Management of COVID 19-SARS Pandemic In The Offices of Rex Moulton-Barrett, Effective March 16th 2020

The following applies to all employees in the offices of Rex Moulton-Barrett, MD

Should an employee think they may have been in contact with a person who might have had a COVID-19 SARS exposure, as defined:

a. Contact person who has traveled in the last four weeks to: South East Asia including China, Korea, Japan, Singapore, Malaysia or Europe and / or
b. The contact person reports and/or: cough, fever, myalgia, shivering, shortness of breath and / or
c. The contact person has tested positive for COVID-19 SARS

Note that symptoms and signs usually appear between 1-14 days, average 5 days after exposure, but a contact person may shed virus for up to 1 month even after becoming asymptomatic or even if that person was asymptomatic

or if the current employee:

d. Is symptomatic for either / and: cough, fever, shortness of breath

Then the following Protocol regarding the employee should be applied immediately:

a. If the employee is coughing place a N95 facemask and a face shield on the Employee
b. The employee should leave the work place Immediately
c. obtain testing by nasal and / or oropharyngeal swab: green kit for Lab Corp and Red Kit Quest.
d. The test for COVID-19 SARS can be performed in our office. Each Test Kit has specific instructions on how to perform in office (see below under "The Test Kit' for details), strict Anti-viral using all COVID-19 infection precautions by the staff obtaining the swab must be adhered to: yellow gown, gloves, facemask and face-shield by the person obtaining the swab. Then after the employee has left, the room should be cleaned using the same precautions and a U/V light 20 minute application to that room, the hands of the staff who handled the Employee and the swab should undergo a vigorous soap and water scrub for at least 20 seconds. The gown, gloves and facial shield/mask should be discarded into a covered biohazard container. The swab kit should be kept at 2-4C for less than 4 days and the reference lab: LabCorp or Quest should be contacted and physician/PA/NP request form signed and correctly labeled with name and date and request for "COVID-19 PCR swab test"
e. Remain away from the work place until your test result comes back negative or until the employee has 2 negative swab tests at least 1 day apart if there was a positive swab test previously
f. If the employee's symptoms worsen then they should contact their primary care physician and discuss whether or not acute medical care including hospitalization may be warranted

Conditions for which we will refuse patient care:

a. Patient does not require acute care following surgery performed under our care and:
b. Patient reports recent travel within 14 days South East Asia including China, Korea, Japan, Singapore, Malaysia or Europe and / or
c. Patient reports and/or: cough, fever, shivering, myalgia, shortness of breath and / or
d. Patient has tested positive for COVID-19 SARS and does not have 2 proven nasal / oropharyngeal swab negative test of at least 1 day apart.

Unavoidable Patient Care with High Probability of COVID-19 SARS Test Positivity

a. strict Anti-viral precautions by the staff must be adhered to: yellow gown, gloves, facemask and face-shield by the person obtaining the swab.
b. Then after the employee has left, the room should be cleaned using the same personal protective precautions and
c. Apply a U/V light 20 minute application to that room,

d. the hands of the staff who handled the Employee and the swab should undergo a vigorous soap and water scrub for at least 20 seconds (soap destroys the surface spikes of the COVID–19 virus rendering it unable to attach to respiratory mucosal surfaces).
e. The gown, gloves and facial shield/mask should be discarded into a covered biohazard container
f. Avoid facial touching throughout the day.
g. The use of hand sanitizers should have at least 70% isopropyl alcohol and 30% soap

The PCR Nasopharyngeal / Oropharyngeal Test Kits

The 2 main test kits available currently in the USA currently are no FDA approved: LabCorp and Quest.

Lab Corp will not provide testing on site. Rather the test kit is to be sent to them by courier. The kit has a green bottle with swab. The swab may be collected from a paper cup with a deep sputum cough up into a paper cup and then swab at least 0.2mls or by individually swabbing either the nose or oropharynx, and collect at least 0.2mls then place the swab into a viral transport medium, after placing in 2-3mls of multi-microbe media, the swab is discarded before sending and again attempt to collect a minimum of 0.2mls. Do not use calcium alginate swabs. Label the container either “NP” or “ OP” do not write NP/OP or swab. If swabs are collected from both they should be submitted in 2 separate collection containers. are The form should have the name, address, sex, age, ordering physician name and telephone number, specimen time and date of collection, A CDC ID number is no longer required. Can be refrigerated after collection for up to 72 hours before analysis. The turnaround is 3-5 days.

