilets and other surfaces that are frequently touched in a preliminary report published in late March, which has not yet been peer-reviewed, on the database medRxiv. He will likely start looking at viral contamination of clothing and shoes of health care workers soon, he says.

(U) But he said it was too early to make a correlation between the rate of COVID-19 cases and various hygiene practices across cultures slowing the progression of the disease.

(U) "Overall, I think we will have to wait until this is over to be able to truly see how the pandemic impacts different countries and cultures, but those countries who already practice many rules that some countries are slow to accept, may have an advantage," he said.

(U) A new study by the Centers for Disease Control and Prevention found that about half of health care professionals working in intensive care units carried the coronavirus on the soles of their shoes at a hospital in Wuhan, China, where the outbreak started.

(U) Asked about the effectiveness of Japan's practice of removing shoes before entering the home in protecting against COVID-19, Roess, an expert on global zoonotic infectious diseases, said

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infection from shoes of SARS-Cov-2, the virus that causes COVID-19, is unlikely, but an abundance of caution is still warranted.

(U) "There is evidence that having a no-shoes-in-the-house policy can reduce the risk of pathogens that cause diarrhea, and this is especially important if you have infants or young children who are crawling and putting things in their mouths," she added.

(U) Aside from homes, schools in Japan require students to remove their shoes, which are placed in a shoe rack called a getabako, all the way through high school.

(U) Most temples, shrines, traditional inns, and hot springs resorts require you to remove your shoes -- all in the name of cleanliness. Some restaurants, which also provide cubbyholes, ask patrons to take shoes off. And clothing stores will often request that you remove them before entering a changing booth.

(U) Fearing an explosion of cases, the Japanese government has declared a nationwide state of emergency to curb the spread of the new coronavirus after an alarming growth in cases in urban areas, including Tokyo and Osaka, urging residents to refrain from nonessential outings and some businesses to shut.

(U) Social distancing, however, has been lax in comparison to the strict guidelines being followed in other countries, with not much evidence of people observing the 2-meters-apart distancing goal set by Tokyo's governor, Yuriko Koike, who has asked residents to refrain from being in enclosed spaces, crowded places or in close contact with each other.

(U) Plastic curtains have been installed at many convenience store checkout counters to prevent infections between customers and store employees.

(U) And while schools have closed and universities, cinemas, live music venues, nightclubs, pachinko parlors and internet cafes have been asked to suspend operations in the capital and elsewhere under the state of emergency, Tokyo's restaurants and Japanese-style "izakaya" pubs are still operating, although they have been requested to shut by 8 p.m.

(U) "There is probably still this feeling of 'As long as I have my mask I'll be fine,'" said Fukushima. "But with the declaration of a nationwide state of emergency (on April 16), people here probably will not be in a situation where they can continue saying this."

(U) Scientists are still grappling with many unanswered questions about how the disease can spread, including through people who show little or no symptoms in what might be aerosol transmissions -- fine particles that can stay suspended in the air for hours -- and surface contact transmissions.

(U) What will be the takeaways learned from various cultures in a world utterly transformed by the COVID-19 pandemic?

(U) Life in the United States could also be radically different with social distancing measures enduring until 2022, including waiters using face masks and gloves and throwaway menus, until a vaccine is found, according to researchers at the Harvard School of Public Health. But will it become more like Japan?

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(U) "There is evidence that wearing masks, good hand hygiene, and practicing social distancing are the best ways to halt the spread of the virus. Cultural norms in Japan include some of these and time will tell if those are, in fact, why Japan has lower COVID-19 infection and death rates than other countries," Roess said.

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Antibodies a hot topic in COVID-19 research Hutch scientists tap their antibody expertise for new tests, treatments, vaccines JUNE 24, 2020 . BY SABRINA RICHARDS AND SABIN RUSSELL / FRED HUTCH NEWS SERVICE cartoon of antibodies swarming a coronavirus Illustration of Y-shaped immune proteins, known as antibodies, swarming a coronavirus Illustration by Getty Images Since the unwelcome arrival of COVID-19, a class of tiny, Y-shaped proteins in our blood called antibodies has emerged as a focus of attention for researchers hoping to find a way to treat it, a vaccine to prevent it and tests to confirm whether a person has gotten over it.

One of the workhorses of the human immune system, antibodies are part of our natural defenses against infectious diseases. Their role is to recognize features of invading microbes. Swarms of antibodies can block infection by jamming a virus's ability to enter a healthy cell or by flagging already infected cells for destruction, like a building inspector's red tags.

Antibodies are standard tools used in medical research and a component of many cancer drugs. Most vaccines work by stimulating production of antibodies against viruses or bacteria. Antibodies can also tell us more about the spread and severity of viruses. So, when the pandemic struck, dozens of scientists at Fred Hutchinson Cancer Research Center set their existing work aside and began applying their antibody-wrangling skills.

