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COVID-19: New disease and chaos with panic, associated with stress

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COVID-19 (**coronavirus disease – 2019**) caused by SARS-CoV-2 (also known as 2019-nCoV) is a new infectious disease by etiology, but in manifestations it has some similarities with SARS (Severe Acute Respiratory Syndrome) that ravaged several countries of the world around 2003. Coronaviruses are RNA containing microbes that 'hijack' mammalian cells to replicate themselves intracellularly, just to be released in large quantities. SARS-CoV-2 first replicates in the upper respiratory tract, as opposed to SARS-CoV viruses in the 'old' SARS that attack the lower respiratory tree, especially the lungs and cause severe pneumonia. About 80% of COVID-19 patients are mild, some of them are even asymptomatic and only about 10-20% require hospitalization because of pulmonary edema and rapidly developing bronchopneumonia that often leads to multiorgan failure, especially in older patients with chronic comorbidities or immunocompromised system (e.g., obesity, diabetes mellitus, cardiovascular diseases). The overall worldwide mortality is about 1-2%, but some of the genetic variants of the virus caused 4-6% mortality, especially in densely populated areas, like Northern Italy, New York city, Spain. In the most severe cases a 'cytokine storm' (a massive release of cytokines) have been described that aggravate the initial damage in the lungs and heart. Epidemiologically, the true incidence and prevalence of COVID-19, most likely, will never be known because of uneven testing in most of the countries for the viral RNA and/or for the developed IgM and IgG antibodies against the virus. From public health perspectives, the hardest hit areas of the world are those that were not prepared, had a poorly organized or underfunded public health service, and/or did not follow the preventive measures such as social distancing, isolation and frequent hand washing. The poor organization of public health services, especially if associated with initial denial of the rapid spread of the disease lead to chaos, panic and, predictably, severe distress in many people.

Keywords: COVID-19, pathogenesis, cytokine, public health, distress, mental health

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COVID-19: нова хвороба та хаос із панікою унаслідок стресу

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COVID-19 (**coronavirus disease – 2019** (коронавірусна хвороба 2019)), викликана вірусом SARS-CoV-2 – етіологічно нова інфекційна хвороба, але у проявах має певні подібності із SARS (Sever Acute Respiratory Syndrome), яка мала місце у кількох країнах у сіті у 2003 р. Коронавіруси є РНК-вмісні агенти, які атакують клітини савців, щоб реплікуватися внутрішньоклітинно з подальшим вивільненням у великих кількостях. SARS-CoV-2 розмножується у верхніх дихальних шляхах, на відміну від SARS-CoV вірусів, які спричиняли так

званий старий SARS, атакуючи нижні дихальні шляхи, а також легені, призводячи до важкої пневмонії. Близько 80% хворих на COVID-19 пацієнтів мають легкі симптоми, дехто навіть не має жодних, і тільки 10-20: потребують госпіталізації у зв'язку з набряком легень і швидкопрогресуючою бронхопневмонією, яка часто призводить до поліорганної недостатності, особливо у старших пацієнтів із хронічними коморбідностями та скомпроментованою імунною системою, як-от ожиріння, цукровий діабет, серцево-судинними захворюваннями. Загальносвітова смертність є близько 1-2%, але деякі генетичні варіанти вірусу викликали смертність 4-6%, особливо у густонаселених регіонах, таких як Північна Італія, місто Нью-Йорк, Іспанія. У найважчих випадках був описаний «цитокіновий шторм» (масове вивільнення цитокінів), що посилював пошкодження легень і серця. Епідеміологічно справжній рівень первинної захворюваності і поширеність COVID-19, правдоподібно, ніколи не будуть відомі через нерівномірне тестування у більшості країн з метою виявлення вірусної РНК і/або циркулюючих антитіл IgM та IgG до вірусу. З перспективи Організації Охорони Здоров'я найбільше постраждали ті регіони, які були найменше підготовані, мали не досить організовану або недофінансовану систему охорони здоров'я і/або не впроваджували превентивних заходів, як-от соціальне дистанціювання, ізоляція та часте миття рук. Погана організація служб охорони здоров'я особливо пов'язана з первинним запереченням швидкого поширення хвороби призводила до хаосу, пініки та, передбачувано, значного дистресу у багатьох людей.

Ключові слова: COVID-19, патогенез, цитокіни, громадське здоров'я, дистрес, психічне здоров'я.

COVID-19 (**coronavirus disease – 2019**) caused by SARS-CoV-2 is the subject of lot of scientific rapid publications and of news media coverage, because of its rapid, pandemic spread. The name of the virus originates from a similar coronavirus which caused the also pandemic SARS (Sever Acute Respiratory Syndrome) around 2003, and as we will see below, there are some similarities

and differences between the old SARS and the new COVID-19. One of the best examples of urgency and the need for rapid distribution of objective scientific information is the fact that a recent issue of *Science*, one of the best scientific journals in the world, dedicated the cover page and most of its content to COVID-19. The other best weekly scientific journal *Nature* also

devotes substantial coverage in every issue during the last two months. Furthermore, the electronic daily *Nature Briefs* is an excellent platform for the fast dissemination of new data and new developments in COVID-19.

This short review article is written at the beginning of April 2020, i.e., within about two months after the declaration of pandemic by the World Health Organization (WHO) and since only a few peer-reviewed scientific papers have been published in reputable journals, I also quote data from credible news organizations, such as the BBC, daily Guardian, Japan Times, The New York Times, Washington Post and Wall Street Journal. The review is divided into sections on the etiology, i.e., the new virus, then to new disease COVID-19 and its epidemiology, followed by the ensuing chaos and panic that was bordering on hysteria, associated with stress in several countries.

The etiology: SARS-CoV-2

Viruses are virtual 'cells', or nuclei without cytoplasm. This definition implies that viruses cannot live long and multiply without entering mammalian cells, essentially hijacking the cell genetic material and its endoplasmic reticulum in the cytoplasm. Then they multiply in the animal or plant cells, just to be released in a large number, often destroying their host cells that helped the virus to survive and multiply.

Viruses can be classified by many criteria, but probably the most useful distinction is

dividing them into DNA and RNA-containing viruses [1]. SARS-CoV-2 is an RNA virus, the 7th coronavirus so far identified (Table 1). The name of coronaviruses originates from their protein-containing corona-like nuclear membranes. As the SARS-CoV-2 picture on the cover page of *Science* (Fig. 1) shows, out of viral membrane protein spikes are

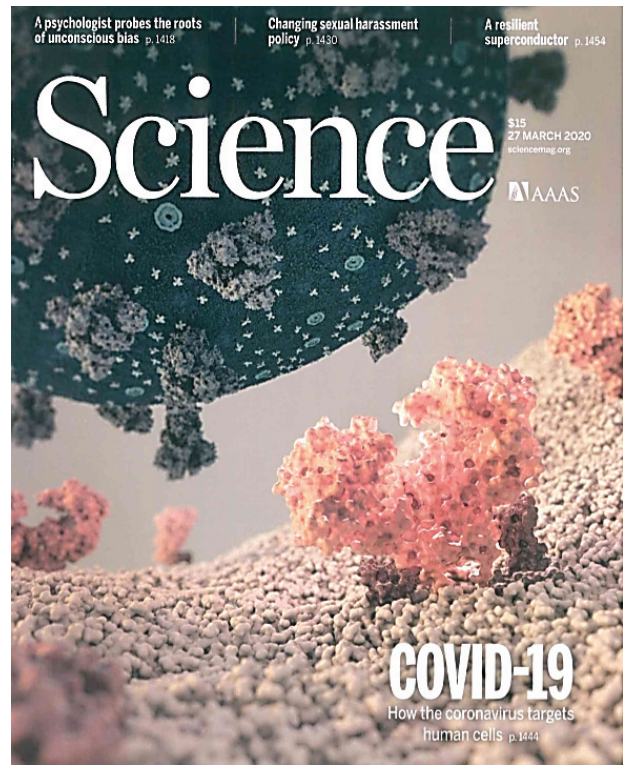


Figure 1. Title page of *Science*, on March 27, 2020, one of the best scientific journals in word, devoted to COVID-19

Table 1.

Human Coronavirus Types

Coronaviruses are named for the crown-like spikes on their surface. There are four main sub-groupings of coronaviruses, known as alpha, beta, gamma, and delta.

Human coronaviruses were first identified in the mid-1960s. The seven coronaviruses that can infect people are:

Common human coronaviruses

1. 229E (alpha coronavirus)
2. NL63 (alpha coronavirus)
3. OC43 (beta coronavirus)
4. HKU1 (beta coronavirus)

Other human coronaviruses

1. MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS)
2. SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome, or SARS)
3. SARS-CoV-2 (the novel coronavirus that causes coronavirus disease 2019, or COVID-19)

From: <https://www.cdc.gov/coronavirus/types.html>

protruding and serve as the invasion tools for coronaviruses. Namely, these can attach to the ACE-2 (angiotensin-converting enzyme 2) receptor in our cells and after endocytosis, the virus can access the intracellular machinery of the mammalian cell. The receptor attachment and endocytosis are the first steps in the viral hijacking of our cells and the process is best illustrated in a figure published in the Science Times supplement of the New York Times [2].

Since discoveries in basic sciences are often not accepted and appreciated, it's worth mentioning that the first coronavirus was discovered in the 1960s by virologist June Almeida, who grew up in Glasgow, UK and left school at age 16, but subsequently mastered electron microscopy as a lab technician and went on to obtain a Ph.D. Her discovery could have been recorded even sooner: an earlier paper featuring her images was rejected as "just bad pictures of influenza" [3].

SARS-CoV-2 is remarkably similar not only to the initial SARS-inducing coronavirus from 2003, but also to RNA viruses that caused the Middle East Respiratory Syndrome (MERS) a few years ago, and the seasonal common cold ("flu"). These coronaviruses mutate very rapidly, and this is one of the main reasons why it is so difficult to develop long-lasting vaccine against influenzas, i.e., almost every year new mutations occur, hence new vaccines need to be produced. A recent issue of Science published not only the molecular structure of the SARS-CoV-2 (also known as 2019-nCoV), the virus genome but also the structure and composition of protein-membrane and the protruding spikes [4] (Fig. 2). The latter is particularly important for designing new drugs that may block viral attachment via the spikes to the ACE-2 receptors on mammalian cells. But the accompanying review article in this issue of Science provided another startling revelation: since December 2019 more than 350 genomic variants of new coronaviruses have been identified around the world... Furthermore, apparently new mutations occur almost every other day! [5]

The analysis of these genetic variants also revealed what was suspected during the preceding weeks, i.e., the deadly virus that suddenly appeared in nursing home patients

in Washington state of the USA jumped from animals to humans in the state of Washington and apparently was not imported from China. Furthermore, another deadly virus variant originated in or around Munich, Germany, and was somehow transferred to Italy. Also, the coronavirus which hit New York City so hard was apparently transported from Europe [5]. These great genetic variations in SARS-CoV-2 are one of the reasons for different mortality rates which were around 6% in Italy, 4% in Washington state, while 1-2% in China & USA.