Quest will not provide testing on site. Rather the test kit is to be sent to them by courier. The name for the test is SARS-CoV-2RNA, Qualitative Real-Time RT-PCR, test code: 39433. This test should be written on it’s own request and not part of other request tests.
Preferred sample: 1 nasopharyngeal and or one oropharyngeal swab collected in a multi-microbe media (M4) VCM medium green cap tube or equivalent UTM. Again the swabs should not be mixed from the 2 sites and if both are tested then 2 separate collection containers should be submitted with appropriate labelling. Alternatively a sputum sample collected in a plastic leak proof container can be used which is sent directly to the lab. Using the swab a minimum of 0.35mls should be collected. The medium or the sterile leak-proof container should be kept at 2-8 Celsius, and picked up same day. Do not use cotton or calcium alginate swabs to collect specimen.

How to obtain a ‘nasopharygeal’ swab: in fact it is a nasal cavity swab: insert the swab into the nostril parallel to the palate: **it must go at least 8cm along the floor to reach the nasopharynx.** Leave the swab in place for a few seconds to absorb secretions. Then repeat the same procedure on the contralateral side then place the swab in the culture media collection tube

How to obtain a oropharyngeal swab: swab the posterior pharynx avoiding the tongue

How to obtain a Nasopharyngeal wash/aspirate or nasal discharge: collect 2-3 mls into a sterile leak-proof, screw-cap sputum collection cup or sterile dry container. Refrigerate at 2-8 degrees. Celsius. Do not use sputum induction.

How to package the specimen: Place in a plastic biohazard bag with 2 pieces of gauze and then place in a second biohazard bag with an ice pack. The specimen must have the name of the patient, the date and the NP or OP specimen site written on the collection container and the order request form with all the above mentioned information stated on the request.

Finger Stick IgM / G test Kits

There are no kits which are manufactured in the US as of 3/24/2020 that test for the presence of acute phase reaction antibodies to COVID-19 antigens. There are 3 major Chinese companies (see below), 1 South Korean:http://sdbiosensor.com/xe/product/7662, 1 German (see below) , 1 English company https://www.alphabiolabs.co.uk/workplace-testing-services/coronavirus-testing-kit/ who are currently manufacturing such kits (see below for full details).

In common none are 'FDA approved', but are allowed under the Emergency Act recently enacted by our government. Specificity is high (few false positives) but sensitivity (few false negatives) results have to be confirmed and are purported to vary from 70-95%. These are 8-20 minute in office tests and involve a single finger stick and in some kits a pipette to test chamber followed by the addition of a reagent and color change for positivity: some IgM and some IgM and IgG. For further details see below.

Serology

Unlike the current test kits which are available in the US which utilize oro/nasopharynx swab tests, serology tests require a blood sample and measure antibodies which may indicate current and or previous exposure depending on which antibody is measured.

The IgM antibody takes 5-10 days from the time of exposure to make an antibody.

The IgG antibody indicates immune reaction to past exposure.

Serology tests are becoming available in the US through importation companies.

Over time our office will be using a total of 4 kits, including the kit listed above Test Country:

a. 20/20 test kits: Purported to be FDA 'cleared' only one import from China (see '1.' below) , finger stick IgM and G, 95% sensitivity and specificity, immediate results:
Here is the company which is FDA approved: https://2020gene.com/
The test itself, The Wondfo SARS-CoV-2 Antibody Test based on lateral flow method, approved by the NMPA on Feb 22 as the country's first POCT test for the SARS-CoV-2, can detect both IgM and IgG antibodies in human serum, plasma and whole blood samples within 15 minutes, effectively accelerating the on-site screening for suspected patients. Additionally, the test requires no special equipment to conduct, and can be stored and transported at room temperature, according to Wang Jihua, president of the company headquartered in Guangzhou.The other three antibody test products

b. Test Country: IgM test, listed above: https://testcountry.com/products/coronavirus-covid-19-rapid-test

c. Confirm Laboratories, San Diego, CA :https://www.confirmbiosciences.com/covid19-instant-coronavirus-test-kit/ which utilizes VivaCheck Laboratories, from China

d. Able Diagnostics, of San Diego, also utilizes Vivacheck Laboratories of China: https://www.ablediagnostics.com/contact.html

