Introduction

As the COVID-19 continues to impact the wealth and welfare of our society, much remains to be understood about the pandemic and its impact. Hence, the importance of using scientific research, facts and data for a better understanding of the nature of the pandemic, as well as its associated public health issues, to drive policy making in addressing challenges related to healthcare and wellbeing of the population. This newsletter is intended to provide a weekly overview on the latest information on health-related topics surrounding the COVID-19 pandemic, covering five main themes: infection control and prevention, diagnosis and testing, treatment and therapy, training for healthcare professionals and exit strategies. Each edition of the newsletter will cover a specific sub-theme under the five main themes, providing up to date information on available resources, research, data and studies, along with policy recommendations and implications, based on scientific evidence and facts, for decision makers to utilize in developing polices and measures to address the challenges associated with COVID-19 within the healthcare sector.
• Singapore approves use of antiviral drug for Covid-19 patients CNN
• New Study Shows Hydroxychloroquine Doesn’t Prevent Covid-19 Coronavirus Infection Forbes
• Coronavirus: Asymptomatic transmission still an ’open question’ BBC
• Monster or Machine? A Profile of the Coronavirus at 6 Months NY Times
• The novel coronavirus attacks the lungs. A biotech company sees a common enzyme as key to protecting them STAT
• Fauci Warns That the Coronavirus Pandemic Is Far From Over NY Times
• Study identifies potential approach to treat severe respiratory distress in patients with COVID-19 NIH
• Modelers Suggest Pandemic Lockdowns Saved Millions From Dying Of COVID-19 NPR
• Coronavirus hospitalizations rise sharply in several states following Memorial Day Washington Post
• Testing funds shortfall imperils Covid-19 fight, health groups warn Financial Times
Executive Summaries

Infection Control and Prevention:

Point of care testing: The United States Food and Drug Administration has authorized the use of the GeneXpert tests outside of BSL-2 laboratories and patient care settings. Working with specimens should take place in a validated biological safety cabinet (BSC) or primary containment device. Non-propagative diagnostic laboratory work should be conducted at facilities and procedures equivalent to BSL-2 and propagative work at a containment laboratory with inward directional airflow (BSL-3). Appropriate disinfectants should be used in a lab settings.

Diagnosis and Testing:

Group screening is proposed as an easy to implement solution to increase the testing capacity of current available laboratory infrastructure and test kits. Pooling samples is recommended for asymptomatic individuals and for those from areas with low levels of positive test results(<5%). This grouping of samples would occur before the RT-PCR amplification step and individuals would only be tested in the case of a positive pool batch test result. This technique would allow for mass screening required to lift lockdown restrictions while substantially reducing the number of tests needed as well as the associated costs of testing.

Treatment and Therapies:

The spectrum of COVID-19 ranges from a mild respiratory illness to a severe disease requiring hospitalization in up to a third of patients, with frequent progression to acute respiratory distress syndrome (ARDS) and a high mortality. Acalabrutinib, a selective BTK inhibitor, was administered off-label to 19 patients hospitalized with severe COVID-19. 72.7% of patients in the supplemental oxygen had been discharged on room air. These results suggest that targeting excessive host inflammation with a BTK inhibitor is a therapeutic strategy in severe COVID-19 and has led to a confirmatory international prospective randomized controlled clinical trial. These findings should not be considered clinical advice but are being shared to assist the public health response to COVID-19. While BTK inhibitors are approved to treat certain cancers, they are not approved as a treatment for COVID-19. This strategy must be tested in a randomized, controlled
clinical trial in order to understand the best and safest treatment options for patients with severe COVID-19.

**Training of Healthcare Professionals:**

We describe a novel and innovative method to train healthcare workers and lab personnel on donning and doffing personal protective equipment (PPE).

