Vaccine Safety

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e are now near the end of the second year of the COVID-19 pandemic, and it has been a year since the first International System Safety Society (ISSS) Conference coronavirus presentation. This past year has seen the development and distribution of several vaccines, as predicted in the previous publication about the pandemic. These new weapons against disease will save millions of lives all over the globe in the next few years — and they were developed faster than any vaccine in medical history. Yet these same vaccines have been the victim of numerous allegations from the start. In fact, their strongest virtue — the speed with which they were developed and distributed — is seen by their critics as a fault, possibly resulting in an unsafe or insufficiently tested product. Is there any truth to these claims? How do these vaccines work? And how are they made?

In order to establish an orderly, technically accurate, objective, and comprehensive record of the events of these times that is accessible to the general public and of some use to posterity, this second publication has been prepared. It is also hoped that this report will mitigate some of the concerns that people have about vaccine safety.

Introduction

Although this publication can be read as a stand-alone paper, it would be best to first read its predecessor, "COVID- 19" [Ref. 1]. The author assumes that the reader is familiar with the background material developed in that publication. Therefore, such foundations will not be repeated here except by citation or a brief descriptive comment. As previously predicted [Ref. 1], the fall 2020 and winter 2021 seasons have seen a frightening number of coronavirus cases and deaths. According to the Centers for Disease Control and Prevention (CDC), as of May 24, 2021, the total number of cases in the U.S. was 32,933,337 and the total number of coronavirus deaths in the U.S. was 586,793 [Ref. 2]. The development of several vaccines and the coming of the warm months seems to have damped the rise in cases and brought infection levels down to "acceptable" levels for the moment. Also, "horror headlines" in the press have largely disappeared. But there is a new terror — complacency! Many people are refusing to be vaccinated [Refs. 3 & 4]. Instead, they would rather take their chances with the "wild-type" infection because they think the vaccine is unsafe. The internet seems to be the current vehicle for rumors surrounding vaccine

safety in the U.S. [Ref. 5]. But before responding to these rumors, the readers need to extend the background they have previously gleaned [Ref. 1].

Herd Immunity

The concept of *herd immunity* is not hard to understand. It is simply this: *If enough people in a population are vaccinated against a disease, the disease will eventually die out in that population.* A simple calculation will put this concept into sharper focus. Suppose each infected person infects five other people while they are incubation carriers [Ref. 1]. After that, it will be assumed that they are quarantined. The number five is called the *Reproduction Number* and it is a *chain reaction multiplicity factor.* A value of three might be a better average [Ref. 6], but in a crowded environment like a city, five is probably more realistic.

Let "t" be the time interval during which a host is an incubation carrier. For the coronavirus, t ~ five days; see Figure 3 of the author's previous publication [Ref. 1]. In this case, after n time intervals t, the number of infections will be 5^n . And, if n = 6, then the total number of infections is 15, 625. At this point, an infection is very noticeable to public health officials. How long will it take for a coronavirus infection to reach this level? It will take a total time T = nt, or T =(6)(5) = 30 days. Something of this kind is what happened in the U.S. Now, suppose a vaccine is available that is 100% effective, and assume that 80% of a population is vaccinated (i.e., 80% are made immune). In that case, the effective multiplicity factor is unity because, on the average, only

Editor's Note: This paper represents the scientific knowledge from a snapshot in time of the early 2021 timeframe. One particular point is that full vaccination is now (i.e., December 2021) considered to be two initial doses of mRNA vaccine, plus a booster of the mRNA vaccine, six months after the second dose.

one out of the five people a carrier might infect will become a carrier themselves. And $1^n = 1$ no matter how many time intervals t pass (i.e., n can equal anything). Therefore, the infection cannot spread. And, if more than 80% of a population receives such a vaccine, the multiplicity factor will be less than unity, and the number of cases will approach zero as n approaches infinity. That's "herd immunity"!

These calculations, however, suppose that a 100% effective vaccine is available. Real coronavirus vaccines are not 100% effective. Therefore, according to this simple model (a rough approximation for the U.S.), it will require *more* than 80% of individuals in the U.S. to complete their vaccination schedule before herd immunity can be established [Ref. 3]. A poll released on March 9, 2021 indicated that one out of four Americans (especially black and Hispanic citizens) will refuse the COVID-19 vaccine [Refs. 3 & 4]. Furthermore, some groups, such as non-English speakers and rural Americans, may be having problems gaining access to the vaccine. In fact, there may be a variety of groups that are each hesitant to vaccinate for their own reason.

