The Scientific Foundation of Defense Against Covid-19

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The corona is a serious disease

According to recent data, the number of corona death in Israel is 536 so far out of 72,584 (Aug. 3, 2020) who have been infected, or 0.74%. The corresponding numbers (approximately) in the USA are about 140,000 dead from about 4 million infected which is approximately 3.5%. The prevalence of infected persons in Israel is approximately 0.78% of the population and in the United States, approximately 1.2% of the population. There are differences between the countries but they are not important to understanding the overall severity of the corona disease: about a percentage of the population was infected and about a percentage of them died from the disease. To get a perspective, let's examine the corresponding data regarding the seasonal flu; for this purpose we use the CDC data in the US. In the last decade between 2.8% and 13.6% of US residents have been infected with flu every year and among them between 0.13% and 0.14% died. The comparison clearly shows that the number of flu patients is much larger than the Covid-19 sufferers, but the mortality rate among those who contacted Corona is nearly 10 times greater than the rate of death from the flu. This is a significant factor that makes the Corona a much more dangerous disease than the seasonal flu.

https://www.cdc.gov/flu/about/burden/index.html

How do epidemics spread?

Epidemics (including the Corona) spread in a chain reaction. The concept of "chain reaction" comes from nuclear physics. It describes how atoms of fissile material (e.g. uranium 235) emit neutrons that cause additional atoms in proximity to emit neutrons in a chain sequence. The higher the concentration of the fissile material (uranium), the greater the speed of propagation of the chain reaction. When the fissile uranium concentration is large and its total mass is large enough ("critical mass") the chain reaction can be so fast that we get a nuclear explosion. Nuclear reactors regulate the chain reaction by limiting the concentration of the fissile material and by absorbing some of the emitted neutrons, for example by graphite rods that prevent the neutrons from hitting other atoms of the fissile material. When you want to speed up the chain reaction, graphite rods are partially removed from the water that surrounds the uranium and the chain reaction and heating of the reactor are accelerated, producing more steam, and thereby increasing electricity production. This process has been recognized and known since the Manhattan Project during WWII and even earlier.

Epidemics are like a nuclear chain reaction. Each active patient is analogous to an atom of fissile uranium. The viruses that the patient emits are analogous to neutrons and the surrounding people close to the patient are parallel to the additional uranium atoms in the reactor. As the patient emits more viruses and as more people are near the patient, the more active a chain reaction of infection is generated. The presence of many patients emitting viruses close to vulnerable people, increases the risk of spreading the infection. Maintaining distance slows down the chain propagation.

What are the graphical rods in a nuclear reactor analogous to? These are the masks that reduce the risk that viruses emitted by a patient will be delivered to another person. Keeping social distance and using masks are completely parallel to the concentration of the fissile material and the use of the graphite rods. It is interesting to note that the mathematical equations describing the kinetics of epidemics spread are very similar to the equations governing a nuclear reactor.

What happens to a nuclear reactor when the uptake of neutrons wrongly falls? The chain reaction goes out of control and a catastrophe such as the Chernobyl disaster is created. The lack of cooperation of the public in wearing the masks and in keeping of social distance may send the pandemic out of control with wave after wave of morbidity.

The physical analogy does not end here. For example, in a given population there are super-shedders (like "hotter" or " more concentrated" fissile material). There are also people who are super-vulnerable, such as those who have a poor immune system (e.g. dialysis patients, patients on steroids, patients with acquired immune deficiency (AIDS) and patients on certain types of chemo.

As of today, we do not know the “Minimal Infective Dose” and we must assume that in certain unknown number of cases it is sufficient to have a single virus penetrate and root to cause the disease! The Corona, the flu, the measles and other viruses replicate and multiply in the epithelial cells that cover the respiratory system. It is important to remember that during embryonic development, the cells that cover the conjunctiva are also created from respiratory epithelia and therefore can be infected by corona virus while other cells in the body (e.g. skin) are less vulnerable or not vulnerable at all.

Absolute protection versus statistical protection

The criteria for **Absolute** protection are: (a) full sealing around the mouth and nose, and around the eyes; (b) maximum blockage against particles (at least 99%); and (c) filtration of particles that starts from a diameter of 0.1 microns.