**Exit Strategies:**

For policymakers to consider herd immunity, a national strategy will need to rely on seroprevalence datasets, which will involve mass community and reliable antibody testing to determine who is immune, as well as a comprehensive assessment of the capabilities and capacities of the healthcare system to support a large number of the population being infected. Given that for COVID-19, approximately 60% of the population will need to be immune in order to achieve herd immunity naturally, without the presence of a vaccine, and that most countries are far from this target point, herd immunity might not be the right approach, as it is likely to lead to hundreds of thousands of additional deaths worldwide. Rather, containment policies should continue while herd immunity can be achieved more safely through a vaccine.
Introduction:

The main goal of this section is to provide interim guidance on laboratory biosafety related to the testing of clinical specimens of patients that meet the case definition of coronavirus disease (COVID-19). Health laboratories must adhere to appropriate biosafety practices. Any testing for the presence of SARS-CoV-2, the virus that causes COVID-19 or of clinical specimens from patients meeting the suspected case definition should be performed in appropriately equipped laboratories, by staff trained in the relevant technical and safety procedures.

Recommendations for minimal working conditions associated with specific manipulations in the laboratory

Risk assessment:

The first step in ensuring biosafety is to perform a risk assessment. Each laboratory should conduct a local site-specific activity-specific risk assessment to ensure it is competent to safely perform the testing with appropriate risk control measures. Risk assessments and mitigation measures are dependent on:

1. Point of care (POC) or near-POC assay:

The CDC defines point of care (POC) tests as: “tests that are intended to supplement laboratory testing, making testing available to communities and populations that cannot readily access laboratory testing, and bolstering testing to address emerging outbreaks quickly”. POC assays such as GeneXpert were recently released for COVID-19 testing of samples.
such as nasopharyngeal swabs, nasal wash, and aspirate. The sample manipulation and the level of aerosol generation is minimal. The United States Food and Drug Administration (FDA) has authorized the use of the GeneXpert tests outside of BSL-2 laboratories and patient care settings. They may be performed on a bench without employing a biosafety cabinet, only when the local risk assessment so dictates. The following conditions should be fully met:

- Performed on a diaper or large paper towel in a well-ventilated area free of clutter.
- Appropriate PPE is worn similar to other manual testing, such as but not limited to a full-length long (elastic) sleeved lab coat, safety goggles or glasses, and disposable gloves.
- Risk assessment should inform the use of respiratory protection as a supplementary precaution.
- Staff well trained in good microbiological practice and procedure (GMPP).
- No rush or increased pressure for test turnaround time.
- A validated infectious waste process, including excess specimens, should be conducted.
- Decontaminate the instrument after each run by using an EPA-approved disinfectant for SARS-CoV-2.

2. Initial processing (before inactivation) of specimens

Initial processing should take place in a validated biological safety cabinet (BSC) (Figure 1) or primary containment device.

3. Non-propagative diagnostic laboratory work:

Detecting viral RNA by nucleic acid amplification test (NAAT), for example, rRt-PCR with nucleic acid sequencing, should be conducted in a facility using procedures following Biosafety Level 2 (BLS-2). All procedures should be conducted in a certified class II BSC.

4. Propagative work:

Virus isolation in cell culture and initial characterization of viral agents recovered in cultures of SARS-CoV-2 specimens should only be conducted in a Biosafety Level 3 (BSL-3) laboratory using BSL-3 practices. Only trained and competent personnel in laboratories meeting additional essential containment requirements and practices BSL-3 should be conducting these processes. Site- and activity-specific biosafety risk assessments should be performed to determine if extra biosafety precautions are warranted based on situational needs.
5. Procedures with a High Likelihood of Generating Droplets or Aerosols:

Procedures with a high likelihood of generating aerosols or droplets should be done using either a certified class II BSC or additional precautions to provide a barrier between the specimen and personnel. Examples of these additional precautions are PPE, such as a surgical mask or face shield, other physical barriers, like a splash shield; centrifuge safety cups; and sealed centrifuge rotors to reduce the risk of exposure to laboratory personnel. Site- and activity-specific biosafety risk assessments should be performed to determine if additional biosafety precautions are warranted based on situational needs, such as high testing volumes, and the likelihood to generate infectious droplets and aerosols.