The U.S. administration considers the problem of non-vaccination severe enough to have sent Vice President Kamala Harris to Atlanta, Georgia, on June 18 to rally support for vaccination in the state, especially within the Black community [Ref. 7]. And the administration's goal to "partially vaccinate" (meaning that at least one shot out of a series of two has been administered) 70% of the U.S adult population by July 4, 2021 [Ref. 7] will probably not be sufficient to *stop* the spread of COVID-19 and its variants; but it will slow down the spread. Therefore, it might not be possible to establish herd immunity in the U.S. until public opinion changes concerning vaccine safety.

That change may be difficult since it has been suggested that willingness to vaccinate is also dependent on people's political views [Refs. 3 & 4]. As each side "digs in" and hardens their opinions, a pragmatic commonsense approach becomes less and less likely. At the time the author wrote this article (May 19, 2021), only 38% of the U.S. population had been fully vaccinated (according to usafacts.org's "Vaccine Progress Tracker"). At the time of final review of this paper, according to the "Vaccine Progress Tracker" (updated July 4, 2021), only 48% of the U.S. population was fully vaccinated and 56% had received at least one dose (as of July 8, 2021, the CDC claims 67.2% for partial vaccination while no figure was given for full vaccination).

The pandemic is not over, and we could still have a very serious problem in the U.S. that might flare up again in the next fall/winter cold and flu season. The "anti-vaxxers" will significantly exacerbate the problem, as may new coronavirus strains. And the American administration's incautious decision to increase refugee immigration by 5.2 times for 2021, and more than an order of magnitude (10.4 times) for 2022, from 2020 levels of 12,000 will not help matters at this time [Ref. 8]. In general, travel into and within the country poses a consistent risk of re-infection, especially given our inconsistent policies and adherence to screening and quarantine protocols. However, the apparent natural immunity of children, as well as ongoing vaccination efforts, will help.

It's an unstable situation and it is difficult to know exactly how it will develop, but there are certainly dangers that can, and should, be mitigated by informed public policy and education of the general public. In particular, the U.S. is simply going to have to do a better job of reaching out to minorities to convince them of vaccine safety.

The Central Dogma

In order to explain how the modern vaccines are made — and how they work — it is necessary to understand the flow of genetic information within a cell. A *gene* is part of a gigantic DNA molecule that makes up one *chromosome*. All the chromosomes together make up the total inheritable material that resides in the nucleus of a cell and are collectively called the *genome* [Ref. 9].

The human genome has 46 chromosomes. The chromosomes themselves are tightly coiled to save space, but when a cell needs a certain protein — for example, an enzyme to carry out some necessary cellular chemical reaction — a small part of a chromosome is "unwound" and copied (*transcribed*) by a very special protein "tool" called *DNA-directed RNA polymerase* (which, following the usual terminology, will just be referred to as RNA polymerase for short) to produce something called *messenger RNA* (or *mRNA*) [Ref. 9].

Now, recall from Reference 1 that RNA polymerase has been discussed before in connection with the replication of RNA viruses. That was *RNA-dependent RNA polymerase*, which was deliberately referred to by its more common name *replicase* to avoid confusion with the type of polymerase discussed here. Think of the genome as a library from which books cannot be borrowed, but parts of them can be copied by RNA polymerase. That copy (mRNA) can pass through the nuclear membrane to a macromolecular micro- machine, called a *ribosome*, that *translates* mRNA from the language of nucleic acids into the language of proteins [Ref. 1].

A protein is nothing more than a string of amino acids that naturally folds itself into complex shapes useful for biological processes. Humans employ 20 different amino acids to build proteins [Ref. 1]. This passage of information from DNA to mRNA to proteins is called the *Central Dogma*, and for two decades, it was thought that this was the *only* way genetic information could travel (See Figure 1 — blue pathway).



Figure 1 — *Information flow within a cell: A) the normal Central Dogma (blue), and B) under the action of the enzyme reverse transcriptase (red).*

The discovery of the first human retrovirus by R.C. Gallo in 1980 revolutionized biochemist's understanding of how genetic information can flow in cells. Retroviruses carry their genetic information as RNA, as do the coronaviruses. However, retroviruses carry something else in their nucleocapsid — a few molecules of an enzyme protein called reverse transcriptase. Their RNA also encodes for *reverse transcriptase*.