An example of a **statistical** defense is a non-sealed 95-N Mask, that is made of material that only blocks 95% of the particles if they are greater than 0.3 microns. The transparency used in front of the user’s eyes also serves as a statistical defense since it is open to aerosols around it and below it.

How are masks and filters tested and classified?

Masks and filters have been tested for many years (since 1919) when the first standards for protective masks against toxic gases (CBRN) and industrial particles were formulated. The US National Institute of Occupational Safety and Health (NIOSH) was among the first to set standards and tests methods. Only in the 1990s of the previous century, the FDA became involved in setting standards for protection of healthcare personnel in the face of the TB epidemic. We will focus here on the tests of devices used to protect against penetration of particles and microorganisms. The main parameters that are currently being tested are filtration index and resistance to flow. The filtration index is the ratio between the amount of particles that are blocked by the mask or filter to the total amount of particles in the air (expressed in percentages) (e.g. if a mask is exposed to a flow of air containing 100,000 particles per cubic cm and only 4000 penetrate the filtration index is 100 X

(100,000-4000) / 100,000 = 96%. This test is done when the flow containing the particles is transmitted at a standardized rate through the filter or mask (usually 85 liters per minute). A mask at a level of "95" blocks 95% of the particles and allows max 5% of them to penetrate.

During the test, the mask (or filter) is attached (hot-melt glued) to a flat board with a hole in its middle that is placed on the lower rim of the 8130 TSI shown in the photograph. The top cylinder then forcefully drops and is sealed to the board with the mask glued to it. Air that contains tiny particles (less than 0.1 microns) is streamed from the top cylinder through the mask or filter, to the bottom part of the device. The particles concentration is measured before and after the transition through the mask/filter and the filtration index is determined.

When a paper mask is checked (i.e. "surgical" mask), it is simply placed on the lower rim and the upper cylinder is tightened and the air is blown with the particles through it. The calculation is the same.

What is important to understand is that these tests are laboratory tests in synthetic conditions, that is, without placing the mask on the face of a breathing person. This means that the leak factor around the mask margins is not included in the determination of filtration factor. The extent of the leak depends on the shape of the user's face and the actions in progress. Movements of the head and neck, speech, increased respiratory flow, and laughter can greatly affect the extent of the sealing. To value the overall protection of a protective kit (both mask and filter), the number of particles must be measured in an air volume outside the mask and inside the mask during each maneuver. Such a measurement can be made with a standard particles counter or a dedicated device such as the PortaCount model 8048 of TSI. This device includes a two-channel particles counter as well as a particle generator that releases particulate in the desired diameter range. Such a measurement is also called Fit-Test. It is required in situations where optimal protection is important. Tests of filters and masks are performed in laboratories and are regulated by the authorities. In Israel, filter tests by the TSI 8130 device are performed by the Standards Institute.

N95 masks According to the American terminology, are essentially equivalent to PPF2 by the European terminology while N99 (US) masks are parallel to PPF3 in European. They block 94-95% and 98-99% of particles, respectively. All these are "half-face" masks (mouth and nose coverage) and are usually for one-time use. Full-face masks cover the eyes in addition to the mouth and nose. Examples are 3M lines 6000 and 7000 and ViriMASK. The ViriMASK is equivalent to the N99/PPF3 in terms of respiratory protection.

What is the physiological meaning of "It is hard to breathe with a mask"?

Even healthy people have a hard time breathing with protective masks, especially with masks of N95 and N99 types. This has several reasons: (1) resistance to flow through the mask; (2) accumulating carbon dioxide (and decreased oxygen); and (3) heat load and humidity. The physiological overload is sometimes added to a psychological load of claustrophobia and anxiety. The latter were more widespread among patients with lung and heart diseases who experienced events of shortness of breath due to their illness. What is the mechanism of each of the physiologists?