Berlin-based Pharmact has already started shipping a 20-minute immunoassay containing three SARS-CoV-2 antigens: the N protein and the S1 and S2 domains of the S protein. It is designed to detect any patient antibody that recognizes these protein structures. It aims to scale production to one million tests during the month of April. As is typical for such a test, it detects both immunoglobulin (Ig) M and IgG antibodies, which are released during the initial and later stages of an infection, respectively. It has conducted validation studies that compared its test with PCR, using samples from 114 infected patients and 126 uninfected controls. The test scored highly in terms of specificity. "We had a true negative rate of 100% — zero false positives," says Gunther Burgard, medical director at Pharmact. Its sensitivity was lower, however, as the IgM response does not offer

a strong initial signal. During the early stage of the infection (days 4–10), the IgM component of the test provides a sensitivity of just 70%. This rises rapidly to 92.3% between days 11 and 24, and the IgG component of the test offers a sensitivity of 98.6% during this phase of the infection. Overall, the test has a false negative rate of 13%, Burgard says.

Summary of Tests Available

TABLE 1 SELECTED COMMERCIAL RAPID TESTS FOR SARS-COV-2

Developer	Test	Description	Status
Guangzhou Wondfo Biotech (Guangzhou, China)	Wondfo SARS-CoV-2 antibody test	Lateral flow 15-minute immunoassay that detects IgM and IgG antibodies directed against SARS-CoV-2	National Medical Products Administration EUA in China; CE mark in Europe
Innovita Biological Technology	SARS-CoV-2 antibody assay	Lateral flow 15-minute immunoassay that detects IgM and IgG antibodies directed against SARS-CoV-2	National Medical Products Administration EUA in China
Jiangsu Medomics Medical Technologies (Nanjing, China)	SARS-CoV-2 rapid combined IgM/IgG antibody test kit	Lateral flow 15-minute immunoassay that detects IgM and IgG antibodies directed against SARS-CoV-2	Shipping
Mammoth Biosciences	SARS-CoV-2 DETECTR	30-minute lateral flow assay	In validation studies
Pharmact (Berlin)	SARS-COV-2 Rapid Test	POC 20-minute test for detecting SARS-CoV-2 exposure through identification of IgG and IgM antibodies	CE-marked and shipping
Snibe Diagnostic(Shenzhen, China)	MAGLUMI 2019-nCoV IgM/IgG kit	Automated central laboratory rapid test that runs on MAGLUMI chemiluminescence immunoassay system	CE mark received 19 February 2020
Sona Nanotech (Halifax, Nova Scotia)	Rapid SARS-CoV-2 antigen detection test	Lateral flow screening test for S1 domain of SARS-CoV-2 S1 protein	Assay development and testing with GE Healthcare Life

			Sciences underway
Sherlock Biosciences, Cepheid	Rapid CRISPR-based tests for SARS-CoV-2 and other pathogens	Combines SHERLOCK Cas12 and Cas13 enzymes for nucleic acid detection with Cepheid's GeneXpert test-processing instruments	Intended as proof of concept for a broad product development alliance in infectious disease
Zhejiang Orient Gene Biotech (Zhejiang, China)	COVID-19 IgG/IgM Rapid Test	Solid-phase immunochromatographic assay	Aytu Bioscience has sublicensed US distribution rights from L.B. Resources (Hong Kong) and plans to obtain EUA; already has CE mark
Biomerica	Rapid POC IgM/IgG antibody test	$10 lateral flow immunoassay	Commenced shipping samples; seeking FDA EUA approval
Caspr Biotech	Ultrasensitive, rapid, and portable coronavirus SARS-CoV-2 sequence detection	Based on CRISPR-Cas12	Proof of principle evaluation
Sugentech (Daejeon, South Korea)	SGTi-flex COVID-19 IgM/IgG	Ten-minute lateral flow immunoassay that detects IgM and IgG antibodies directed against SARS-CoV-2	CE Mark
Cepheid	Xpert Xpress SARS-CoV-2	Rapid PCR test that runs on GenXpert benchtop system – delivers result in two hours from sample collection to delivery of result	Received FDA emergency use authorization
Xiamen AmonMed Biotechnology (Fujian, China),	COVID-19 IgM/IgG test kit (Colloidal gold)	Ten-minute lateral flow immunoassay that detects IgM and IgG antibodies	CE Mark

directed against SARS-CoV-2

Proposed Protocol to Resume Work In The office from May 1st 2020

All employees (including myself) within 6 feet of patients will:

1. wear N95 masks without exhalation valves
2. wear protective glasses and a disposable gown
3. wear non latex gloves during patient care.