It should be also acknowledged that coronaviruses are the etiologic factors in zoonosis, i.e., diseases when the pathogens jump from wild or domestic animals. SARS-CoV-2 in Wuhan, China apparently jumped from bats to other animals (e.g., civets, cats, wild dogs) that are sold as delicatessens in 'wet markets' that are so popular in China. New studies also indicate that animals exposed to severe or frequent environmental stressors, like temperature extremes, starvation, overcrowding (in farmed or domestic animals), shed the viruses much easier to other animals and humans, than healthy and well-bred animals [6]. It is also interesting that coronaviruses that are pathogens to us, do not make the host animal sick. And these zoonoses are becoming more frequent with global warming, adding one more example of environmental stressors affecting human health.

The new disease: COVID-19

It is interesting that the etiologic virus is new, actually novel, and the disease it creates is also new and unusual. Although it has a few similarities with other viral respiratory diseases, it also demonstrated major differences. The original SARS virus in 2003 attacked mainly the lower respiratory tract, especially the lung, and created severe bronchopneumonia that was exceedingly difficult to treat. The SARS-CoV-2, on the other hand, attaches mostly to the upper respiratory tract, e.g., nose and nasopharynx [7]. This differential target specificity is the main reason that COVID-19 starts with a dry cough, often before the detectable fever, within 3-5 days after exposure.

Then, depending on the immune status of the infected person, the clinical progression may include the spread of the virus to the

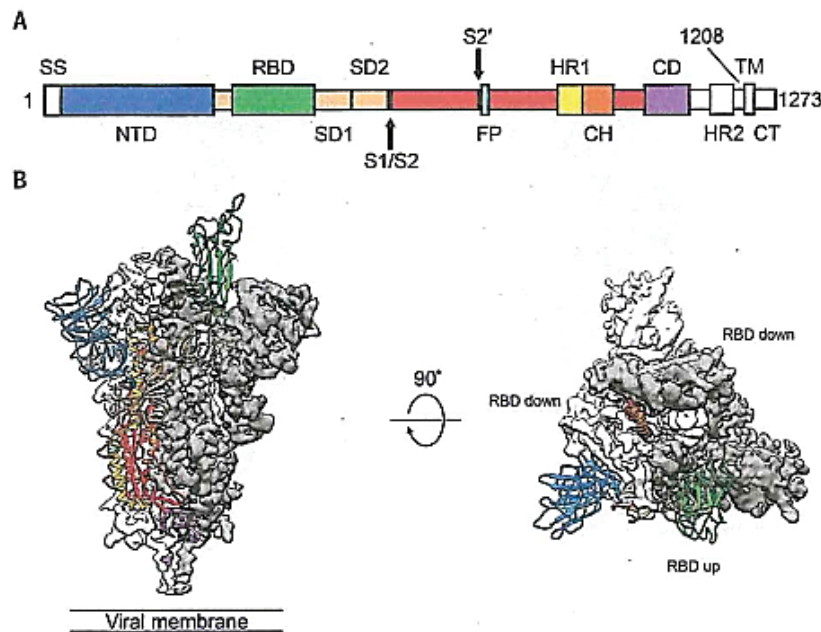
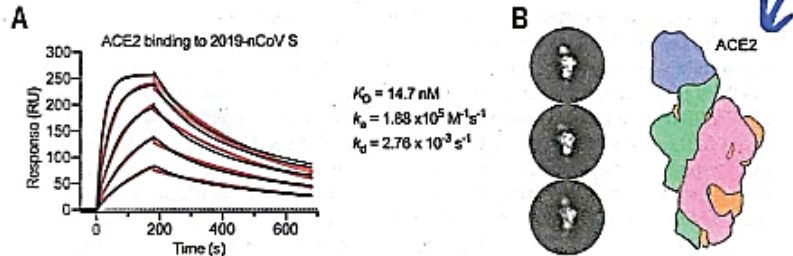


Fig. 3. 2019-nCoV S binds human ACE2 with high affinity. (A) Surface plasmon resonance sensorgram showing the binding kinetics for human ACE2 and immobilized 2019-nCoV S. Data are shown as black lines, and the best fit of the data to a 1:1 binding model is shown in red. (B) Negative-stain EM 2D class averages of 2019-nCoV S bound by ACE2. Averages have been rotated so that ACE2 is positioned above the 2019-nCoV S protein with respect to the viral membrane. A diagram depicting the ACE2-bound 2019-nCoV S protein is shown (right) with ACE2 in blue and S protein protomers colored tan, pink, and green.



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CORONAVIRUS

Cryo-EM structure of the 2019-nCoV spike in the prefusion conformation

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The outbreak of a novel coronavirus (2019-nCoV) represents a pandemic threat that has been declared a public health emergency of international concern. The CoV spike (S) glycoprotein is a key target for vaccines, therapeutic antibodies, and diagnostics. To facilitate medical countermeasure development, we determined a 3.5-angstrom-resolution cryo-electron microscopy structure of the 2019-nCoV S trimer in the prefusion conformation. The predominant state of the trimer has one of the three receptor-binding domains (RBDs) rotated up in a receptor-accessible conformation. We also provide biophysical and structural evidence that the 2019-nCoV S protein binds angiotensin-converting enzyme 2 (ACE2) with higher affinity than does severe acute respiratory syndrome (SARS)-CoV S. Additionally, we tested several published SARS-CoV RBD-specific monoclonal antibodies and found that they do not have appreciable binding to 2019-nCoV S, suggesting that antibody cross-reactivity may be limited between the two RBDs. The structure of 2019-nCoV S should enable the rapid development and evaluation of medical countermeasures to address the ongoing public health crisis.

Figure 2. Cryo-EM (electron microscopic) structure of 2019-nCoV (also known as SARS-CoV-2) spike proteins (adapted from Science, March 13, 2020)

lower respiratory tract, including the alveolar sacs of terminal bronchi. There, since the alveoli are covered by thin epithelial layer what the virus attacks, defensively releases VEGF/VPF (vascular endothelial growth factor/vascular permeability factor) from the surrounding connective tissue and macrophages. The peptide then increases vascular/capillary permeability, plasma fluid escapes, and often fills the alveolar sacs. This resulting pulmonary edema impairs, in severe cases completely blocks the oxygenation of venous blood that normally happens in the healthy lung. The resultant tissue hypoxia causes more VEGF/VPF release, because of the upregulation of HIF (hypoxia inducible factor) that triggers the increased synthesis and release of VEGF/VPF.

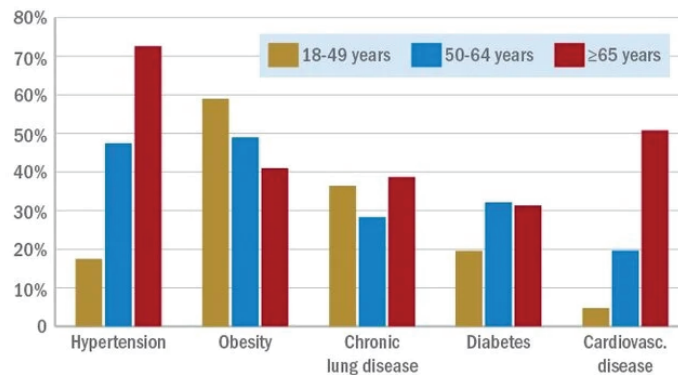
This early vascular damage in the pathogenesis of pulmonary edema is not unique to the lung. My research lab systematically demonstrated this in the initial stages of gastric erosions and ulcers, as well as in the molecular pathogenesis of ulcerative colitis [8-11]. Like in experimental ulcerative colitis, where anti-VEGF neutralizing antibodies prevented the full development of colitis, now after clinical reports showed that the blood levels of VEGF in severely ill COVID-19 patients were markedly elevated [12], clinical trials with commercially available anti-VEGF drugs like Avastin (bevacizumab) and Lucentis (ranibizumab) are in treating COVID-19 patients are appearing [12, 13].

The rapidly developing pulmonary edema is the reason for shortness of breath, and the need for respiratory ventilators in severely ill COVID-19 patients. If increased vascular permeability and edema, which are the first stage in any acute inflammation, not treated early, the cellular stage of inflammation is ensuing when infiltration of leukocytes in the next response to early tissue damage. This may progress to mild or severe bronchopneumonia that is the cause of death in the minority of COVID-19 patients. Fortunately, in about 80% of patients, the symptoms are mild or moderate, and only in 10-15%, the outcome is death. But the main concern from the public health point of view is that 5-20% of the infected people remain asymptomatic, i.e., unknowingly they may spread the virus, especially if they do not wear appropriate masks [14, 15].

Comorbidities and pathogenesis of COVID-19:

- Another important clinical and public health pattern is emerging that seems to be consistent from the very early reports from China to the most recent cases in Italy, Spain & USA: the hospitalized patients who suffer the most severe outcome are those who have other underlying chronic diseases, such as diabetes mellitus (DM), obesity, hypertension, chronic lung and cardiovascular diseases (Fig. 3) and/or naturally compromised drug-induced immune suppression [16, 17]. The underlying mechanism is not clear, but a few elements in the pathogenesis of very severe COVID-19 are emerging, e.g., nonre-

Underlying conditions among adults hospitalized with COVID-19



Note: Based on data from the COVID-19–Associated Hospitalization Surveillance Network for patients hospitalized in 99 counties in 14 states from March 1-30, 2020.

Source: MMWR. 2020 Apr 8;69(early release):1-7

Figure 3. Major comorbidities associated with COVID-19 and their age-dependent distribution (modified from MMWR – Morbidity & Mortality Weekly Reports, April 8, 2020)

sponsive or poorly responsive immune system and the already existing tissue damage in the lungs and heart. It may be like the obesity-DM type 2 connection: obesity leads not only to non-responsive insulin receptors but also to sluggish immunity which allows the proliferation and dissemination of coronaviruses in the body. New reports are also emerging indicating "multi-organ failures" in a deadly form of the disease: inflammation in heart muscle, especially around the conduction system in the heart resulting in fatal cardiac arrhythmias. The existing atherosclerotic plaques become more prone to rupture that will lead to, often occlusive, thrombus formation, which is aggravated by abnormal blood coagulation, as first reported in patients from Wuhan, China [17]. In patients with COVID-19-related pneumonia, 10% had venous thromboembolism that contributed to their death. Almost half of COVID-19 patients have blood or protein in their urine, indicating kidney damage. Gastrointestinal (GI) symptoms and signs (e.g., nausea, vomiting, diarrhea) have also been reported and the GI signs may precede or follow the upper respiratory manifestations [18].