1. Resistance to flow – in order to pass air through a mask you need to create a pressure differential. The pressure in the mouth and nose area should be lower ("negative") than the atmospheric pressure during inhalation and higher than atmospheric pressure ("positive") during exhalation. We generate negative pressure in every inhalation by expanding the chest and lowering the diaphragm that causes the lung to increase its size and thereby cause

pressure inside it to be lower. The negative pressure draws the air through the bronchial tree. When we breathe deeper and faster (for example during exercise or when we have high fever) we need to produce a more negative pressure in the chest and increase the "respiratory work". We need to produce more negative pressure in the chest even when the bronchi become narrower than usual, as happens in an asthma attack. When the breathing muscles work harder to generate air flow and supply oxygen, we feel "shortness of breath." We measure the resistance to air flow in units of cm of H_2O per liter per second. One cm of H_2O is the pressure that creates a 1 cm-high water column in a straw. The resistance to air flow of the bronchial tree of a healthy person is 1-1.5 centimeters of water per liter per second. This value is very small and therefore at rest, when the respiratory flow does not exceed 1 liter per second, we do not feel any respiratory load. During a mild asthma attack, an additional pressure of 2-4 cm of water per liter per second is required for the air flow to the lungs to be sufficient. In severe asthma, resistance can grow by more than 10-fold. Https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4500056 It is not surprising that breathing with the N95 mask is difficult. Its resistance to flow is 2-3 cm H_2O per liter per second, just like a mild asthma attack. When one is required to perform mild to moderate physical activity with an N95 mask (e.g. attend to an ICU patient), the respiratory flow increases and with it the need for generating pressure. Reducing the resistance to flow is crucial to prevent respiratory distress when breathing with a protective mask.

2. The accumulation of CO_2. The volume between the nose and mouth and the inner surfaces of the mask contains at the end of exhalation the air that came from the alveoli. It is rich with CO_2 (about 5.6%, compared to 0.03% in the environment) and low in oxygen (about 16% instead of 21%). This volume is called "The Dead Space". In our bronchial tubes there is a dead space. In the subsequent inhalation this air is first to enter. It is clear that if the body needs a sufficient amount of fresh air to reach the alveoli of the lung in each breath, (say 450 milliliters) and the size of the dead space of the bronchi is 150 milliliters, each breath volume should be 450 + 150 = 600 milliliters. These are the normal values of an adult at rest. If we now add another dead volume by rebreathing the air in the space between the mouth and the nose and the mask, we will have to increase the volume of each breath or alternatively breathe more times per minute (faster). If we can’t do so, the CO_2 level in the alveoli and in the blood will rise. When we try to move a larger and faster volume in every breath through a mask with a great resistance (see section 1) in order to compensate for a large dead space, we need to work harder. Initially we can do so, but later fatigue may develop and the CO_2 level may rise. A significant increase in CO_2 levels in the blood causes widening of the brain blood vessels causing headache, dizziness and nausea.

3. Heat and moisture overload may cause discomfort. The air we exhale contains 100% humidity at a temperature of 37 degrees Celsius. These are the conditions where most people seek air conditioning. On the other hand, these conditions are not different from those experienced by more than half of the Earth's population during considerable parts of the year. Air conditioning and a fan help mitigate the heat load. Masks that have a built-in blower that force air through a filter, brings fresh filtered air into the breathing space of the mask and ease the discomfort. Exhalation should also be through a filter (additional)

to protect the user's environment in case the user is a carrier of the virus. Mask with a blower can certainly be an optimal solution.

How do you prevent the risk of infecting during commercial flights?

The passenger cabin on commercial flights contains pressurized and warmed up air. Air compression and heating consume a lot of energy (= $$$) and therefore airlines try to save by reducing the replacement of air in the cabin. Instead, they use filters that can block particles. When smoking on airplanes was allowed, filters were used extensively and they were effective enough to prevent, almost entirely, the spread of cigarette smoke throughout the cabin. When the smoking on board was stopped, the air flow through the filters and filtering efficiency was reduced. The result was a savings to airline companies on the one hand, and the emergence of Air Travel Respiratory Infection Syndrome on the other. It is enough that one person coughs and sheds viruses in the passenger compartment for the viruses to reach all passengers and cause infection.

To cope with this phenomenon we should: (1) increase the rate of airflow through the filters; (2) Increase the entry of fresh air; (3) Use filters that can filter out virus particles (that is, 0.1 microns and above); And (4) demand that all passengers and flight personnel use the best available protection equipment (Best Available TECHNOLOGY – BAT).

What is the difference between droplet spread and aerosol dispersion?