When a cell is infected by a retrovirus, the contents of its nucleocapsid is emptied into the host cell's *cytoplasm* (a jelly-like substance enclosed by the outer cell membrane). Then the reverse transcriptase forms a piece of double-stranded DNA from the retroviral RNA (also called vRNA). This new, chemically active piece of DNA can pass through the nuclear membrane and become incorporated into the host cell's genome. Thereafter, every time the infected host cell divides, it must also pass on the instructions for producing more retrovirus particles (virions), including instructions for producing more molecules of reverse transcriptase to be incorporated into the nucleocapsid of daughter virions.

Typically, the production of daughter virions begins when the DNA that was made from the vRNA is "switched on" by some biochemical signal after a period of dormancy. As the viral parts collect in the host cell's cytoplasm, they self-assemble into virions capable of infecting other cells. Eventually, the host cell becomes so filled with virions that it bursts (lyses) to release its infectious particles and begin the cycle of infection all over again. This is what happens during an acquired immunodeficiency syndrome (AIDS) infection [Ref. 10]. Therefore, retroviruses allow genetic information to pass from RNA back to DNA – *the reverse of the Central Dogma*!

Figure 1 summarizes the reverse information flow (red pathway). Although retroviruses have been responsible for many frightening diseases, they are also a powerful tool of genetic engineering and can insert a useful protein producing gene into an easily grown host such as a yeast.

The Making of a Vaccine

Three major vaccines are being used in the U.S. today: the Moderna vaccine, the Pfizer/BioNTech vaccine, and the Johnson & Johnson vaccine. However, others do exist. Recall from Reference 1 that development of human immunity to COVID-19 requires a coronavirus protein. This foreign protein is recognized as "not-self" by the human immune system. Consequently, the body tries to destroy it.

Usually, the protruding "Spike" (or "S") glycoprotein is used to stimulate immunity because, without that protein on the surface of the viral envelope, the coronavirus cannot recognize, or bind to, its host cell prey (see Figure 1 of Ref. 1). The Moderna and Pfizer vaccines utilize the Central Dogma pathway to produce "S" and, consequently, immunity within the human body [Refs. 4, 10 & 11].

How is this done? The process is complex, but begins with the coronavirus itself.

Unlike polio virus, coronavirus is very difficult to breed. Therefore, making a traditional vaccine by simply growing copious amounts of virus and then inactivating them with chemicals or radiation, or breeding an attenuated active strain to stimulate immunity is also difficult. Instead, the genetic material is removed from a small amount of coronavirus. This can easily be done by breaking the virus apart in a solution (essentially dissolving its parts) and then centrifuging the result to separate out the RNA. Once the RNA is isolated, it can be cut into fragments with a nuclease (an enzyme that chops up RNA) and the fragments separated by chromatography, electro*phoresis*, or some other method (and there are many; Mathews and Van Holde, 1996). The fragment that encodes for "S" then needs to be copied (amplified) many times. One might think that the desired RNA fragment





Figure 2 — The structure of tris. Left) Planar projection. Right) "Ball and stick" 3D space molecular model; black = carbon, red = oxygen, blue = nitrogen, light blue round beads = hydrogen. This molecule also goes by several other names: Tromethamine, tris (hydroxymethyl) aminomethane, and most properly, the IUPAC name 2-Amino-2- (hydroxymethyl) propane-1,3-diol. As the reader knows from Figure 5 of Reference 1, amines (like tris) are weak bases. It is the nitrogen atom that wants to accept an acidic hydronium ion.

could be copied directly by using the enzyme *replicase*, but, as pointed out in Reference 1, this copying process is not very faithful.

And so, if you base a large-scale copying process on replicase, you might end up with tons of mutated RNA fragments that are good for nothing. Another amplification process is called a *polymerase chain reaction* (PCR) [Ref. 9] and it starts by turning a fragment of RNA into a fragment of DNA using the enzyme reverse transcriptase. DNA looks like two strings that have been twisted together. And, if they are carefully heated, the strings unravel. This is called "melting." Each string can then be used as a template to grow its complement so that you end up with *two* twisted strings. These two complete DNA fragments can then be reheated again to begin the cycle all over – reheating, growth, reheating, growth, etc. After each cycle the number of DNA fragments doubles. When you have enough DNA fragments you can turn them back to RNA fragments with RNA polymerase. PCR has been used to test for coronavirus virions as described in Reference 1, but again copying fidelity is not as high as one would like. Hence, the 20% false negative errors associated with some virion tests [Ref. 1].