4. undergo weekly finger stick acute IgM testing in office with in office documentation on file

5. all patients who are scheduled for out-patient surgery according to Am College of surgeons 'Tier 1 a or b ' will undergo history screening, physical exam including pulmonary examination and a finger stick IgM testing during their pre-op, if negative they will continue with surgery, if positive they will contact the Dept of Health and their primary care physician and will proceed to home isolation followed by swab PCR testing.

6. all patients on the day of surgery will undergo a second finger stick IgM testing. if negative surgery will proceed and if positive it will be cancelled and they will contact the Dept. of Health and their primary care physician and will proceed to home isolation followed by swab PCR testing.

7. all staff at the San Leandro Surgery center will undergo weekly finger stick testing IgM and if negative will continue work, if positive, they will contact the Dept of Health and their primary care physician and will proceed to home isolation followed by swab PCR testing.

Relevant information:
Am Col Surgeons recommendations for out patient surgery:

https://nam02.safelinks.protection.outlook.com/?url=https%3A%2F%2Fwww.facs.org%2Fabout-acs%2Fcovid-19%2Finformation-for-surgeons%2Ftriage&data=02%7C01%7Clindaj%40sutterhealth.org%7Cb181e2fd43634481226208d7ce785d52%7Caef453eadaa243e0be62818066e9ff63%7C0%7C0%7C637204888664696320&sdata=%2FLO75VxK7uJeoC059iDCcDOTxklC02sT87Ndwsce8oc%3D&reserved=0

Finger Stick IgM testing sensitivity and specificity

COVID-19 Rapid Test - $9.95 per test
- Item Number: HE-Cassette-COVID19
- Rapid results in 2-5 minutes
- Detection window IgM: Symptomatic 3-5 days, Asymptomatic 7 days
- 'Accuracy over 95%' sensitivity and specificity more likely 90%
- Small sample sizes
- CE Marked
- Shelf life of 24 months from manufacture date

https://testcountry.com/products/coronavirus-covid-19-rapid-test

Epidemiology

The current assumptions based on some recent calculation is that up to 75% of the US population may become infected and roughly 0.3-1% of those infected will become severely ill with an

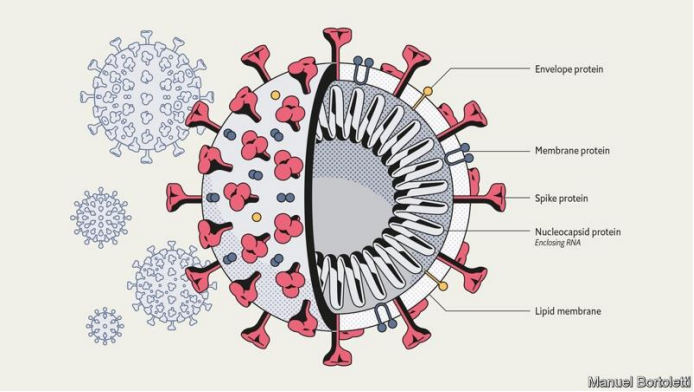
estimated 1 million deaths in the US mostly in the elderly and the people with pre-existing major medical problems in particular pulmonary illness.

It is unclear if there will be seasonality, ie warmer weather reduction in cases.

Social distancing and hand hygiene have an impact on the containment of the virus. Some new at-home suggested precautions include washing cloths using soap products every 1-2 days and preventing outside cloths from entering the home. The extent of these extreme measures has yet to be determined.

Following a COVID-19 infection it is not clear the conveyed immunity which is generated, specifically can the person become re-infected. Later we will know better whether mutations are relevant to reinfection and to what extent mutations might be clinically relevant.

BackGround



There are 2 groups of viruses: DNA viruses- that contain DNA material in order to reproduce and RNA viruses which have genetic material to help make the DNA to then reproduce. RNA viruses include. CoVID-19-SARS, Influenza, The common cold virus, HIV, SARS, and Ebola are all RNA viruses. Because the RNA has to code for DNA production it is more prone to mutations and errors which can explain the genetic variation and changes over time when it comes to testing and the formation of effective vaccines.