Very recent data and publications indicate that the multi-organ involvement and pathogenesis of COVID-19 is more complex and detrimental than initially thought. This is very nicely integrated and illustrated in a very recent review article in Science [19] (Fig. 4). It confirms that although the initial target in the pathogenesis is the respiratory tract, including the lungs, with direct damage to the alveolar epithelial and endothelial cells, other organs are also involved, especially in the minority of very severe cases. In this sequence, damage to the liver, kidney and the GI tract has been documented, but lesions in the heart, blood vessels, and brain are the major contributors, in addition to pulmonary edema, to the cause of mortality in very ill COVID-19 patients. The figure also includes the recently identified early sign and symptoms in this disease: the loss of smell because of viral proliferation in the nose in some of the infected people.

Thus, regarding the frequently discussed question "how SARS-CoV-2 kills" certain patients, i.e., by direct organ damage or via "cytokine storm" (reviewed in the next section), we could probably state that by both pathways [20].

The 'cytokine storm' – Among the complications of COVID-19, a new syndrome, the 'cytokine storm' is emerging. 'Cytokine storm' is a massive release of inflammatory cytokines, in a second wave of secondary cytokines (Fig. 5) in response to SARS-CoV-2 or influenza virus, i.e., when the release of defensive cytokines is much larger and last longer than in the usual inflammatory response to microbial or viral invasion [20]. The 'storm' may occur during the clinical course of COVID-19 and rarely in influenzas, and it often kills the patient... Even worse, it may develop 3-5 days after recovery in healthy-looking individuals and may exacerbate pulmonary edema, pneumonia, and cardiac complications.

Very recent studies started to shed light on the molecular mechanisms of 'cytokine storm'. Namely, during infection, our T-lymphocytes are activated to release cytokines which trigger additional T-lymphocytes to be made, which release more cytokines. Among the proliferating lymphocytes, cytotoxic T-cells roam the body and kill infected cells to stop the increased production of viruses that cause COVID-19 [20]. Normally, cytotoxic T-lymphocytes target only infected cells, but when the immune response goes into overdrive, these cytotoxic T-cells and the massive release of cytokines damage or kill healthy cells in our organs, especially in the lungs and heart. This storm is the major cause of mortality in about half of the 20% of hospitalized COVID-19 patients. Fortunately, it is relatively easy to diagnose the 'cytokine storm' by laboratory tests that show elevated serum ferritin level (the usual 200 ng/ml goes up to 500-800 ng/ml), accompanied by also increased serum D-dimer proteins and lactate dehydrogenase enzyme, originating from liver and heart [20].

Because of the clinical importance of 'cytokine storm', recent intensive research revealed an additional molecular/biochemical pathway: "glucose metabolism pathway [is] critical to the dysregulated immune response that kills many infectious disease patients, including those with COVID-19" [20]. The other main culprit is the transcription factor interferon regulatory factor 5 (IRF5) which is critical for pro-inflammatory cytokine production, and if it is genetically deleted in mice, the animals are protected against influenza-induced cytokine storms. During the

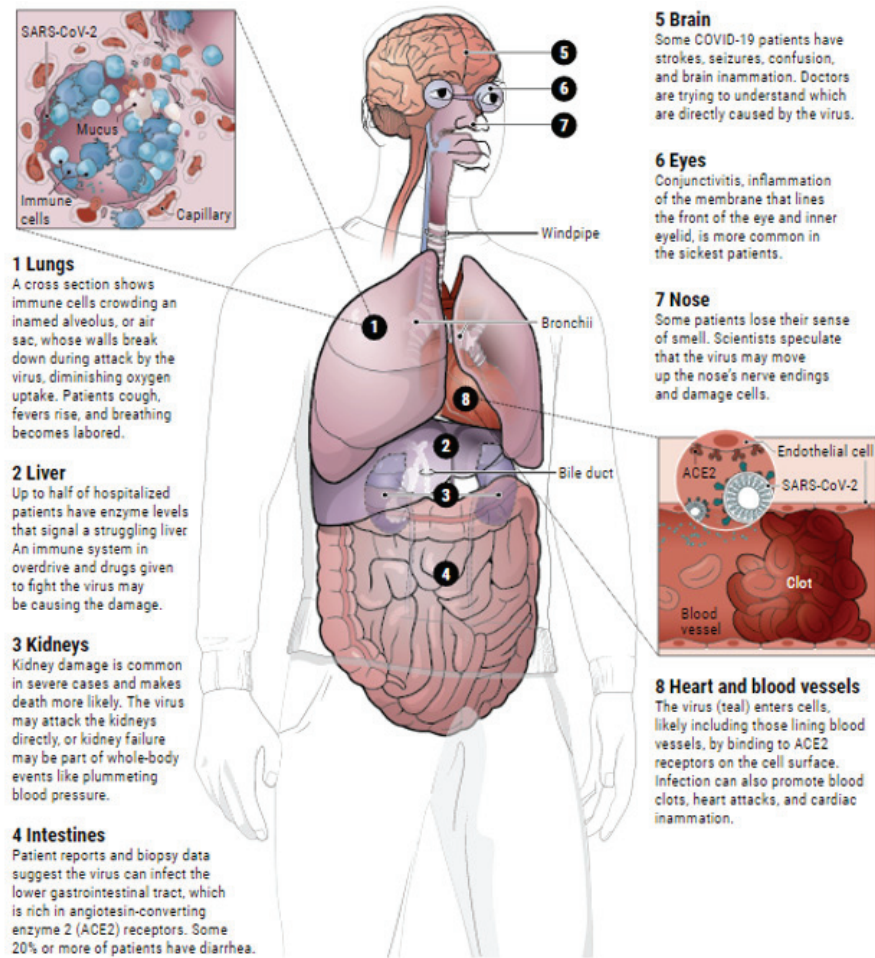


Figure 4. The multi-organ involvement in the pathogenesis of COVID-19 (modified from Science, April 17, 2020)

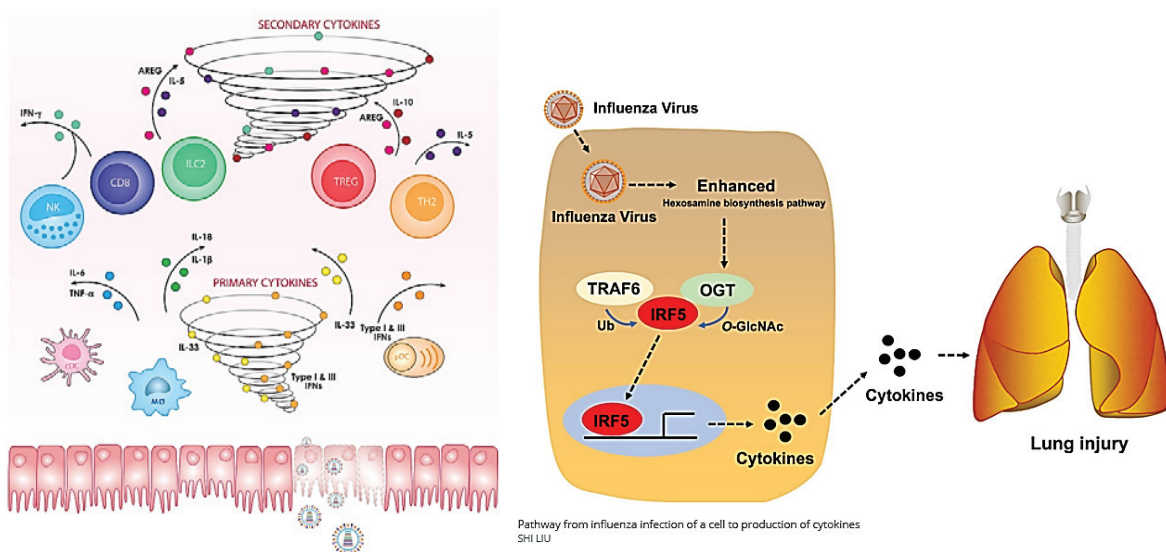


Figure 5. The 'cytokine storm': illustrating the importance of primary & secondary cytokines (adapted from Guo XJ et al. *Semin. Immunopathol.*2017; 39: 541-550), and its new molecular mechanism involving glucose metabolism (adapted from Williams R., *The Scientist*, April 15, 2020)

inflammatory response to infections, glucose metabolism is upregulated, in part to provide an energy source to our immune cells. The specific glucose metabolism pathway now identified is the hexosamine biosynthesis pathway which leads to the production of uridine diphosphate N-acetylglucosamine (UDP-GlcNAc)—pronounced UDP-GlickNack (Fig. 6). This nucleotide sugar is sometimes added to proteins in a process called O-GlcNAcylation. Namely, O-GlcNAcylation of IRF5 is necessary for the cytokine-producing activity of transcription factor IRF5 [21]. The research team also showed that patients infected with influenza coronavirus have higher blood glucose levels and more O-GlcNAcylation of IRF5 than healthy controls. Furthermore, blood glucose levels correlated tightly with levels of inflammatory cytokines [19].

Tests for COVID-19 detection. - The growing number of approved tests around the world (so far more than 25 tests have been approved by the USA FDA), the confusion, as well as intentional and unintentional misinformation, is also spreading in the news and social media, often even in the scientific literature. Thus, it is important to clarify some facts and to distinguish the two types of tests so far available in most of the countries:

- Direct detection of SARS-CoV-2 (the new official name of the virus) which causes COVID-19: These tests detect the viral RNA fragments in the mucus secretion (obtained by upper respiratory tract swabs that are inherently prone to error) or in the blood (more reliable and accurate). These biochemical methods usually involve PCR (polymerase chain reaction) tests that could be performed, until recently, only in specialized molecular pathology labs. At the end of March 2020, the FDA approved a very rapid PCR test that can be performed in office/desktop type "ID NOW" instruments produced by Abbott Labs. These instruments are in common use to detect influenza and other viral or bacterial products. With this technique, positive qualitative results can be seen in 5 mins, negative ones in 13 mins. To measure the viral levels of RNA in the blood, samples still must be sent to specialized labs. A very recent study, in part originating from China indicates that "throat washing outperforms nasopharyngeal swabs for coronavirus detection" [22].