The only way to amplify an RNA fragment with high fidelity is to use the method employed by the phar-

maceutical companies. Amplification starts the same way as does PCR amplification. A small fragment of RNA that encodes for "S" is turned into a small fragment of DNA by reverse transcriptase. The small fragment of DNA has "sticky" ends so that another enzyme called a *circularizing protein* can change it into a small ring called a plasmid [Refs. 10 & 13]. Some bacteria, like *E. coli*, harbor *plasmids*, and when the bacteria reproduce, so do the plasmids.

Then you have the problem of changing all those plasmids back into RNA fragments. First, the E. coli have to be broken open and the plasmids separated out by filtration or centrifugation. The rings can then be cut and straightened with still another enzyme called a *linearizing protein*, and RNA polymerase can be used to produce RNA fragments that encode for "S." *If one of these RNA fragments is introduced into a cell, it essentially acts as a messenger RNA (mRNA), and will be translated into an "S" glycoprotein.* Recall from Reference 1 that a glycoprotein is a protein with a sugar moiety (fragment or piece) attached, and the only places in a cell capable of producing "S" glycoproteins are the ribosomes of a cell's endoplasmic reticulum (ER) (see Figure 6 of Reference 1).

All *eukaryotic* cells (i.e., the cells of higher organisms — anything from yeast to man) have an ER, so why

not infect a batch of yeast with the amplified mRNA fragments and let the yeast produce "S", which can then be harvested for vaccine production? Or, better yet, take a retrovirus, remove its genome and replace it with an mRNA fragment. Then, let the retrovirus infect a yeast cell? Since the retroviral capsid already contains reverse transcriptase, the mRNA fragment that encodes for "S" will be integrated into a yeast cell's DNA. Then the yeast cell, and all its daughter cells, will produce "S" as a byproduct of their metabolism. Copious amounts of this genetically modified yeast can be grown in tanks with a 100,000 to 150,000 liter capacity!

All of these things can be done, but why bother? *It is more direct, safer, more natural, faster (production-wise), and cheaper, to directly infect human cells with the mRNA fragments and let the ER of human cells produce "S" to stimulate immunity (the Central Dogma "blue" pathway shown in Figure 1). This is why the Moderna and Pfizer vaccines are called "mRNA vaccines," and they are the latest innovation in immunology!* The Moderna vaccine contains 100 micrograms (µg) of mRNA per dose, while the Pfizer vaccine contains 30 µg [Ref. 4].

But how are human cells infected with mRNA fragments? Now that is something quite interesting. In the old days (a few years ago), when biochemists wanted to infect a cell with RNA, they coated the surface of gold microspheres with RNA and then accelerated them into the outer cell membrane. The micro-bullets entered the cytoplasm and the semi-fluid cell wall healed behind it.

That was a workable procedure to infect a few cells in a petri dish, but how do you infect a whole organism (like a person)? Recall from Figure 2 in Reference 1 that a lipid (fatty) bubble can be prepared that has a composition similar to a cell's outer membrane. It is called a *micelle*. Both the Pfizer and Moderna vaccines employ lipid micelles. But, the schematic drawing of a micelle in Figure 2 of Reference 1 doesn't do the little devil justice.

Actually, the micelle is much more complex and is composed of several lipids. Each vaccination consists of 0.5 cc of vaccine, and of this, 1.93 mg are lipids (Moderna composition [Ref. 14]); SM-102, polyethylene glycol (PEG) 2000 dimyristoyl glycerol (DMG), cholesterol, and 1,2-distearoyl-sn-glycero-3- phosphocholine (DSPC). The Pfizer lipid composition is similar.¹ If the interior of a micelle contains a few mRNA fragments encoding "S," and is injected into a person, the tiny micelle will eventually contact a cell wall (cell membrane) within the human body. Then the micelle and the cell will unite (fuse). The mRNA will then enter the cell and production of "S" can begin at any ER ribosome. That is how the Moderna and Pfizer vaccines are made, and how they basically work.

The micelles also serve another purpose. They help protect the chemically unstable mRNA from destruction during delivery. Protecting the mRNA from the body's immune system is harder than you might think. So there is a lot of science here worth a Nobel Prize. Nevertheless, the micelles are fragile and must be maintained at the proper pH and temperature [Ref. 1]. It is for this reason that these vaccines contain *buffers* (to keep the pH constant), a preservative (to protect the fatty micelles), and are kept refrigerated (to slow down deterioration of the vaccine by chemical reactions).