Environmental Specimen Testing: Procedures that concentrate viruses, such as precipitation or membrane filtration, can be performed in a BSL-2 laboratory with unidirectional airflow and BSL-3 precautions, including respiratory protection and a designated area for donning and doffing PPE. The donning and doffing space should not be in the workspace. Work should be performed in a certified Class II BSC. This guidance is intended for only those laboratories that perform virus concentration procedures, including wastewater/sewage surveillance testing, and not for public health or clinical diagnostic laboratories that handle COVID-19 clinical specimens or laboratories that perform culture and isolation of SARS-CoV-2.

Decontamination

Decontaminate work surfaces and equipment with appropriate disinfectants with proven activity against enveloped viruses by using an EPA-approved disinfectant for SARS-CoV-2. This may include but not limited to: sodium hypochlorite (bleach) (e.g. 1,000 ppm (0.1%) for general surface disinfection and 10,000 ppm (1%) for disinfection of blood spills), 62-71% ethanol, 0.5% hydrogen peroxide, quaternary ammonium compounds and phenolic compounds. Manufacturer’s recommendations for use, such as dilution, contact time, and safe handling must be followed.
Table 1  
Summarizes the biosafety recommendations for minimal working conditions associated with specific manipulations in laboratory.

<table>
<thead>
<tr>
<th>Lab Procedure</th>
<th>Example</th>
<th>Biosafety level</th>
<th>Specific Recommendations</th>
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| **Point of care (POC) or near-POC assay**          | GeneXpert: for COVID-19 testing of nasopharyngeal swab, nasal wash and aspirate | May be performed on a bench without employing a biosafety cabinet | -Performed in **a well-ventilated area** free of clutter.  
-Appropriate PPE is worn  
-Staff well trained in good microbiological practice and procedure (GMPP)  
-A validated infectious waste process should be used.  
-Decontaminate the instrument after each run by using an EPA-approved disinfectant for SARS-CoV-2. |
| **Initial processing (before inactivation) of specimens** |                                                                         | BSL-II          | See Figure 2  
-Biosafety Safety cabinet (BSC)  
-Primary containment device.                                                                                                                                  |
| **Non-propagative diagnostic laboratory work:**    | Detecting viral RNA by nucleic acid amplification test (NAAT) for example rRt-PCR with nucleic acid sequencing | BSL-II          | See Figure 2  
-Biosafety Safety cabinet (BSC)  
-Primary containment device.                                                                                                                                  |
| **Propagative work:**                              | -Virus isolation in cell culture  
-Neutralization assays                                                                                                                                   | BSL-III         | See Figure 2  
Additional precautions:  
-**PPE:** laboratory workers should wear protective equipment, including disposable gloves; solid-front or wrap-around gowns, scrub suits, or coveralls with sleeves that fully cover the forearms; head coverings; shoe covers or dedicated shoes; and eye protection (goggles or face shield).  
-Risk assessment should inform the use of respiratory protection (e.g. N95 or more) |
Figure 1: Class II Biological safety cabinet (BSC)

Schematic representation of a Class IIA1 biological safety cabinet.
A, front opening; B, sash; C, exhaust HEPA filter; D, rear plenum; E, supply HEPA filter; F, blower.

WHO-Laboratory biosafety manual-Third addition 200
Figure 2: Main features of a BSL-II lab

*Diagram graphics kindly provided by CUH2A, Princeton, NJ, USA*

*Labelling based on the interim laboratory biosafety guidance related to COVID-19 by the WHO (May 13, 2020) and the CDC Interim Laboratory Biosafety Guidelines (June 5, 2020)*

**Centrifugation of specimens using**

Sealed centrifuge rotors or sample cups. These rotors or cups should be loaded and unloaded in a BSC.