- Measuring the antibodies against SARS-CoV-2 in the plasma, obtained by centrifugation the venous blood samples: Recently approved methods use only saliva or a drop of blood, obtained after needle pick of fingers, as source material for the qualitative detection of specific IgG and IgM. Thus, these tests do NOT detect the virus, only our antibodies that develop in a few days or weeks after the exposure, irrespective if a person is sick, or asymptomatic. Positive results may also indicate that the patient is immune to this virus. This is the medical reason why people with the defective or drug-suppressed immune system are so susceptible to COVID-19, i.e., since they cannot develop antibodies against the virus.

It's also important to understand that there is no such thing as "drive through testing" – only drive-through sample collection (of swabs) that need to be sent to specialized labs, where the results may be ready in 2-4 days.

Prevention and treatment. - As with any infectious disease, the best medical approach to COVID-19 caused by the SARS-CoV-2 is to eliminate, kill the bug... But since there is no truly affective, FDA-approved antiviral drug for this disease, we must rely on our own immune system. Naturally, our immune cells, mostly B-lymphocytes and plasma cells develop IgG & IgM antibodies against virtually all pathogenic bacteria and viruses. If a patient recovers from an infectious disease, these antibodies can be recovered and concentrated from their plasma. The purified or synthetic antibodies may then be administered to severely ill patients and this has been the standard of medical care for more than 100 years before antibiotics became available following World War II.

During the COVID-19 pandemic, this kind of natural plasma transfusion has been used successfully and several companies, as well as government agencies, are rushing to synthesize large quantities of effective IgG & IgM antibodies. But until these antibodies will become commercially available, we may use other natural products. Among these, our first line on nonspecific defense against almost any type of cell & tissue injury is the antioxidant system which protects against oxidative stress in our body:

- Vitamins C and E are the best known – but we have to take them in higher doses than the 'daily recommended amount'. The water-soluble vitamin C need to be ingested in 1-2 grams/day (e.g., 1 g or 1000 mg tablets in the morning and evening). The lipid-soluble vitamin E, if taken as 400 IU (180 mg), is probably enough every other day.
- Selenium (Se) is an essential trace element for animals and humans that need to obtain selenium from dietary sources. Plants convert selenium mainly into Se-methionine & selenocysteine which are potent antioxidants. Furthermore, glutathione peroxidase (GPx) is a selenium-containing antioxidant enzyme & the GPx/glutathione system is a major defense against oxidative tissue damage (stress). Since the about 30 selenoproteins are also immunomodulators, we need to consume at least 200 micrograms of organic selenium tablets, obtained usually from yeast (the inorganic selenium present in 'multivitamins & multimineral' tablets is not absorbed from our gut).
- Zinc is not a direct antioxidant and no COVID-19 magic bullet but has shown to help with other coronaviruses that also cause common cold. There zinc lozenges helped to shorten the misery phase (e.g., running nose, soar-throat) of common colds.

Since the COVID-19-inducing virus accumulates and proliferates in the upper respiratory tract, i.e., nose and nasopharynx/throat (as opposed to SARS-inducing coronavirus which attacks the lower respiratory tract, like lungs and lower bronchi), based on experience with zinc lozenges in common cold, the natural alcohol (22% ethanol) present in Listerine-like lozenges may also be helpful in the current pandemic (e.g., some of us use Listerine gargles several times a day...) Nevertheless, let us keep everything in perspective: all these are temporary measures until vaccine and new, specific antiviral drugs will become widely available.

It should be emphasized that we are referring here only to chemical means of prevention, and this should be parallel or preceded by physical means of prevention, such as frequent hand-washing with soap and water, wearing masks (Fig. 6) in public spaces as well as a social

distancing of at least 2 m. Be aware that not all masks created equal: the most effective ones are the N95 masks that exclude 95% of the very small, tiny particles (i.e., 0.3 microns, in comparison the human hair is about 70 microns). (Fig. 6). The next best masks the medical/surgical ones that have 3-ply of special material and protect against 60-80% of small particles.

Another important dictum of public health and preventive medicine is that 'if primary prevention fails, we have to start secondary prevention', i.e., treatment. As stated before, there is no approved drug treatment for COVID-19 in any country of the world, - but there is the emerging pipeline of potentially other medicines that proved to be effective in other viral or bacterial diseases [23]. Among these, apparently, the most effective seems to be is remdesivir which was used successfully again Ebola virus, and several controlled clinical trials are now on the way with this drug around the world; University of California Irvine (UCI) Medical Center, under the leadership of Dr. Alpesh Amin was the first to start clinical trial with remdesivir. Other drugs in the pipeline are chloroquine and hydroxychloroquine which have long been used for treatment of malaria, rheumatoid arthritis and lupus, but these drugs have a narrow therapeutic window and people who used these for COVID-19 prevention without medical supervision often died because of cardiac toxicity [19, 20]. Chloroquine derivatives block the attachment of SARS-CoV-2 virus spikes to ACE-2 receptors on human cells. Colchicine is an FDA-approved anti-inflammatory drug to treat gout and pericarditis but now applied to mitigate the 'cytokine storm' in severe COVID-19 patients, along with or independently from the also potent anti-inflammatory glucocorticoids. A group of researchers at the Montreal Heart Institute and the University of Montreal aggressively investigate to stop the overproduction of immune cells and cytokines that damage the lungs in the 'cytokine storm', resulting in acute respiratory distress and multi-organ failure (19, 20). But as much as these drug trials and investigations are important now, these are not replacement for the intensive research to find specific antiviral drugs and vaccines to treat or prevent COVID-19, respectively.

N95

The N95 is the most recognizable and effective mask. Its name means it can block at least 95 percent of tiny particles — 0.3 microns — that are the hardest to capture. An average human hair is about 70 to 100 microns wide.



Medical

Medical masks come in a few varieties and are less effective than N95s: Some filter as much as 60 to 80 percent of small particles under lab conditions. When worn properly, they can help prevent the spread of the coronavirus by catching droplets when you cough or sneeze.



Homemade

With medical masks in short supply, many have turned to making or buying homemade ones. Depending on the fabric and how it's made, a homemade mask can sometimes protect the way a simple medical version does. And any face covering is better than nothing.



Homemade With Filters

This is another homemade mask, made from 100-percent cotton t-shirts, with a pocket sewn in to hold an additional filter.



We used a coffee filter in this mask. Paper towels have also been tested. One experiment found that two layers of paper towels on their own blocked between 23 and 33 percent of 0.3-micron particles.



Figure 6. The various forms of masks (modified from the New York Times, <https://www.nytimes.com/interactive/2020/health/coronavirus-best-face-masks.html?auth=login-email&login=email>)

COVID-19 epidemiology and public health

If we learned anything so far from the pandemic of this new disease is the importance of public health that my former dean at the Harvard School of Public Health Dr. Howard Hyatt defined 'our patient is the nation'... Most countries of the world neglect the funding for public health, dismantle, diminish, or under-fund national surveillance and preventive programs.

The USA is one of the worst examples in this and now we are paying a price for it (Fig. 7). Most of the nation-states of Eastern Europe do not even have modern schools/faculties of public health at university levels... Even worse is the almost total lack of education of our children about the basic principles of public health and epidemiology in our elementary and high schools. Should we then be surprised that people accept misinformation about the

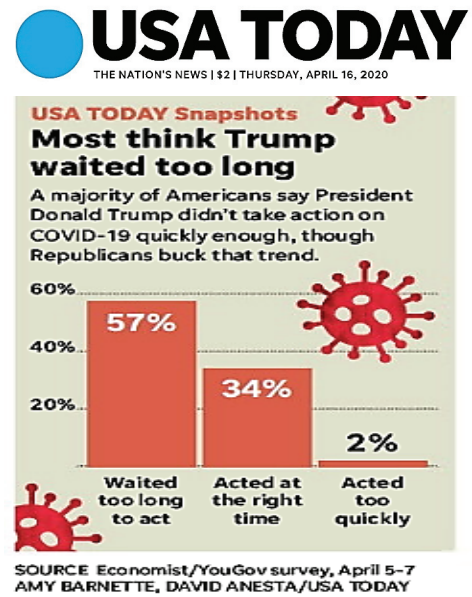


Figure 7. One of the main reasons for the late response to COVID 19 in the USA & the public reaction to it in mid-April 2020 (modified from the Los Angeles Times & the USA Today, respectively)

pandemic, do not follow or outright resist preventive measures? Or that our TV, radio, print news, and social media keep repeating scary news about the TOTAL number of virus-positive people and daily new cases, also emphasizing only the daily deaths...

One of the first principles of epidemiology is that we should not look only at the total number of cases, but rather the ratio of cases per unit of population or percent (%) of the total population in the state or county/region or city. For example, as I am finishing this review article in the middle of April, the total number of COVID-19 positive cases world-wide has been 2,243,512, with 154,209 deaths, while the USA had on April 17, 2020, 701,475 cases and 37,054 deaths (24). If we look at these numbers as a ratio, e.g., per 100,000 or millions of people, we get a very different and more realistic picture wherein both the number of COVID-19 cases and the number of deaths in Spain, Switzerland, and Italy show the worst statistics (Fig. 8). It is interesting that some of these statistical comparisons, originating from Europe and USA, do not include Chinese data – in part, because by numerous experts believe that the 'Chinese data are suspect', they keep changing, e.g., even in the middle of April 2020, the Chinese death toll suddenly jumped, apparently due to their initial underreporting thousands of cas-

es in some parts of China... Nevertheless, as the colored world map indicates (Fig. 8), it is probably safe to assume that the number of COVID-19 patients in China was not as prevalent as in some countries of Europe or in some states of the USA.

Another scary example of lack of epidemiologic insights and public health perspectives is not being able to distinguish the prevalence (total number of cases in a population) from incidence (new cases per day or week or month) and reporting these numbers only in daily totals. In California, we have seen the daily deluge of TV news and other news/social media reporting the TOTAL numbers that enhance the anxiety, bordering on hysteria in some segments of the society. Surely, every new case and death are a tragic example of our inability to save lives, but if we look at these numbers as PERCENT changes, the most recent data indicate much rosier, almost encouraging picture (Fig. 9). Namely, the percent changes in both new cases and deaths in California are dropping and started to 'flatten the epidemiologic curve', most likely because California was the first (on March 15, 2020) state, among the 50 states of the in the USA, to order a strict 'stay at home order' and closing all public gatherings, including sport events, schools, restaurants, bars, and non-essential businesses.