The interconnectedness of the modern world has been a boon for SARS-CoV-2. Without planes, trains and automobiles the virus would never have got this far, this fast. Scientists around the world are focusing their attention on its genome and the 27 proteins that it is known to produce, seeking to deepen their understanding and find ways to stop it in its tracks. The resulting plethora of activity has resulted in the posting of over 300 papers on and the depositing of hundreds of genome sequences in public databases.

The assault on the vaccine is not just taking place in the lab. As of February 28th China's Clinical Trial Registry listed 105 trials of drugs and vaccines intended to combat SARS-CoV-2 either already recruiting patients or proposing to do so. As of March 11th its American equivalent, the National Library of Medicine, listed 84. This might seem premature, considering how recently the virus became known to science; is not drug development notoriously slow? But the reasonably well-understood basic biology of the virus makes it possible to work out which existing drugs have some chance of success, and that provides the basis for at least a little hope.

Even if a drug were only able to reduce mortality or sickness by a modest amount, it could make a great difference to the course of the disease. As Wuhan learned, and parts of Italy are now learning, treating the severely ill in numbers for which no hospitals were designed puts an unbearable burden on health systems. As Jeremy Farrar, the director of the Welcome Trust, which funds research, puts it: "If you had a drug which reduced your time in hospital from 20 days to 15 days, that's huge."

Little noticed by doctors, let alone the public, until the outbreak of SARS (severe acute respiratory

syndrome) that began in Guangdong in 2002, the coronavirus family was first recognized by science in the 1960s. Its members got their name because, under the early electron microscopes of the period, their shape seemed reminiscent of a monarch's crown. (It is actually, modern methods show, more like that of an old-fashioned naval mine.) There are now more than 40 recognized members of the family, infecting a range of mammals and birds, including blackbirds, bats and cats. Veterinary virologists know them well because of the diseases they cause in pigs, cattle and poultry.

Virologists who concentrate on human disease used to pay less attention. Although two long-established coronaviruses cause between 15% and 30% of the symptoms referred to as "the common cold", they did not cause serious diseases in people. Then, in 2002, the virus now known as SARS-COV jumped from a horseshoe bat to a person (possibly by way of some intermediary). The subsequent outbreak went on to kill almost 800 people around the world.

Some of the studies which followed that outbreak highlighted the fact that related coronaviruses could easily follow SARS_COV across the species barrier into humans. Unfortunately, this risk did not lead to the development of specific drugs aimed at such viruses. When SARS-CoV-2—similarly named because of its very similar genome—duly arrived, there were no dedicated anti-coronavirus drugs around to meet it.

A SARS-CoV-2 virus particle, known technically as a virion, is about 90 nanometers (billionths of a meter) across—around a millionth the volume of the sort of cells it infects in the human lung. It contains four different proteins and a strand of RNA—a molecule which, like DNA, can store genetic information as a sequence of chemical letters called nucleotides. In this case, that information includes how to make all the other proteins that the virus needs in order to make copies of itself, but which it does not carry along from cell to cell.

The outer proteins sit athwart a membrane provided by the cell in which the virion was created. This membrane, made of lipids, breaks up when it encounters soap and water, which is why hand-washing is such a valuable barrier to infection.

The most prominent protein, the one which gives the virions their crown- or mine-like appearance by standing proud of the membrane, is called spike. Two other proteins, envelope protein and membrane protein, sit in the membrane between these spikes, providing structural integrity. Inside the membrane a fourth protein, nucleocapsid, acts as a scaffold around which the virus wraps the 29,900nucleotides of RNA which make up its genome.

Though they store their genes in DNA, living cells use RNA for a range of other activities, such as taking the instructions written in the cell's genome to the machinery which turns those instructions into proteins. Various sorts of virus, though, store their genes on RNA. Viruses like HIV, which causes aids, make DNA copies of their RNA genome once they get into a cell. This allows them to get into the nucleus and stay around for years. Coronaviruses take a simpler approach. Their RNA is formatted to look like the messenger RNA which tells cells what proteins to make. As soon as that rna gets into the cell, flummoxed protein-making machinery starts reading the viral genes and making the proteins they describe.

First contact between a virion and a cell is made by the spike protein. There is a region on this protein that fits hand-in-glove with ace2, a protein found on the surface of some human cells, particularly those in the respiratory tract.

ace2 has a role in controlling blood pressure, and preliminary data from a hospital in Wuhan suggest that high blood pressure increases the risks of someone who has contracted the illness dying of it (so do diabetes and heart disease). Whether this has anything to do with the fact that the virus's entry point is linked to blood-pressure regulation remains to be seen.