Buffered solutions resist changes in pH when foreign acids or bases are added. A buffer consists of an acid and its salt. In the case of the Moderna vac-

The composition of the lipid micelles used by Pfizer and Moderna may seem overly complex, but this is not the case. Each component contributes some necessary property. For example, the cholesterol is a membrane "stiffener" (i.e., it makes the lipid bilayer membrane less fluid) [Ref. 9]. The micelles must have just the right strength, fluidity and elasticity — strong enough to carry its precious mRNA cargo to the target cells, but weak enough to release that cargo when needed. A decade before the pandemic, biochemists were studying membranes because they realized that they were key to understanding how life began on Earth. It is thought that the first cells were nothing more than lipid micelles with prokaryotes (simple life forms like bacteria) trapped within. What is the proof for such an astounding statement? It comes from the cells themselves. It was discovered that some of a cell's organelles (structures within the cell's semi-liquid cytoplasm), for example the mitochondria (the cell's energy factories), *contain their own DNA!* This fact has led to the speculation that over time symbiotic relationships developed between prokaryotes captured within a bag-like lipid micelle. The result was the eukaryotic cell of modern higher life forms (anything from yeast to man)! Here one can see how a seemingly esoteric line of research led to one of the most practical discoveries of our age! Although it may seem like the new vaccines were "rushed," this was not the case because it was preceded by a decade of patient preparatory research.

¹Each 0.3 cc dose of the Pfizer vaccine [Ref. 50](CVS, 2021) contains lipid micelles made from cholesterol, and 1,2distearoyl-sn-glycero-3-phosphocholine (DSPC) like the Moderna vaccine. The Pfizer vaccine also contains the lipids ALC – 0159 and ALC – 0315. The first is a PEG/lipid conjugate that is the N,N-dimyristylamide of 2-hydroxyacetic acid, O-PEGylated to a PEG chain mass of about 2 kilo Daltons. In plain parlance, it is a PEG polymer with a molecular weight of about 2000 Daltons (a Dalton is the weight of one hydrogen atom) that is attached to an amide moiety (fragment). This PEG/lipid conjugate takes the place of the PEG polymer used by Moderna. The other lipid, ALC – 0315, is a macromolecule with a molecular weight of 766.29 g/mole and an empirical formula of $C_{48}H_{95}NO_5$. This lipid is a replacement for the proprietary SM-102 lipid used by Moderna with an empirical formula of $C_{44}H_{87}NO_5$.

cine, the acid is acetic acid (0.043 mg/0.5 cc vaccination, or 1.434×10^{-3} M) and the salt is sodium acetate (0.12 mg/0.5 cc vaccination, or 2.927 x10⁻³ M) [Ref. 14]. The pH of a buffered solution is governed by the Henderson-Hasselbalch equation [Ref. 15] and, for the concentrations of acetic acid and sodium acetate just given, results in a pH of about 5.07, which is a little low.² Recall from Reference 1 that a micelle is stable at a slightly acidic pH in the $5 \rightarrow 7$ range. Therefore, a second buffer (0.31 mg of tromethamine per 0.5 cc vaccination plus 1.18 mg of tromethamine hydrochloride) is also employed by Moderna [Ref. 14]. Tromethamine $(C_4H_{11}NO_3)$, formula weight 121.136; Figure 2), commonly referred to as "tris," forms a very popular buffer when mixed with its hydrochloride ($C_4H_{11}NO_3.HCl$, formula weight 157.597) [Ref. 15], and is usually used in the pH = $7 \rightarrow 9$ range.

Repeating the Henderson-Hasselbalch calculations for the tris / tris HCl buffer system yields 8.40.² Now comes a very difficult question, "What is the pH of a solution that contains *both* buffering systems?" Experimentally, the amount of tris and tris HCl (also written as "tris.HCl," "trisH⁺.Cl⁻," or "trisH⁺Cl⁻") needed to produce a pH near the center of the optimal micelle range can be determined by direct addition to an acetic acid / sodium acetate buffered solution. In effect, a new buffer has been created out of the previous two.^{2, 3} Although tris is a popular biological buffer, it has a side effect — *headaches!* Many vaccinated individuals do complain of headaches.

Sucrose (common sugar) is used as a preservative by both Moderna and Pfizer for two reasons. First, it tends to retain necessary water in the vaccine solution. The colligative properties of sucrose, the replacement of surface water molecules with molecules of sucrose, minimizes evaporative loss. Furthermore, a sugar solution has a high *osmotic pressure*, meaning that water wants to go into the solution rather than leave it. Second, the sugar also retards the growth of bacteria, molds and yeast that might otherwise try to metabolize the lipids. Therefore, 43.5 mg of sucrose are used per 0.5 cc vaccine dose (Moderna, [Ref. 14]).