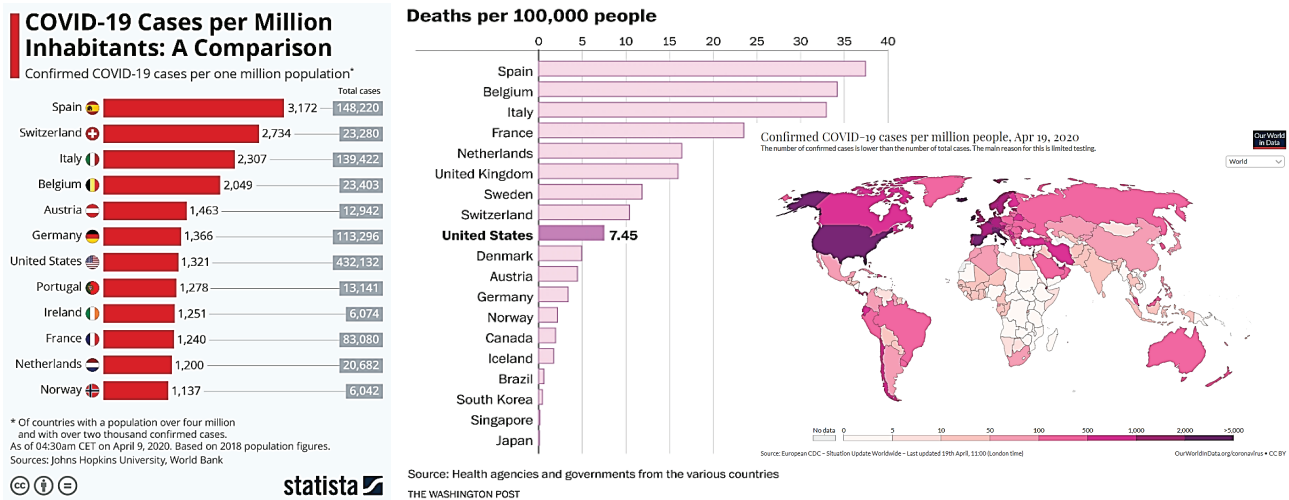


Figure 8. COVID-19 cases per million of inhabitants and deaths per 100,000 people in various countries of the world (sources are indicated in the figures)

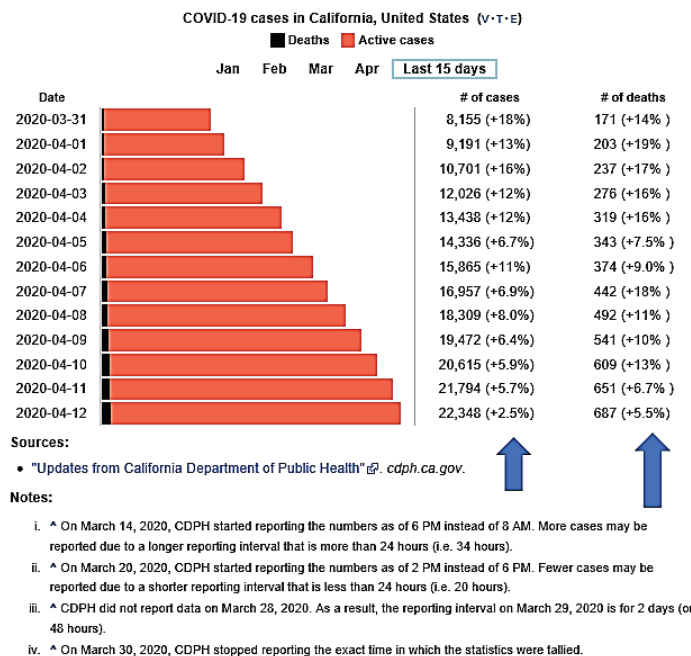


Figure 9. Comparisons of TOTAL number of new cases of COVID-19 and related deaths vs. the PER CENT daily changes (source as indicated in the figure)

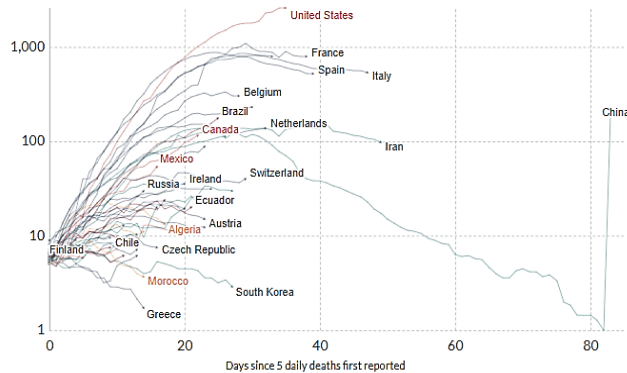
Bending the curve and case fatality ratios. 'Flattening the curve' is frequently used term during this pandemic both in the scientific literature and in the lay press. It also refers to flattening the peak in the rapidly rising incidence of new cases that may overwhelm the capacity of the healthcare system in any community. The underlying logic is that if we slow the occurrence of new cases, e.g., by social distancing, contact tracing, and isolation, the slow rise of new COVID-19 cases could be

handled by the available outpatient clinics and hospital beds. Epidemiologically, it refers to the decreasing the daily incidence of new cases or COVID-19 deaths, eventually reaching a pick, then starting a decline. As shown in Fig. 10, most of the countries started this decline, except the USA, due to multiple reasons, as we will see later in this review.

Another important epidemiologic and public health parameter is the 'case fatality ra-

Daily confirmed COVID-19 deaths: are we bending the curve?

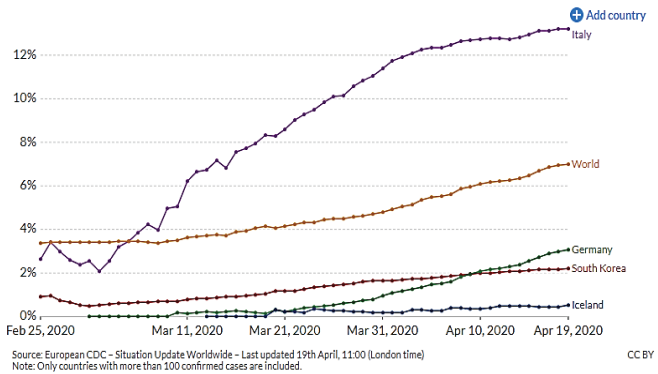
Shown is the 7-day rolling average. Limited testing and challenges in the attribution of the cause of death means that the number of confirmed deaths may not be an accurate count of the true number of deaths from COVID-19.



Source: European CDC - Situation Update Worldwide - Last updated 19th April, 11:00 (London time)

Case fatality rate of the ongoing COVID-19 pandemic

The Case Fatality Rate (CFR) is the ratio between confirmed deaths and confirmed cases. During an outbreak of a pandemic the CFR is a poor measure of the mortality risk of the disease. We explain this in detail at [OurWorldInData.org/Coronavirus](https://ourworldindata.org/coronavirus)



Source: European CDC - Situation Update Worldwide - Last updated 19th April, 11:00 (London time)
Note: Only countries with more than 100 confirmed cases are included.

Figure 10. Daily COVID-19 deaths and the case fatality rates in several countries, in time-dependent fashion from mid-February to mid-April 2020 (sources are indicated in the figure)

ratio' that refers to the ratio between confirmed deaths and confirmed clinical cases (Fig. 10). In this COVID-19 pandemic, in the case fatality statistics, unfortunately, Italy is on the top of the curve, much above the world average, while Germany, South Korea, and Iceland are below the world average. Iceland, in this case, deserves special attention... Probably because it is a relatively small, isolated country, led by enlightened public health and political leaders, the majority of the population was tested, a few cases have been detected, then traced and isolated. Then it should not be surprising to all of us that from the public health point of view, Iceland is the best country in the world, especially in this pandemic.

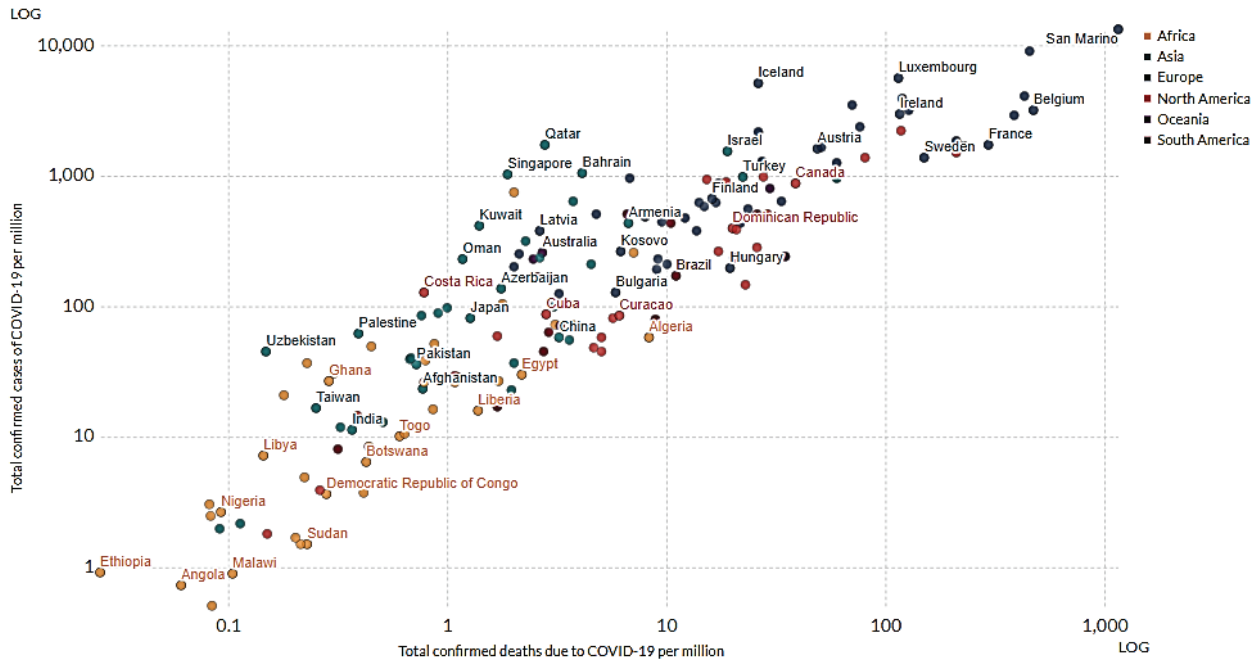
This brings us to another surprising, sad conclusion: we should not blame only China since most of the declared "new cases" are unreliable since it depends on what part of the population has been tested either for SARS-CoV-2 RNA fragments or antibodies against it... The USA is probably one of the worst examples in this, since test kits, despite all the promises and predictions are still lagging... How can we then tell what the REAL incidence of disease is if we do not test the majority of the population? Even worse (and only a public health-trained pathologist can say or write this), we can only count death bodies with great certainties. This is one of the reasons that we have this surprising distribution of COVID-19 confirmed cases vs. deaths per million population (Fig. 11): African countries (in the lower left of the distri-

bution) have low death rates because they don't test the majority of their populations, while wealthy countries of Europe that try to test most of their inhabitants have the highest rates of confirmed COVID-19 cases of death rates per millions of their population (Fig. 11). Sadly, we will never know the real prevalence and incidence, because the large parts of the population were not tested (25), either because of the non-availability of test kits or poor organization of public health services or for other reasons. More concerning is what the recent results and estimates in California indicate: the more realistic prevalence of COVID-19 cases maybe 40-50 times higher than the current infection rates indicate...