**A controlled ventilation system** that provide an inward flow of air without recirculation.

- Air HEPA filtered
- When exhaust air from the laboratory is discharged to the outdoors, it must be dispersed away from occupied buildings and air intakes.
- Air discharged through HEPA filters

**Autoclaves** or other appropriate means to decontaminate infectious materials near the lab or inside the lab.

**Doors** are kept closed and are posted with appropriate hazard signs.

**Biohazard warning signs** are posted near the lab.

**Biological safety cabinets II (BSC-II): aerosol generating procedure**

**A dedicated hand-wash sink** should be available in the laboratory.

**Contaminated wastes** separated from the general waste stream.
Global Covid-19 Test Shortages lead to a new innovative strategy: Group Screening
An adapted technique allows more people to be tested using fewer tests.

Group screening is proposed as an easy to implement solution to increase the testing capacity of current available laboratory infrastructure and test kits. Pooling samples is recommended for asymptomatic individuals and for those from areas with low levels of positive test results (<5%). This grouping of samples would occur before the RT-PCR amplification step and individuals would only be tested in the case of a positive pool batch test result. This technique would allow for mass screening required to lift lockdown restrictions while substantially reducing the number of tests needed as well as the associated costs of testing.

Urgent public health needs continue to push global efforts to increase testing.

Testing has been a central component in effective control strategies employed in several countries to limit and suppress the spread of SARS-CoV-2. Countries with limited testing capacity such as the United States (US), have struggled to contain the spread of the virus and have prioritized testing specific groups. Several other countries have struggled with challenges surrounding test delivery, processing capacity, and specimen collection, regardless of affluence. However, urgent public health needs continue to push global efforts to increase testing.

Testing can be scaled within current laboratory infrastructure and available test kits for certain cases using sample pooling techniques.

Important first steps to expand testing include: relaxing and streamlining regulatory requirements and procedures, granting testing approval to non-government health laboratories such as academic diagnostic labs as well as university research laboratories, introducing flexibility regarding RNA extraction methods and amplification instruments, and indigenous manufacturing of testing supplies. That said, successful scaling up of testing is achievable within the current laboratory infrastructure and available test kits. The strategy, named sample pooling, is a well-established and safe procedure adapted for use in coronavirus diagnostics. The procedure, which

1 Diagnostic Testing for Severe Acute Respiratory Syndrome-Related Coronavirus 2
Matthew P. Cheng, Jesse Papenburg, Michael Desjardins, Sanjat Kanjilal, Caroline Quach, Michael Libman, Sabine Dittrich, and Cedric P. Yansouni Annals of Internal Medicine 2020 172:11, 726-734
has been used for HIV and Tuberculosis screening in the past, consists of combining several individual samples together into one batch to test for the presence of the virus in a number of individuals at once. If the pooled sample test yields a positive result, indicating at least one person in the batch has the virus, all individuals in the batch are then tested. However, if the pooled sample comes back negative, a larger number individuals will have successfully been tested using fewer tests, reducing costs and barriers to mass testing².

**Sample pooling is optimal and most cost efficient in areas of low prevalence (<5% positive rates) and for mass screening of asymptomatic individuals.**

While countries like the US, Ghana, India, and Germany are developing their own sample pooling techniques, the testing strategy is not without its limitations ³. In the pioneering study published in The Lancet, a range of 4-30 samples is suggested for optimal accuracy and efficiency. The grouping of the samples into one batch should take place before RT-PCR amplification ⁴. Sample pooling is recommended as cost efficient for areas in low prevalence (<2% test positivity rates) based on recommendations from the Indian Council of Medical Research and for surveillance among asymptomatic individuals, excluding individuals with known contact with confirmed cases, in areas with test positivity rates between 2-5%⁵. However, another study from University of Southern California (USC) suggests an area with a positive test rate of about 5% to be suitable for sample pooling. The same USC study estimates this approach can reduce testing costs by at least half, adding up to “tens of billions of dollars saved”, despite factoring in reliability concerns and testing errors. The USC study suggests an optimal pool size of 4 samples per batch, and indicates a pool size of 11 to be too large. An example of 100 subjects from a company split into 20 groups of 5 individuals each is given. If 5% (or 1 individual from 5/20 of the groups) tested positive and 5 groups of 5 had to be independently tested the company will have paid for 45 tests versus 100 if the samples were not pooled. Testing errors is a concern with sample pooling as it is with individual tests, but the USC study notes that in some cases, errors are reduced when the samples are pooled. Until Kuwait is able to scale up individual testing efforts, case pooling may be an innovative and feasible solution to our testing limitations⁶.