Once a virion has attached itself to an ace2 molecule, it bends a second protein on the exterior of the cell to its will. This is tmprss2, a protease. Proteases exist to cleave other proteins asunder, and the virus depends on tmprss2 obligingly cutting open the spike protein, exposing a stump called a fusion peptide. This lets the virion into the cell, where it is soon able to open up and release its RNA.

Coronaviruses have genomes bigger than those seen in any other RNA viruses—about three times longer than HIV's, twice as long as the influenza virus's, and half as long again as the Ebola virus's. At one end are the genes for the four structural proteins and eight genes for small "accessory" proteins that seem to inhibit the host's defenses (see diagram). Together these account for just a third of the genome. The rest is the province of a complex gene called replicase. Cells have no interest in making RNA copies of RNA molecules, and so they have no machinery for the task that the virus can hijack. This means the virus has to bring the genes with which to make its own. The replicase gene creates two big "polyproteins" that cut themselves up into 15, or just possibly 16, short "non-structural proteins" (nsps). These make up the machinery for copying and proofreading the genome—though some of them may have other roles, too.

Once the cell is making both structural proteins and RNA, it is time to start churning out new virions. Some of the RNA molecules get wrapped up with copies of the nucleocapsid proteins. They are then provided with bits of membrane which are rich in the three outer proteins. The envelope and membrane proteins play a large role in this assembly process, which takes place in a cellular workshop called the Golgi apparatus. A cell may make between 100 and 1,000 virions in this way, according to Stanley Perlman of the University of Iowa. Most of them are capable of taking over a new cell—either nearby or in another body—and starting the process off again.

Not all the RNA that has been created ends up packed into virions; leftovers escape into wider circulation. The coronavirus tests now in use pick up and amplify SARS-CoV-2-specific RNA sequences found in the sputum of infected patients.

Because a viral genome has no room for free riders, it is a fair bet that all of the proteins that SARS-CoV-2 makes when it gets into a cell are of vital importance. That makes each of them a potential target for drug designers. In the grip of a pandemic, though, the emphasis is on the targets that might be hit by drugs already at hand.

The obvious target is the replicase system. Because uninfected cells do not make RNA copies of RNA molecules, drugs which mess that process up can be lethal to the virus while not necessarily interfering with the normal functioning of the body. Similar thinking led to the first generation of anti-hiv drugs, which targeted the process that the virus uses to transcribe its RNA genome into DNA—another thing that healthy cells just do not do.

Like those first HIV drugs, some of the most promising SARS-CoV-2 treatments are molecules known as "nucleotide analogues". They look like the letters of which RNA or DNA sequences are made up; but when a virus tries to use them for that purpose they mess things up in various ways.

The nucleotide-analogue drug that has gained the most attention for fighting SARS-CoV-2 is remdesivir. It was originally developed by Gilead Sciences, an American biotechnology firm, for use against Ebola fever. That work got as far as indicating that the drug was safe in humans, but because antibody therapy proved a better way of treating Ebola, remdesivir was put to one side. Laboratory tests, though, showed that it worked against a range of other RNA-based viruses, including SARS-COVID, and the same tests now show that it can block the replication of SARS-CoV-2, too.

There are now various trials of remdesivir's efficacy in covid-19 patients. Gilead is organizing two in Asia that will, together, involve 1,000 infected people. They are expected to yield results in mid- to late-April. Other nucleotide analogues are also under investigation. When they screened seven drugs approved for other purposes for evidence of activity against SARS-CoV-2, a group of researchers at the State Key Laboratory of Virology in Wuhan saw some potential in ribavirin, an antiviral drug used in the treatment of, among other things, hepatitis c, that is already on the list of essential medicines promulgated by the World Health Organisation (who).

Nucleotide analogues are not the only antiviral drugs. The second generation of anti-HIV drugs were the "protease inhibitors" which, used along with the original nucleotide analogues, revolutionized the treatment of the disease. They targeted an enzyme with which HIV cuts big proteins into smaller

ones, rather as one of SARS-CoV-2's nsps cuts its big polyproteins into more little nsps. Though the two viral enzymes do a similar job, they are not remotely related—HIV and SARS-CoV-2 have about as much in common as a human and a satsuma. Nevertheless, when Kaletra, a mixture of two protease inhibitors, ritonavir and lopinavir, was tried in sars patients in 2003 it seemed to offer some benefit.