Experience with other viruses is guiding efforts to track and counter SARS-CoV-2, the cause of COVID-19.

From flu to SARS-CoV-2

Dr. Jesse Bloom is an expert on influenza and how that virus interacts with the antibodies we produce against it. The Hutch researcher and Howard Hughes Medical Institute investigator is turning his expertise to the study of

SARS-CoV-2 and our immune responses to it, starting with local children.

He and Dr. Adam Dingen, a research scientist in Bloom's lab, collaborated with Dr. Janet Englund, an infectious disease researcher at Seattle Children's, to examine prevalence of SARS-CoV-2 infection in Seattle-area children. Although kids make up nearly a quarter of the nation's population, less than 2% of confirmed coronavirus cases are among them.

"That sets up this question: Are kids protected from infection and not getting infected, or are they still getting infected and we're missing them?" Dingen said.

The researchers screened blood samples from 1,076 youngsters who had visited the hospital in March and April of this year, when COVID-19 infections began picking up steam. They tested sera - the clear liquid left over when clotting factors and cells are filtered from blood - for antibodies that bind the novel coronavirus. If the screen finds them, the child is called seropositive. It means they had been exposed to COVID-19, had developed antibodies to the virus and were likely immune to it.

The team found only one seropositive child in March, but the seroprevalence increased in April, with just over 1% of those tested showing evidence of SARS-CoV-2-binding antibodies. A majority of those seropositive children had not been suspected of having COVID-19.

Dr. Jesse Bloom

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Dr. Jesse Bloom has developed a way to test whether antibodies drawn from blood samples can neutralize SARS-CoV-2, the virus responsible for COVID-19.

Photo by Robert Hood / Fred Hutch News Service The researchers also tested whether the children's antibodies could block the virus from infecting cells, a phenomenon known as neutralization. Most of the kids' antibodies easily passed a test developed by Bloom, and one child's sera was particularly potent. Bloom said it was too early to gauge how the potency of children's immune responses to coronavirus compare to those of adults. "But we can say that despite the fact that kids are often asymptomatic or only have a mild sickness, they're certainly mounting quite good immune responses," he said.

The 1% infection rate in this small group of kids aligns with infection estimates for all age groups in the Seattle area developed using epidemiological models. Most of the children who tested positive for past exposure to SARS-CoV-2 came to Seattle Children's for other health concerns, showed few to no symptoms consistent with COVID-19, and were not suspected of being infected during their hospital stay. Consequently, the researchers said their findings also suggest that only screening children with COVID-19 symptoms will likely miss many cases, and that measures to control the spread of the coronavirus should not focus exclusively on those who are clearly sick.

Bloom said it is also difficult to compare the study's infection rates in children with those reported in adults, because the kids' antibody tests indicate there was a prior infection, while adults are most often tested for the presence of the virus itself using a nasal swab instead of a blood sample. Unlike the children in the hospital study, who were mostly asymptomatic, adults are typically tested because they have some symptoms, such as a fever and cough, consistent with COVID-19.

A biological record of past infections

Antibodies are released by immune cells known as B cells. We make a huge variety of antibodies to help protect against the wide array of microbes we may encounter. Prior to infection with a given pathogen, we have relatively few B cells whose antibodies can bind to it.

Infection changes this: The B cells whose antibodies recognize the infecting pathogen multiply and start churning out enormous amounts of antibodies.

Even long after the pathogen has been conquered, a few lingering B cells will continue making antibodies to help stave off a second infection. These antibodies in our blood serve as a biological record, so antibody tests are an easy way to assess whether we have been infected with a specific pathogen.

Hutch researchers (left to right) Drs. Andrew McGuire, Leo Stamatatos and Justin Taylor Drs. Andrew McGuire, Leo Stamatatos and Justin Taylor Photos by Robert Hood / Fred Hutch News Service Dr. Justin Taylor and colleagues are using sophisticated tools developed in his lab to gain a deeper understanding of how our B cells respond to SARS-CoV-2. Much of their focus is on pre-existing immunity that people develop early in life to four other, less harmful coronaviruses that cause common colds.

"We all have pre-existing immunity. We've all been exposed," said Dr. Jim Boonyaratankornkit, a research assistant in the Taylor Lab.

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That exposure, much of it occurring in early childhood, is one reason scientists think may explain why COVID-19 occurs in very few children. Head colds come early and often, triggering a strong antibody response. But as people age, that immunity may wane, and that may influence how older people respond to the arrival of the new coronavirus.

So, the researchers are studying the B-cell responses to SARS-CoV-2 in the blood of people of various ages. Using selected snippets of the virus, they want to see if they prompt a direct defense against it, or possibly cause the body to attack its own tissues. They want to see if SARS-CoV-2 stirs up antibodies against the old cold viruses, potentially stopping it as it appears to happen in kids; or if the immune systems of adults are fooled into mounting an ineffective defense against the old viruses, leaving them vulnerable to this new and deadlier strain.