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6 “A Testing Strategy to Get Americans Back to Work and School.” USC Schaeffer, University of Southern California, 5 May 2020,

7 “A Testing Strategy to Get Americans Back to Work and School.” USC Schaeffer, University of Southern California, 5 May 2020,
“The same USC study estimates this approach can reduce testing costs by at least half, adding up to “tens of billions of dollars saved” despite factoring in reliability concerns and testing errors.”
Treatment in development: Potential approach to treat severe respiratory distress in patients with COVID-19

Early data from a clinical study suggest that blocking the Bruton tyrosine kinase (BTK) protein provided clinical benefit to a small group of patients with severe COVID-19. Researchers observed that the off-label use of the cancer drug acalabrutinib, a BTK inhibitor that is approved to treat several blood cancers, was associated with reduced respiratory distress and a reduction in the overactive immune response in most of the treated patients. The findings were published June 5, 2020, in Science Immunology. The study was led by researchers in the Centre for Cancer Research at the National Cancer Institute (NCI), in collaboration with researchers from the National Institute of Allergy and Infectious Diseases (NIAID). These findings should not be considered clinical advice but are being shared to assist the public health response to COVID-19. While BTK inhibitors are approved to treat certain cancers, they are not approved as a treatment for COVID-19. This strategy must be tested in a randomized, controlled clinical trial in order to understand the best and safest treatment options for patients with severe COVID-19.

Fig. Model of BTK-dependent hyper-inflammation in severe COVID-19.1

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1 M Roschewski et al. Inhibition of Bruton Tyrosine Kinase in Patients with Severe COVID-19
**Why Acalabrutinib?**

The BTK protein plays an important role in the normal immune system, including in macrophages, a type of innate immune cell that can cause inflammation by producing proteins known as cytokines. Cytokines act as chemical messengers that help to stimulate and direct the immune response. In some patients with severe COVID-19, a large amount of cytokines are released in the body all at once, causing the immune system to damage the function of organs such as the lungs, in addition to attacking the infection. This dangerous hyper-inflammatory state is known as a “cytokine storm”. At present, there are no proven treatment strategies for this phase of the illness. The study was developed to test whether blocking the BTK protein with Acalabrutinib would reduce inflammation and improve the clinical outcome for hospitalized patients with severe COVID-19.

**The Clinical Study**

This prospective off-label clinical study included 19 patients with a confirmed COVID-19 diagnosis that required hospitalization, as well as with low blood-oxygen levels and evidence of inflammation. Of these patients, 11 had been receiving supplemental oxygen for a median of two days, and eight others had been on ventilators for a median of 1.5 (range 1-22) days. Within one to three days after they began receiving Acalabrutinib, the majority of patients in the supplemental oxygen group experienced a substantial drop in inflammation, and their breathing improved. Eight of these 11 patients were able to come off supplemental oxygen and were discharged from the hospital. Although the benefit of Acalabrutinib was less dramatic in patients on ventilators, four of the eight patients were able to come off the ventilator, two of whom were eventually discharged. The authors note that the ventilator patient group was extremely clinically diverse and included patients who had been on a ventilator for prolonged periods of time and had major organ dysfunction. Two of the patients in this group died.