When we sneeze or cough, we generate air flow at a huge speed. The role of cough is to sweep and rake with the air stream the layer of the mucus that covers the airway, and to break it into small particles. It is an important role that prevents the accumulation of secretions that may block the airways. At the same time there is an environmental scattering of particles. Since the beginning of microbiology as a science and especially with the beginning of understanding tuberculosis, we are educated from childhood to block the air flow of cough with the hand or, preferably, with the elbow. It's certainly not enough, so in eastern cultures it is accepted (even before the corona) to wear a protective mask as part of the common mutual manners. Also, the customs of greeting a person by bowing while maintaining a proper distance (as opposed to the kisses and hugs in Mediterranean countries) are part of the culture and help prevent spread of infection long before the corona appeared. The problem is that the scattering of particles in a trajectory with sufficient kinetic energy can overcome gravity for a distance of 1-3 meters. However, this is only one kind of dispersion, because with each cough and sneeze, there are also very small particles that are under 10 microns in diameter. These tiny particles, especially those that are under 2.5 microns, tend to remain suspended in the air for a long time while moving together with the air flow as if they were molecules. In fact, they are even affected by the Brownian movement of the gas molecules. This aerosol is scattered all over, and it is easy to see it if you spurt a spray of perfume or deodorant in a room. It is possible to feel the scent long after the splash. While the volume of these particles is low, their surface area (relative to volume) is large and lots of virus particles can be adhered to the surface of these small particles. If at the beginning of the corona plague, "experts" felt that spread is only by droplets, it is now fully accepted that the virus's transmission by aerosols is an important vector. In this context, it is necessary to mention that the relatively large area of the eyes' surface is made of respiratory epithel which makes them vulnerable to landing and the culture of viruses. Protection against sprays and eye protection are crucial to creating barriers against contacting Covid-19.

Is it possible to establish decisions about the closing/opening of various compounds and activities on scientific considerations? Do we know enough?

Everyone remembers the debate that became political about closing or opening gyms in Israel. Looking from the side, it seems that each party has established its position on hunches. They were not able to make an informed decision. But it doesn't have to be this way and any political or lobbying pressures can be removed from the equation. Decisions can be based on objective criteria. It is true that it is necessary to use probability (or calculation of odds and risks) but we already have enough data to pinpoint the criteria. This chapter does not claim to determine the actual values for the criteria but to point to the process by which the criteria should be calculated. The basis for the determination is: "What is the chance (risk) that a virus penetrates and infects a particular person in a particular space, while performing certain activity when protected by a specific protective gear?"

To do this we offer to use the following parameters:

1. What is the expected viral load? Clearly, the load in a Corona ward is much larger than in places where the chance to encounter a virus spreader is low. This is the probabilistic calculation that on one end has 100% risk and at the other end there is no risk (e.g. in open air where there is no one around). The number of carriers in a community divided by the population can be used as a simplistic benchmark. For example, in the city where there are 100,000 inhabitants and 100 active patients, the expected statistical load is 0.1%.
2. Is the air in which we are staying replaced with fresh air frequently or filtered? Here you can assume that on one side of the spectrum is the free air in which the dilution and mixing are almost endless, and on the other side there is a closed hall that is not ventilated and does not have any filters. In this case the presence of a virus distributor will increase the concentration of viruses in the air and the risk of infection will continue to rise with time. Hence, the time of exposure in this case is an important factor. Obviously, in a space that refreshes the air in a controlled and measured way, the risk decreases. For example, if the air in a hall that has a volume of 300 cubic meters is refreshed 10 times/hour by using a pump that can blow 3000 cubic meters per hour, the concentration of the virus particles is reduced 10 times, thereby reducing the risk (or allowing more people to share the space). Another option is to move the air through dense filters that are able to block the virus particles. If we know the efficacy of the filter, it is a simple calculation to determine the risk mitigation
3. Shielding: Protection should always be two-way, i.e. the protective mask protects both the user and the environment. Here too, this is the probabilistic element: For example, the paper mask ("surgical") which most of us use in public prevents the distribution of droplets emitted while coughing and sneezing (see a previous chapter) at a level of about 85% when used correctly (on the nose and mouth together). As such, there's a 15% risk of spreading. There is also a 15% risk of penetration. Basic probability considerations indicate that the total risk of transferring a virus when two people wear a paper mask is equal to the product of the risks, namely 0.15 X 0.15 = 0.0225 or 2.25% only. This is a very significant drop in overall mutual risk as compared to not wearing anything (i.e. 100% risk). When using masks of type N95 the protection increases to 95% and the risk decreases to 5% and thus the risk of mutual exposure decreases to only a quarter of a percent (0.05 X 0.05 x 100 = 0.25%). When using an N99 rated mask (e.g. 3M or

ViriMASK) the individual risk decreases to 1%, and the mutual risk to 0.01%.