Comparison of COVID-19 calamities vs. other pandemics. – When we are in the middle of the public health crisis, it is natural to assume that it is terrible, we have never seen something similar or never lived through, but we have to put this pandemic in perspective... The best example is probably the influenza epidemic that returns almost every fall or winter and it is caused by another coronavirus: when a lot of people are panicking about COVID-19, they forget that they may get "flu" more likely than the new disease... The prevalence of "flu" is almost 10 times higher than that of COVID-19, but fortunately, 'flu' mortality is lower (0.1 % vs. 1-2 % of COVID-19). But, despite lower mortality of 'flu', because of its much higher prevalence, more people die of influenza than that of COVID-19.

COVID-19: Confirmed cases vs. deaths per million, Apr 19, 2020

Both measures are expressed per million people of the country's population.
 The confirmed counts are lower than the totals. The main reason for this is limited testing.



Source: European CDC - Situation Update Worldwide - Last updated 19th April, 11:00 (London time)

OurWorldInData.org/coronavirus • CC BY

Figure 11. COVID-19 cases vs. deaths per million people, worldwide (sources are indicated in the figure)

Another useful comparison is to compare deaths in each country with other main causes of mortality. In the USA, the CDC (Center for Disease Control and Prevention) This season CDC estimates that, as of mid-March, between 29,000 and 59,000 have died due to influenza illnesses. Add to that the misery of hundreds of thousands of flu-related hospitalizations and millions of medical visits for flu symptoms this season. This is like the current COVID-19 deaths of more than 37,000 in the USA. This year's flu season will be possibly less severe than the 2017-2018 season when 61,000 deaths were linked to the virus. Globally, the World Health Organization (WHO) estimates that the flu kills 290,000 to 650,000 people per year, vs. the COVID-19-related more than 155,000 deaths until now [26].

Comparison with other seasonal infectious diseases may give us some hope since most of the other seasonal diseases show a clear pattern of waxing and waning over the years (Fig. 12) [27]. The incidence of these diseases decreases for several reasons, one of these being the warm weather, like with influenza... Population density is another major factor for the rapid

spread and high prevalence of infectious diseases (Fig. 13). Expert opinions are sharply divided with COVID-19; some predicting a drop in new cases during the summer, but others, especially some of my alumni at the Harvard School of Public Health doubt that. New data on the prevalence and incidence of new COVID-19 cases in hot Brazil and Australia indicate that this new disease may persist even during the hot and wet summer months... There are also pessimistic predictions that the second wave of COVID-19 cases might be much worse than the initial prevalence.

COVID-19: Chaos, panic and stress

Chaos and anxiety are often seen in epidemics, especially when it grows to a pandemic level. As a recent article stated, "crisis response has always been chaotic" (Fig. 14) which might be an exaggeration but citing the example of 'Spanish flu' (1918) and the Great Depression (1933) in the USA, the article quips "we start with inertia, bestir ourselves with hubris, move on to bungling, and spice things with venality" [28]. These articles also analyze the mistakes and lessons learned from the 1918 pandemic, com-

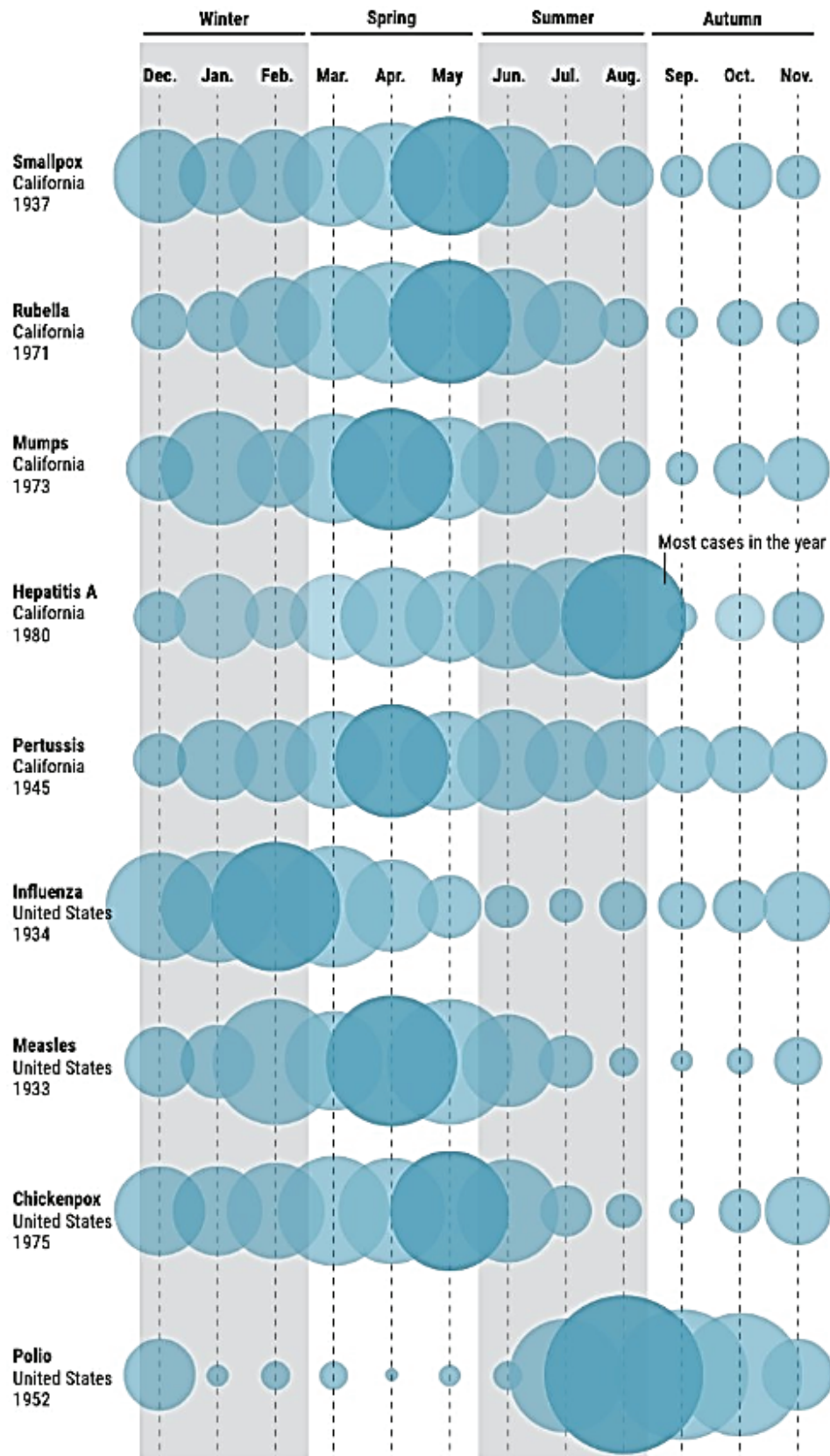


Figure 12. The seasonal waxing and waning in the epidemics of several diseases, in historical perspectives (modified from *Science*, March 20, 2020)

The New York Times

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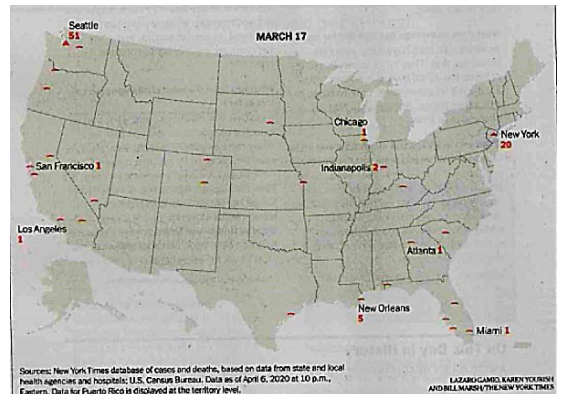
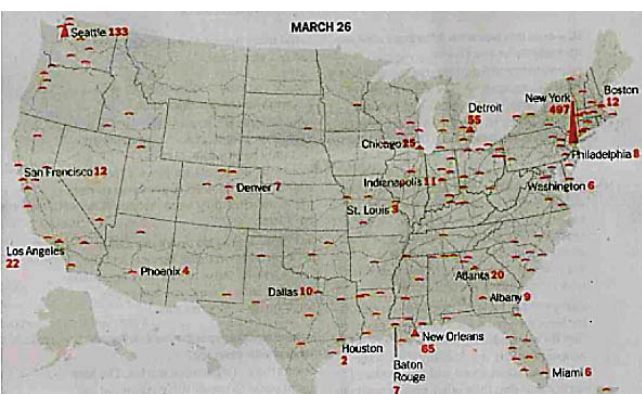
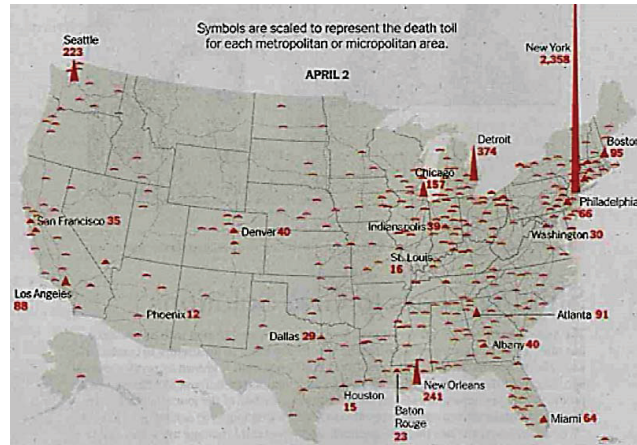
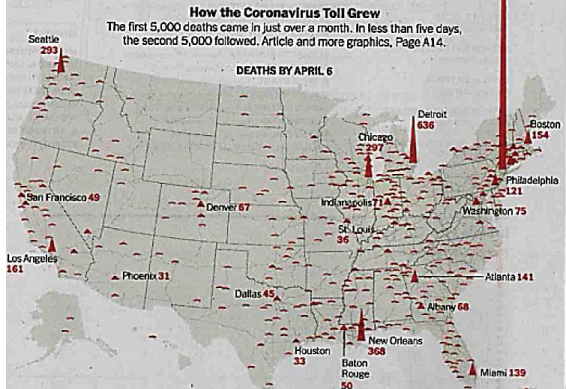