"We're asking whether this pre-existing immunity guides or misguides our immune response. Do they help us fight off the infection, cause damage or do nothing at all?" Boonyaratanakornkit said.

The answers to those questions are needed as researchers develop vaccines or antibody therapeutics against COVID-19. The behavior of our immune system, never simple, may be more important than the virus itself in determining whether a vaccine will work, or whether an infected person becomes only mildly ill or will end up in critical care, on a ventilator or dead.

A deeper understanding of how antibodies to SARS-CoV-2 can bind and neutralize the virus is critical to building an effective vaccine and antibody-based therapies for infected patients.

Dr. Jim Boonyaratanakornkit

Fred Hutch researcher Dr. Jim Boonyaratanakornkit Photo by Robert Hood / Fred Hutch News Service
Hutch researchers led by Bloom have developed an experimental assay that allows researchers who don't have access to the highest biosafety-level laboratories to safely measure antibody neutralization of SARS-CoV-2. The test measures how well the antibodies perform against a harmless virus that has been genetically engineered to carry SARS-CoV-2 spikes, so it mimics the real virus. This "pseudovirus" can be used to test COVID-19 vaccines or antibody therapies in a lab setting without having to use the dangerous wild virus, which can only be tested in highly secure facilities.

That test was crucial for another Hutch team, led by immunologist Dr. Leo Stamatatos, in their studies of antibodies that bind to the distinctive spike on the coronavirus surface, a likely target of vaccines and therapies.

In the journal *Immunity*, Stamatatos and colleagues describe how they identified from the blood of a COVID-19 survivor an extremely potent neutralizing antibody that can block the ability of the virus to lock onto vulnerable cells thought to be its primary target inside the human lung.

The antibody fit so snugly to a spot on top of the SARS-CoV-2 spike that it stopped infection 100% of the time using Bloom's laboratory tests.

"Because it neutralized every viral particle in our assay, it is theoretically a good candidate for a COVID-19 therapy or a vaccine,"

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Stamatatos said.

His team embarked with University of Washington researchers in early March on the effort to identify natural antibody defenses against SARS-CoV-2 shortly after obtaining the precious blood sample from a patient who had recovered from COVID-19.

They developed a test to isolate antibodies that this one patient had naturally developed against the coronavirus and identified 45 different varieties that latched onto one site or another on the knobbly protein surface of the spike. Of these, only three had any ability to block infection.

A top performer

The one antibody that seemed to have hit the bullseye was measured to be 530 times more potent than its nearest competitors: two others that homed in on different parts of the coronavirus spike but only weakly blocked infection.

The top performer, labeled CV30, was extraordinarily good at stopping infection, likely because it locked so securely onto a region at the tip of the spike called the receptor binding domain. That is the same site that has been so problematic for humans, because it connects the top of that spike, like a key fitting into a lock, with a receptor called ACE2 found on the surface of cells that line the deepest recesses of the human lung.

ACE2 acts like a trap door that allows the coronavirus to break into those cells and use its internal genetic machinery to make thousands of new copies of SARS-CoV-2, eventually killing those cells.

Could this antibody, by itself, be key to stopping the pandemic? Stamatatos said very likely no, because the virus would eventually escape through mutation of that closely matched site on its spike. Consequently, researchers are hoping to develop a cocktail of many different neutralizing antibodies.

"Ideally, a cocktail would presumably be better, because the virus has less chance to escape," said study co-author Dr. Andrew McGuire, whose lab performed the genetic sequencing of the antibodies and carried out the neutralization studies using Bloom's pseudovirus test.

Stamatatos and colleagues are now exploring whether the neutralizing antibodies isolated using these techniques could be formulated into a therapeutic infusion that could protect frontline workers from infection, or as a treatment to limit viral replication in an already infected patient.

The structure of the most successful antibodies can also inform research on a vaccine, which would be designed to teach a healthy individual's immune system to generate similar protective proteins if exposed to SARS-CoV-2, blocking infection.

Meanwhile, McGuire has been working on neutralizing antibodies against coronaviruses for several years in a collaboration with biochemist Dr. David Veesler of the University of Washington. Predating COVID-19, the work was initially aimed at SARS and MERS, two deadly epidemics - discovered in 2003 and 2012, respectively - caused by coronavirus cousins of SARS-CoV-2.

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That gave the researchers a jump start on describing the structure of the SARS-CoV-2 spike, and Veesler and McGuire were co-authors of one of the first papers to describe it.

The team hopes to identify an antibody that neutralizes all three types of the deadly coronavirus, which could be developed into an antibody-based therapeutic to treat infection by any one of these coronavirus threats.

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(b)(1); (b)(3):10 USC 424; (b)(3):50 USC 3024(i); Sec. 1.4(c); (b)(6)

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The remaining pages (243-279) are withheld in full citing (b)(1), (b)(3) 10 USC 424 + 50 USC 3024(i), and (b)(6), and are not provided.