4. Distance: The concentration of particles in the air decreases as a function of the distance. For the sake of this calculation, let's assume that air is not moving and has no directionality (by air flow, or coughing or sneezing), and suppose that we released a certain number of particles (say a million) that are floating initially in a volume of one liter. Over time, the particles disperse and occupy the entire space. Assuming the size of space 50 cubic meters (e.g. a room with an area of 4m X 4m = 16 sqm with a height of 3.1 m). This is about 50,000 liters. By simple dilution of the particles in the entire volume, their concentration decreased from a million in one liter to 1,000,000/50,000 = 20 particles per liter. It is easy to see that if a particles distributor stands in the middle of the room, a person who is only 2 meters from the shedder (i.e. near the wall) is exposed to a very small concentration. Social distancing is then an important tool in reducing the viral load and the risk of infection.

5. Susceptibility and vulnerability: Here comes the question of what is the concentration of particles that are dangerous to us? Science on this subject is still unclear. Https://www.nytimes.com/2020/05/29/health/coronavirus-transmission-dose.html experiments in animal studiess have already been carried out, but it is not ethical to perform human infection experiments. In the SARS (bird flu) epidemic, a member Corona virus family, it was found that several hundred virus particles are necessary to cause disease. Below this amount the immune system (assuming it's normal) can overcome the virus and prevent it from penetrating the respiratory tract cells and reproduce. In the MERS epidemic, the minimal infective dose was even larger, several thousand virus units. On the other hand, apparently, for the measles virus, which is also distributed through the respiratory system, it is sufficient for an individual virus particle to cause disease in an unvaccinated person. The currently known scientific material suggest that several hundred particles of virus need to penetrate the respiratory system to induce disease development. However, patients with immunodeficiency, such as patients receiving cytotoxic drugs, steroids, dialysis patients and acquired immunodeficiency patients (AIDS) we should assume that in some cases even a single virus can penetrate into a cell and begin to reproduce. Another look at the extent of the vulnerability is the amount of air that is breathed in and out by a person. If we refer to a comparison between a person who is resting and breathing about 6-7 liters per minute and a person who is doing a physical effort and breathing 60 liters each minute, it is clear that the total burden of the virus exposure grows in proportion to the amount of air that penetrates the lungs. There are of course other parameters of vulnerability and sensitivity, such as disinfection (or lack of) of hands, or frequency of touching ones face, and so on.

6. At what cost? When rationally examining the protection against the Corona virus, the cost must also be taken into account. You can't completely ignore it. During the Gulf War, the state of Israel handed out expensive gas masks for the entire population because of fear from a gas attack from Iraq — the psychological scare of chemical gas attack played an important role in deciding to give gas-masks for the entire population. The questions of cost (in cash) versus benefit (in prevention of morbidity and mortality) are in the eyes of decision makers all the time. Budgets are not endless. For example, when you ask

how many fatal accidents are prevented when investment is made in fixing a road or a dangerous intersection? It is not cynical to calculate the financial value of saving a person's life in a situation where the cake is finite and should be prioritized as rationally as possible. On the issue of the corona, the determination is more complex because there may be a situation in which the capacity of all the hospitalization beds in the intensive and ventilation care units may be exhausted leading to a situation where there may be a drastic increase in mortality. In a situation in which billions are invested in coping with the economic damage of closures and the loss of jobs, a national investment should be considered in the distribution of protective masks at level N99 for the entire population or at least the population at higher risk.

Summary

Understanding the scientific and quantitative parameters of the Corona epidemic can enable rational, weighed, and measured actions to cope with the prevention of the disease while causing minimal economic damage to the country and its people.