**Was Acalabrutinib Successful?**

Blood samples from patients in the study showed that levels of interleukin-6 (IL-6), a major cytokine associated with hyper-inflammation in severe COVID-19, decreased after treatment with Acalabrutinib. Counts of lymphocytes, a type of white blood cell, also rapidly improved in most patients. A low lymphocyte count has been associated with worse outcome for patients with severe COVID-19. The researchers also tested blood cells from patients with severe COVID-19 who were not in the study. In comparison with samples from healthy volunteers, they found that these patients with severe COVID-19 had higher
activity of the BTK protein and greater production of IL-6. These findings suggest that Acalabrutinib may have been effective because its target, BTK, is hyperactive in severe COVID-19 immune cells. The results of this study were used to inform the trial design of the CALAVI (acalabrutinib) randomized, controlled clinical trial, sponsored by AstraZeneca, which will examine the safety and efficacy of acalabrutinib in patients with severe COVID-19, the estimated completion date of the trial is 30 September 2020.

Summary
The spectrum of COVID-19 ranges from a mild respiratory illness to a severe disease requiring hospitalization in up to a third of patients, with frequent progression to acute respiratory distress syndrome (ARDS) and a high mortality. Acalabrutinib, a selective BTK inhibitor, was administered off-label to 19 patients hospitalized with severe COVID-19. 72.7% of patients in the supplemental oxygen had been discharged on room air. These results suggest that targeting excessive host inflammation with a BTK inhibitor is a therapeutic strategy in severe COVID-19 and has led to a confirmatory international prospective randomized controlled clinical trial. These findings should not be considered clinical advice but are being shared to assist the public health response to COVID-19. While BTK inhibitors are approved to treat certain cancers, they are not approved as a treatment for COVID-19. This strategy must be tested in a randomized, controlled clinical trial in order to understand the best and safest treatment options for patients with severe COVID-19.
Donning and Doffing of PPE: A Novel Teaching Method

The safe and optimum operation of a laboratory during the COVID-19 epidemic is dependent on the competence of its staff. Personnel must be given appropriate safety training. Laboratory supervisors, with the assistance of the biosafety officer and other resource persons, play a crucial role in staff training. Only personnel trained in the appropriate procedures in biosafety should be allowed to handle SARS-CoV-2 specimens. An essential part of biosafety is the proper use of PPE by lab personnel while handling and processing COVID-19 diagnostic tests.

Reports that many health care personnel (HCP) contracted COVID-19 despite wearing appropriate PPE resulted in substantial concerns about the effectiveness of the PPE for HCP and laboratory personnel. A recent study describes a refresher training course delivered to HCP incorporating feedback for their performance on donning and doffing PPE effectively and accurately.

To detect contamination, the researchers used a non-toxic fluorescent solution during the PPE training of HCP. The solution was only visible under ultraviolet light.

In the study, HCP donned PPE: a cap, gown, gloves, eye protection, face shield, and an N95 mask. Once the personnel donned their PPE, they went into a room to care for a simulated patient sprayed down with the invisible simulated contagion. They added the fluorescent solution to a simulated albuterol nebulizer treatment that was given to the high-fidelity simulator during the scenario (not in a negative pressure room). After completing the simulated case, the staff remained in their PPE and were led into another room.

The room lights were then turned off before doffing to allow identification of widespread simulated contagion on the PPE, both on the gloves and gowns from directly touching the simulated patient and on the face shields and masks from the aerosolized solution. A blacklight flashlight was used to examine each HCP and identify the presence of any fluorescent solution. Learners then completed the doffing procedure. The presence of fluorescent solution on the learner’s skin represented an exposure to
the contagion and indicated an error was made in the donning or doffing process. The most common error was contaminating the face or forearms during PPE removal. The novel training technique achieved its primary aim of reinforcing the importance of using proper technique to don and doff PPE when caring for patients during the COVID-19 pandemic. It visually demonstrated how aerosol-generating procedures could lead to exposure if proper technique and procedures are not followed. The training method allowed educators and learners to easily visualize any contamination on themselves after they fully doff their PPE. Educators were able to make immediate corrections to each individual’s technique based on visual evidence of the exposure.