Figure 13. The population density-dependent evolution of COVID-19 epidemic in the USA, from mid-March to early April 2020 (adapted from the New York Times)

Crisis response has always been chaotic

By Daniel Akat

If you're trying to understand the disorganization and ineptitude of America's response to coronavirus, you might find it helpful to know there's a single word that captures the situation perfectly: That word is normal. The sad truth is that we've faced many crises in our history, and we almost always make a hash of them. We start with inertia, bestir ourselves to hubris, move on to bungling, and spice everything with venality. Situated far from the world's troubles, we are invariably dragged by complacency and handicapped by federalism, the system that gives us many levels of government to get in each other's way. Unpreparedness is a signal feature of almost every American crisis, from the Revolutionary War right up to our recent stunning lack of ventilators and masks. In 1912, for example, Secretary of War William Danks predicted that we needed only to send some officers into Canada and residents of the British territory would "rally round our standard." In fact, American overconfidence, unreadiness and disorganization led to successive fiascos culminating in the burning of the fledgling nation's capital. In the Civil War, a crisis if there ever was one, the Union cause was imperiled by timid generals, bad equipment, scarce supplies and rampant fraud. When World War II broke out in Europe in 1939, the United States had the world's 18th largest



THE U.S. government made many early missteps in its response to the Great Depression. Above, people line up to receive a federal surplus of potatoes and cabbage in 1933.

We start with inertia, bestir ourselves to hubris, move on to bungling, and spice things with venality.

should have lowered them and failed to backstop banks against devastating runs. FDR tried lots of things, but overall fiscal policy oscillated perversely and may have done little to shorten the nation's ordeal. The Sept. 11, 2001, attacks, aside from a fleeting sense of unity, produced costly and inconclusive wars. And things have rarely turned out well when

rites regulation and a wised-up Fed (itself the belated offspring of the Panic of 1907). The Second World War resulted in the Marshall Plan and helped propel us down the road to equality for black people, women and others. Our latest crisis may finally force us to universalize health-care and find a way to rein in its costs. We might also agree that there are good reasons not to

Outbreak Puts Stress on Links of Food Chain

The nation's food supply chain is showing signs of strain, as increasing numbers of workers are falling ill with the coronavirus in meat processing plants, warehouses and grocery stores. The spread of the virus through the food and grocery industry is expected to cause disruptions in production and distribution of certain staples like pork and chicken, industry executives, labor unions and analysts have warned. The issues loomed nearly a month of stockpiling of food and other essentials by panicked shoppers that have tested supply networks as never before.

Industry leaders and observers say, the food supply remains robust, with hundreds of millions of pounds of meat in cold storage. There is no evidence that the coronavirus can be transmitted through food or its packaging, according to the Department of Agriculture. Still, the illnesses have the potential to cause shortages lasting weeks for a few products. "You might not get what you want when you want it," said Christine McCracken, a meat industry analyst at Rabobank in New York. "Consumers like to have a lot of different choices, and the reality is in the short term, we just don't have the labor to make that happen."

Smithfield Foods became the



BRITANNIA NEWS/GETTY IMAGES

As workers in the industry fall ill, food shortages could reduce choices for weeks. At grocery stores, some employees still have not been given masks.

latest company to announce a shutdown, saying Sunday that it would close its processing plant in Sioux Falls, S.D., after 230 workers became ill with the virus. The plant produces more than 5 percent of the nation's pork. As of Saturday, the plant's Covid-19 cases were more than half of South Dakota's active total, Gov. Kristi Noem said. She called the outbreak an "alarming statistic" and asked Smithfield to shut down the facility for two weeks. The problems at the Sioux Falls pork plant show the food processing industry's vulnerability to an outbreak. Employees often work shoulder to shoulder, and some companies have granted sick leave only to employees who test positive for the coronavirus. Other major processors have had to shut down entire plants.

MOST ACTIVE, GAINERS AND LOSERS

Stock (Ticker)	Class	Chg	%	Volume (100)
19 MOST ACTIVE				
Ford Motor (F)	5.16	-0.2	-3.91	99,933
GE (GE)	7.02	-0.1	-1.08	89,993
Bank of America (BAC)	29.92	-0.3	-1.01	82,024
Cardinal Health (CAH)	11.50	-0.9	-7.41	76,342
Duke Energy (DUK)	29.92	-0.1	-0.67	72,763
American A (AAU)	11.56	-1.0	-8.59	72,307
AMD (AMD)	30.34	+0.1	+0.35	63,703
Marathon Oil (MRO)	42.33	+0.4	+0.95	52,962
Hollander (HOL)	7.65	+0.4	+5.88	46,111
Oakwood Energy (OKE)	6.20	-0.9	-14.02	43,002
19 TOP GAINERS				
Marathon Oil (MRO)	42.33	+0.4	+0.95	52,962
Amgen (AMGN)	266.87	+13.1	+4.91	6,608
Corning (GLW)	81.94	+1.1	+1.31	3,561
AMD (AMD)	30.34	+0.1	+0.35	63,703
Norfolk Southern (NS)	59.77	+2.5	+4.19	11,610
Paycom Software (PAYC)	28.55	+0.1	+0.37	2,543
Acadia (ACAD)	62.25	+2.2	+3.55	8,506
Norfolk Southern (NS)	59.77	+2.5	+4.19	11,610
Baker Hughes (BHU)	31.20	+0.4	+1.26	3,008
Baker Hughes (BHU)	31.20	+0.4	+1.26	3,008
19 TOP LOSERS				
David Bull (DBL)	33.37	-6.0	-17.08	3,429
New York (NYS)	11.26	-1.3	-11.56	2,959
Arcore (ARCO)	3.50	-1.2	-34.29	542
Truist Financial (TFC)	19.14	-0.3	-1.57	10,068
Gap (GPS)	8.22	-0.4	-4.86	11,627
L. Brands (LBR)	12.11	-1.5	-12.37	6,747
Sunderly (SUN)	8.22	-1.4	-17.35	11,044
Parsons (PS)	8.36	-0.4	-4.81	1,522

Stocks that moved heavily or traded substantially on Monday.

Figure 14. Crisis and chaos during the 'Spanish flu' and the Great Depression in the USA, and one of the stressors in the COVID-19 epidemic, like food shortages that may cause hunger in some segments of the population (sources are indicated in the figures)

paring the responses in four cities (Los Angeles vs. San Francisco, and Philadelphia vs. Saint Louis). Cities that shut down public gatherings, closed shops, factories, and schools very early in the 1918 pandemic had a much lower number of influenza cases and mortality, in comparison with those that reacted late or initially denied the existence of any danger [29].

But we do not even have to go back to the early 20th century – we have examples of disorganized or unresponsive leadership in the COVID-19 pandemic: “Where Germany had success in fighting coronavirus, Britain failed: “Johnson proclivity for wartime bravura rings hollow in the midst of a public health emergency” [30]. UK has performed about 350,000 tests and almost completely dropped any attempt of contact tracing – leading to chaos, panic and anger in their population and health-care sector. Germany, on the other hand, gave itself a head start in testing that resulted in much better public health outcomes.

In the Americas, Brazil and the USA are bad examples when and how to react to a pandemic like the COVID-19 storm... Although the WHO announced the pandemic on January 30, 2020, when it was obvious that the new virus was rapidly spreading around the globe, the USA did nothing in the entire month of February; no testing, no suggestions for social distancing or other preventive measures... In some circles, COVID-19 was considered just ‘another flu-like disease that will disappear with warmer weather’... It was only the State of California that on March 15 first announced the state-wide stay-at-home order, closures of schools, shops, and all non-essential businesses... Other states followed that a few days or weeks later.

No wonder then that some segments of the population were bewildered, confused and angry – that lasts until the present days. Furthermore, that led to panic buying of food, toilet papers, sanitizing tools, followed by a rush on face masks, bordering on hysteria. If we combine these stressors and add home isolation, loneliness, depression, and anxiety, the predictable outcome is a stress reaction, i.e., distress. All this could have been prevented by good planning, ‘prepare for the worst, - hope for the best’, and follow the basic tenets of public health and preventive medicine. i.e., test/

detect the disease, isolate the infected person, followed up with contact tracing.

The stress of COVID-19. - As stated above, the distress was almost predicable in this pandemic, also illustrated in Figs. 14&15. “Stress is the nonspecific response of the body to any demand made upon it”, as we stated and discussed in our recently published book on Stress [31]. By definition, stress should be caused by different factors (stressors) eliciting similar neuroendocrine changes, like the rapidly released catecholamines and sustained, elevated levels of secreted glucocorticoids [31]. The multifactorial etiology is almost given in a pandemic like this, e.g., anxiety about what the future may bring, depression, isolation, family arguments in closed quarters, real or perceived food shortages, unemployment, (temporary) loss of income, all culminating in increased domestic violence and suicides. The more psychological, societal, and physical stressors hit us, the more serious is the resultant distress reaction [31, 32].

The distress may involve all segments of the population, but the most severely affected are the healthcare workers (e.g., emergency room and intensive care unit doctors and nurses), and contact tracers. The additional stress on healthcare workers, besides almost all the other factors that hit any segment of the society, are the long hours they must put in, in part because of the shortages of doctors and nurses, lack of sufficient personal protective equipment, triaging patients that cannot be saved either due to lack of respirators or hospital beds, seeing dying patients... No wonder then that in some hospitals nurses and others demonstrate (Fig. 15), demand improvements or a few refuses to work to protect themselves and their families from potential exposure to the new virus. All this is compounded by the fact that thousands of doctors and nurses died worldwide, apparently in a much larger percentage than any other segment of the population.