Another drug which was developed to deal with other RNA-based viruses—in particular, influenza—is Favipiravir (favilavir). It appears to interfere with one of the nsps involved in making new RNA. But existing drugs that might have an effect on SARS-CoV-2 are not limited to those originally designed as antivirals. Chloroquine, a drug mostly used against malaria, was shown in the 2000s to have some effect on sars-cov; in cell-culture studies it both reduces the virus's ability to get into cells and its ability to reproduce once inside them, possibly by altering the acidity of the Golgi apparatus. Camostat mesylate, which is used in cancer treatment, blocks the action of proteases similar to tmprss2, the protein in the cell membrane that activates the spike protein.

Not all drugs need to target the virus. Some could work by helping the immune system. Interferons promote a widespread antiviral reaction in infected cells which includes shutting down protein production and switching on rna-destroying enzymes, both of which stop viral replication. Studies on the original sars virus suggested that interferons might be a useful tool for stopping its progress, probably best used in conjunction with other drugs

Conversely, parts of the immune system are too active in covid-19. The virus kills not by destroying cells until none are left, but by overstimulating the immune system's inflammatory response. Part of that response is mediated by a molecule called interleukin-6—one of a number of immune-system modulators that biotechnology has targeted because of their roles in autoimmune disease.

Actemra (tocilizumab) is an antibody that targets the interleukin-6 receptors on cell surfaces, gumming them up so that the interleukin-6 can no longer get to them. It was developed for use in rheumatoid arthritis. China has just approved it for use against covid-19. There are anecdotal reports of it being associated with clinical improvements in Italy.

Gilead, meanwhile, has enough remdesivir to support clinical trials and, thus far, compassionate use. The firm says it is working to make more available "as rapidly as possible", even in the absence of evidence that it works safely.

The uncertainty is high, but a plausible scenario—one-fifth of the US population will fall ill, and a 0.5% fatality rate—would lead to 327,000 deaths, or nine times that of a typical flu season.

The estimated doubling time of the virus is six days. If that remains constant, as is likely, the close-to-1,300 current cases are the bottom of a sickening ride up an exponential curve of infections.

"In literal terms, we have no idea about the number of cases because nobody has tested to any meaningful extent," says Marc Lipsitch, a professor of epidemiology at Harvard. "Tens of thousands of cases in the us seems plausible," he adds.

A recent study of Covid-19 in China found that 5% of patients needed to be admitted to an intensive care unit (icu), with many needing intensive ventilation or use of a more sophisticated machine that oxygenates blood externally. America has 95,000 icu beds and 62,000 mechanical ventilators, while only 290 hospitals out of 6,000 offer the most intensive treatment. The death rate varies between 0.4-2.9% depending on the polulations health, age and access to advanced medical care specifically ICU ventilators +/- ECMO.

Understanding How The Covld-19 PCR Swab Test Works

The tests to date in common rely on test called PCR-reverse polymerare chain reaction or RPCR.

The RPCR test is only positive if viral particles are present and does not indicate past exposure.

Basically, PCR is a way to extract highly purified RNA, then amplify the 100 of the 30,00 nucleotides in the RNA which is then converted to DNA: which includes 2 specific genes in the SARS=CoV-2 genone. These genes are amplified into billions of copies and then the DNA undergoes gel electrophoresis.

A positive test requires the presence of both genes.

There are currently at least 4 companies that at developed this RPCR test

- bioMérieux NucliSens® systems,
- QIAamp® Viral RNA Mini Kit, QIAamp® MinElute Virus Spin Kit or RNeasy® Mini Kit (QIAGEN), EZ1 DSP Virus Kit
- Roche MagNA Pure Compact RNA Isolation Kit, Roche MagNA Pure Compact Nucleic Acid Isolation Kit, and Roche MagNA Pure 96 DNA and Viral NA Small Volume Kit, and
- Invitrogen ChargeSwitch® Total RNA Cell Kit.

A false negative results are more likely than false positive and the reason is either genetic variability or inadequate viral particles (emphasizing the importance of a minimum of 0.2-0.35mls swab collection technique.

A recent study in China found PCR COVID-19 in the stool of a asymptomatic child 26 days after last viral exposure.

Signature below is to verify I have read the above and will follow this protocol in the immediate future:

Signature Date

Angel Romero

Alondra Alcala

Amy Celaya

Brianna Kirkeby

Keely Tietjen

Lisa Derita

Nancy Huynh