A similar simulation-based approach may be adopted to effectively and efficiently train lab personal that need to handle and process SARS-CoV-2 patient specimens and cultures.

Exit Strategies

Is Herd Immunity a Feasible Exit Strategy?1

While most countries were adopting some form of a containment strategy in trying to mitigate the COVID-19 pandemic, Sweden seemed to take the more relaxed approach, aiming to achieve herd immunity, a point in which a certain portion of the population is immune or shows immunity to the virus.2 There are two approaches in achieving herd immunity: a vaccine or through the natural route of more of the population being infected, and without a vaccine to date, the latter approach of having the majority of the population infected is the only way to achieve herd immunity. Thus, at this point in time, where exit strategies are being developed and implemented, should a herd immunity strategy even be considered?

Most will defer to the case in Sweden to answer this question, comparing how the country has fared, socially and economically, in comparison to other Scandinavian and European countries, as well as other places around the world. While most countries adopted national lockdowns measures which proved to have severe economic impacts, some other countries, mainly in Southeast Asia, were well equipped to implement

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specific and stringent public health interventions, such as test, trace, and isolation measures, with those susceptible having mild restrictions in place (i.e. social distancing)\(^3\). Sweden, on the other hand, opted for more mild interventions, with an emphasis on personal responsibility to slow the spread of the virus; however, their interventions led to a higher case numbers and fatalities, as shown in Figure A\(^4\). As a matter of fact, Sweden and the United States are among the countries with the highest number of deaths per capita\(^5\). The creator of Sweden’s herd immunity approach noted that they were unsure if the relaxed approach was working, after high death rates were observed in nursing homes, which has led to much criticism\(^6\).

**Seroprevalence Surveys**

For herd immunity, one way to decipher how many people have been immune to COVID-19 is to conduct a seroprevalence survey, which involves serology testing, and assessing the data that is acquired\(^1\). Challenges in relation to availability and validity of testing, globally, has been a limiting factor. Nevertheless, several countries in the Europe have implemented serology testing, and what most have observed is that no country is known to have more than 5% of their population immune to the virus. Spain reported a national average of 5%, with an 11% and 7% immunity in Madrid and Barcelona, respectively. In a recent study completed by the Office for National Statistics in the United Kingdom (UK), using 1,000 adults to track levels of immunity, it was shown that the national average was also 5%, with London showing 17% immunity.\(^7\) In New York, it is estimated that roughly 20% of the population has immunity, whereas in Wuhan, China, only 10% of the population is considered immune (Figure B)\(^8\).

Testing will also give an indication into the basic reproductive number (\(R_0\)) of the virus, which in the case of COVID-19, has been shown to be in the range of 2 to 6\(^9\). From an initial cohort of 425 confirmed cases in Wuhan, China, an \(R_0\) of approximately 2.2 was estimated, but more recent estimates places the \(R_0\) more around 5.7. Assuming that the \(R_0\) is somewhere in the middle of the range, at 3, for SARS-CoV-2, the herd immunity threshold would be around 67\%.\(^8\) At this rate, most countries and cities are far from achieving this target and would deal with more fatalities to achieve this target. Although, larger seroprevalence datasets are needed, thus far, the datasets are indicating that natural exposure of COVID-19 might, in the short to medium term, not deliver the required level of herd immunity needed.