Another unappreciated and stress-prone profession are the contact tracers [33] who are doing a critical, often very stressful job in the initial stages of epidemiology: after detecting a virus-positive, symptomatic or asymptomatic patient, they have to speak to the patient, often in their home. Sometimes, they don't let

NATION'S HEALTH

USA TODAY (MONDAY, APRIL 13, 2020) SECTION 2



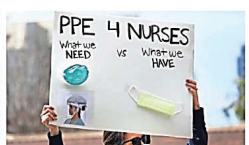
Nurses and other hospital staff practice social distancing as they call for adequate protective equipment during a protest outside Westchester Medical Center in New York on Thursday. (AP Photo/Scott Freedman)

Stress, shortages push nation's nurses to brink

Hospitals: We're trying to preserve the PPE we have

Ken Auletta
USA TODAY

A week after recovering from a fever, nurse Maria Gray was given a surgical mask and assigned to Research Medical Center's ward of patients suspected of having the virus that causes COVID-19. Not knowing the risks, she pulled on the mask and returned to the 100-bed hospital ward that would offer more than 100 beds to patients. She was asked her request and reassigned her to a different hospital floor.



School closures raising parents' stress levels

Many are concerned that their children will fall behind in studies, a new survey shows.

BY BONALI KOHLI

Parents across California are more stressed than usual, and school — or lack thereof — is a major source, according to a statewide survey of 1,500 public school parents commissioned by a nonprofit research and advocacy group.

Most parents gave their schools and districts credit for short-term crisis planning but worry about their kids falling behind academically. The same equity issues long entrenched in California education remain in play during the pandemic, said Xisha Smith Arrillaga, executive director of Education Trust West, which sponsored the survey conducted by the research firm Global Strategy Group from March 26 to April 1.

According to the poll, 89% of parents are concerned about ensuring their children do not fall behind academically during school closures, and 79% are wor-



YADIRA DE LOZA and her second-grader, Paulina, pick up computers at Ellen Ochoa Learning Center.

ried about their children's mental well-being while at home. The poll showed that 86% of parents said their own stress is higher or much higher than usual, and 49% reported that their children's stress was higher than usual.

"Our poll finds that parents crave consistent contact with teachers and equitable access to academic resources," Smith Arrillaga said. The poll found that access to remote learning was not equal. Parents that were either low-income parents, African American par-

ents or Latino parents were less likely to have been in contact with their child's teacher, she said.

At first, when school closures were thought to last only through spring break, parents felt the expectations were manageable, said Araceli Simeon, project director for the Parent Organization Network. But now, as the length of closures stretches into the unknown and financial burdens increase, parents' stress is growing, she said.

"The length of time has been extended as days and

weeks go by," Simeon said. "So right now a part of the stress is coming from the uncertainty and really from not having a clear plan for long-term distance learning or online."

Schools should now think about distance learning plans that extend for six to nine months, and help families understand how to track their students' progress, she said.

Beyond income and race, parents of students with disabilities and English learners reported greater challenges.

Also undocumented parents will not be benefiting from the federal relief that many of us will be benefiting from," said Xishia Cruz-Gonzalez, president of the California School Boards Assn, and an Assn Unified school board member. Because of that financial uncertainty, she said, it is important to "make sure we are communicating with the parents in the language they understand."

A group of educators and school leaders is working to address achievement gaps that are exacerbated by the

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Meditation apps ease angst in stressful time

Exercises, coping tips offered for free

Jazmin Goodwin
USA TODAY

As uncertainty continues to grow around the coronavirus pandemic and life in seclusion mounts, so has the level of stress and anxiety for many consumers.

Popular health and wellness apps are now offering free services to help people cope in the midst of unprecedented times.

Meditation app Headspace announced Monday that it is offering free premium services



Meditation apps including Headspace, Simple Habit and others are offering free services as stress and anxiety rises over coronavirus. (PEOPLEIMAGES/ETTY IMAGES)

Figure 15. Other stressors in COVID-19 pandemic and coping tips, like meditation (sources are indicated in the figures)

the contract tracers in, or if the patient agrees to speak, s/he may deny that they are in danger and refuse to reveal who they were with during the preceding week, since the contacts may also need to go to self-isolation for at least for two weeks, losing potential income for a few weeks... Then, the contact tracers must speak to all the people whose names were revealed to them, going through the same, often unpleasant conversation as with the initial patient. And this could be repeated 10-15 times a day... Thus, that it's not surprising that thousands of contract tracers are needed in the USA, and only after their entry salaries were substantially increased, like in Massachusetts [34], candidates showed up in throws, despite the distress they may face, since the stressful job may relax the financial burden in their families...

We should also mention a few remedies in the pandemic stress, and fortunately, the social media and lay press are full of stress-reduction exercises, diets, and other measures. Among these ones of the simplest, science-proven intervention is meditation, yoga and the easy, seven-minute workout (Figs. 15, 16). All these should be preceded or associated with a healthy diet (with a lot of vegetables, minimal carbohydrates, and salt), plenty of hydration with regular tap water, daily exercise (at least

30 min of walking), breathing exercise, and (if available) plenty of sunshine... If none of these steps help, to avoid going into a deep depression or alcoholism, or domestic violence, obtaining professional help from licensed mental health experts is crucial!

Lessons learned and planning for the future. - Despite all the challenges, chaos, panic and stress associated with the COVID-19 pandemic, we should extract some beneficial lessons. Although there are pessimistic predictions (e.g., 'end of globalization' – actually, we need coordination and cooperation in response to pandemics like the new coronavirus), and truly futuristic musings on 'how pandemic could reshape civilization', a rational, multidisciplinary global plan should emerge.

Among the first things we should be ready to accept that zoonoses, disease caused by viruses jumping from animals to humans, are becoming more prevalent, and these viruses mutate very frequently [5]. This makes very difficult to develop new vaccines and specific antiviral drugs. Next, we should be vigilant that these zoonoses may linger long time, especially in rural areas and if the first symptoms are very nonspecific or flu-like, and they may be detected too late. Also, we must be

Distress reduction:

Get in shape with the best seven-minute workout apps

USA TODAY US Edition 8 Jan 2018 Jennifer Jolly

Here are my favorite seven-minute workout apps.

Johnson & Johnson 7-Minute Workout App

If you're looking for a customizable, well rounded, safe and truly free seven-minute workout app, you can download this one and get to work right this second. It features 12 different 30-second exercises, with five seconds of rest in between.

It's great for beginners and athletes, syncs with your iPhone Health App to take your other daily movement into account, and the workout library has 22 presets that you can customize to create thousands of variations. You can swipe right or left during the exercises to see how much time you have left, watch the instructor or listen to music from your iTunes.

Seven App by Perigee



JUMPING JACKS



The Seven App by Perigee guides users through jumping jacks. THE SEVEN APP

This app has a huge variety of exercises and would have made the #1 spot if it weren't for the fact that even though you can do it for free, you'll end up paying for a subscription to access all of the exercises and motivational tools. Seven has you do each exercise for 30 seconds, with 10 seconds of rest in between. It shows each move with 3D illustrations and written prompts for beginners.



Wahoo 7-Minute Workouts

This app doesn't give you the fancy video demo's or illustrations the ways the others do. If you want to see how to do an exercise, you have to watch a video separately, which is a little jarring. Other than that, it delivers just fine in a series of exercises, with a firm voice to get you through them.

7 Minute Fitness Challenge App

This is another one you can try for free, but you'll end up paying \$2.99 and more for full access to all of the various exercises. I like that the video instructions are led by both male and female trainers, and they do a great job guiding you through each exercise via video, audio, image and text.

Blogilates

The tagline for this one is, "Train like a beast, look like a beauty." Again, you can try it for free but will end up paying \$1.99 to access the timer and another 99 cents to access the best videos. (All About That Butt

is one of my favorites.) It's less about jumping jacks and more about holding a particular pose (like a half squat) until you're crying. The workouts are designed to tone, strengthen and elongate muscles.

7-Minute Workout For Kids

OK, this one if for the kids, but grown-ups can do it to too. With animated instructions, catchy music, and all the basics of the other full-body workouts, this is another top choice overall. The exercises include some more advanced moves, like tricep dips with a chair and push-ups with rotation, so it's a great one to do with your kids.

Yoga Wake Up (iOS only)

This one is different from the others in that it's yoga (duh), but also really mellow. You won't be wheezing or sweating buckets, but you likely will feel better. The best part? You can do the movements from bed.

Figure 16. Distress reduction with the seven-minute workout (adapted from USA Today, January 8, 2018)

ready that the new infectious diseases usually 'explode' in densely populated areas of any country. This was the case with COVID-19 which started in the huge, congested city of Wuhan, China, just to be reincarnated a few months later in the densely populated and industrialized Italian north. The rapid spread of COVID-19 in the USA confirms that, since it 'exploded' in New York city and its surrounding areas that are densely connected by public transportation (e.g., buses, subways, trains, ferries) (Fig. 13). Chicago, Detroit and Seattle have smaller populations, but they heavily rely on public transportation where social distancing is almost impossible to practice and enforce. The high prevalence of cases in New Orleans is apparently caused by the fact that the city ignored the early warnings in middle of February and allowed the hugely popular Mardi Grass street-city wide celebrations and gatherings that actually lasted several days...

This population-density theory of epidemiologic spread of respiratory infectious diseases may also explain the relatively small case number in the huge cities of California, (e.g., Los Angeles County, with its more than 10

million people is like New York City; and San Francisco with the Bay Area, with its 6 million inhabitants) had relatively low prevalence of COVID-19 cases (Fig. 13). These big California cities have minimal public transportation since people traditionally use personal cars, resulting in almost daily, notorious traffic congestions when people sit in their idling cars, well isolated from each other... The other factor is the previously mentioned first state-wide shutdown that the governor of California first introduced in the nation on March 15, 2020.

As with COVID-19, the "asymptomatic transmission is the Achilles' heel" (14) of any existing or emerging epidemic. That is one more reason to rush with the development of new vaccines, but that may take about a year, just for early testing of its effectiveness... Then the mass-production of the vaccines usually requires 2-4 years.

Last, but not least, one of the most important lessons should be that cities, states and regions around the world should not neglect, underfund and underplay the importance of public health, where 'nation is the patient'. This should in-

clude establishing new, modern schools of public health, especially in eastern Europe, and increase the support for existing schools, along with investing in public health education and research. After all, the best treatment of any disease as its prevention, which makes sense even economically. We owe this not only to the

current, post-COVID-19 generation, but also to our children and grandchildren.

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