\(^4\) [https://theconversation.com/herd-immunity-in-europe-are-we-close-139253](https://theconversation.com/herd-immunity-in-europe-are-we-close-139253)


One other important consideration that remains to be understood is how protective the antibodies resulting from an infection (symptomatic or asymptomatic) are, and what percentage of the population would need to have these antibodies to prevent the spread or a resurgence? Understanding immunity required for protection involves the use of titrated transfers of antibodies and T lymphocytes, similar approaches utilized in assessing the correlation of protection for other viruses, such as Ebola. In looking at the 2003 SARS pandemic, also a coronavirus, 90% of the survivors, in one study, had functional, virus-neutralizing antibodies, and around 50% had strong T-lymphocyte responses.\textsuperscript{10,11}

The duration of protection is also important. A recent study from China on rhesus monkeys with immunity showed that the monkeys not re-infected when exposed once again to the virus\textsuperscript{12}. In looking at reports for other coronaviruses, similar to COVID-19, an antibody response was detectable beyond a year after hospitalization. In the case of Middle East respiratory syndrome, antibodies were detectable for 4 years.\textsuperscript{13}

Figure B. The percentage of the population shown to be immune to COVID-19: New York, 19.9%, London 17.5%, Madrid 11.3%, Boston 9.95%, Stockholm 7.3%. Source (https://www.nytimes.com interactive/2020/05/28/upshot/coronavirus-herd-immunity.html)

\textsuperscript{10} Most of these studies, focus on people that were hospitalized, and data is needed for individuals with SARS-CoV-2 infection who have not been hospitalized.

\textsuperscript{11} T Cell Responses to Whole SARS Coronavirus in Humans Chris Ka-fai Li, Hao Wu, Huiping Yan, Shiwu Ma, Lili Wang, Mingxia Zhang, Xiaoping Tang, Nigel J. Temperton, Robin A. Weiss, Jason M. Brenchley, Daniel C. Douek, Juthathip Mongkolsapaya, Bac-Hai Tran, Chen-lung Steve Lin, Gavin R. Screaton, Jin-lin Hou, Andrew J. McMichael, Xiao-Ning Xu. The Journal of Immunology October 15, 2008, 181 (8) 5490-5500; 9

\textsuperscript{12} Reinfection could not occur in SARS-CoV-2 infected rhesus macaques Linlin Bao, Wei Deng, Hong Gao, Chong Xiao, Jiayi Liu, Jing Xue, Qi Lv, Jiangning Liu, Pin Yu, Yanfeng Xu, Feifei Qi, Yaqin Gu, Fengdi Li, Zhiqiang Xiang, Haisheng Yu, Shuran Gong, Mingya Liu, Guanpeng Wang, Shunyi Wang, Zhiqi Song, Wenjie Zhao, Yunlin Han, Linna Zhao, Xing Liu, Qiang Wei, Chuan Qin bioRxiv 2020.03.13.990226

\textsuperscript{13} Channappanavar R, Zhao J, Perlman S T cell-mediated immune response to respiratory coronaviruses. Immunol Res. 2014; 59: 118-128
Thus, while much remains to be understood about the nature and duration of the protection from antibodies, policymakers should emphasize the need for collecting seroprevalence data, to understand the immunity profile of the population (i.e. exposed and immune populations). These datasets, along with considering epidemiological and immunological factors, such as population structure, variation in transmission dynamics between populations, and waning immunity, should be used as the basis for determining whether herd immunity strategies are feasible. Based on the data and information thus far, the consequences of the natural way of achieving immunity, would not only be challenging, but also serious, in the absence of a vaccination program. Rather, the emphasis should be on the need for seroprevalence data to inform decision and policy making, as well as policies that continue to protect high risk and vulnerable populations, including social distancing measures to minimize the impact of the pandemic and prevent a resurgence.

Policy Implications and Recommendations

• Comprehensive seroprevalence data and a holistic understanding of the nature and duration of protection should inform policymakers on the feasibility of a herd immunity strategy, which will rely on:
  • Widespread and reliable antibody testing to determine who is immune. The validity of these antibody tests are extremely important, especially in relation to the practicalities of the implementing lab based testing, versus, serology or at home testing.
  • A full assessment of the capabilities and capacities of the healthcare system, with considerations for providing the infrastructure and resources, are needed.