Everything that the vaccine contains has now been discussed! There are no magnetic microchips, no tracking devices, no homing devices, no listening devices, no delayed action "poisons" — no implants of any kind! And, incidentally, no magnets will stick to your skin at the site of the injection, not unless you superglue them there! Although the technology is complex, the composition of the vaccine itself is fairly simple and straightforward at the top level. The method of construction, contents (all harmless and none of them live), and biochemical function within the human body have now been carefully described for the two leading American vaccines. The author must congratulate the technical staff of both Moderna and Pfizer. It was the "Moon Shot" of this gener-

$$pH = pK_a + \log_{10} ([A^-]/[HA]).$$
(1)

The brackets "[]" denote concentrations measured in *molars* (M; mass in grams/formula wt. in grams, per liter of solution), and pKa is -log10 of the acetic acid dissociation constant (4.757 after taking the logarithm). Substituting the appropriate concentrations and pKa into this last equation yields pH = 5.07, assuming what was mixed stays in the same form (or almost so).

The calculations for the tris/tris HCl system are similar, except that the numerator of the argument of the Log is [tris] = 0.00512 moles/l, the denominator is [tris HCl] = 0.01497 moles/l, and the pKa for tris HCl is 8.075. Substituting these figures into equation 1 yields 8.40.

Now, what is the pH when the *two* buffer systems are combined [Ref. 49]? One might reasonably guess a figure somewhere between the extremes produced by the individual buffers alone, since hydronium ions will be shuttled from the acidic buffer system to the basic system. The complete mathematical solution to this problem is actually quite complicated and cannot be treated here [Ref. 49]. However, a net pH of 6.00 would be ideal since it lies at the center of the micelle stability region. The specifications of the types and initial concentrations of the acids, bases and salts, needed to produce such a result requires machine computation [Ref. 49]. This discussion gives the reader some idea of how a vaccine can be designed on a computer. It is a trend that is likely to continue for these new pH-sensitive vaccines, in spite of concerns by critics who do not understand the role of computers in the design process [Ref. 5]. The buffered vaccine can now be frozen at -70° C (203 K⁰ above absolute zero) (Pfizer) for long-term storage. The micelles are now safe in a protective frozen cocoon of hydronium ions and water molecules until they are ready for their life-saving errand. Finally, it should be noted that the pH of blood is about 6.8 in tissues and veins [Ref. 9]. Therefore, the micelles are still stable after vaccination of an individual.

³ Each 0.3 cc Pfizer dose employs two other buffer systems: 1) potassium chloride / potassium phosphate monobasic, and 2) sodium chloride / sodium phosphate dehydrate [Ref. 50]. Incidentally, the salts potassium chloride and sodium chloride also retard the growth of bacteria, molds, and yeast.

² Given a weak acid reaction of the form HA \leftrightarrow H⁺ + A⁻, where HA is acetic acid, and A⁻ is the acetate ion whose concentration is dominated by the complete disassociation of sodium acetate, the Henderson-Hasselbalch equation states [Ref. 15]

ation, and *it was all very well done!* This author can only hope, Katalin Kariko, that you and Drew Weissman get the Nobel Prizes you both deserve!

The Johnson & Johnson vaccine, however, works a little differently than those just described. In this bold approach, a harmless virus is used to deliver the "S" protein mRNA to the interior of a cell. There have been a few blood clotting problems associated with this product, and information at this time is limited [Ref. 16]. Further complicating matters is the fact that only 6.9 million doses of the Johnson & Johnson vaccine have been administered as of April 14, 2021 [Ref. 16]. So there is only a small sample set to study. As of April 2021, blood clots had developed in the brains of six women between the ages of 18 and 48 within the time period of 6 to 13 days after vaccination. Furthermore, one man who participated in the clinical trial of the Johnson & Johnson vaccine experienced a similar clotting problem [Ref. 17]. Clotting reports have also come in from Europe involving the similar Astra-Zeneca vaccine. The clotting is thought to involve a protein on the surface of blood platelets [Ref. 17].

Blood clots are, of course, very suggestive. Recall from Reference 1 that the envelope of a coronavirus contains a protein called "H-E" (*hemagglutinin-esterase*), as does influenza C. "H-E" causes red blood cells to clump together. The "S" gene and "H-E" gene lie close to each other in the virion transmembrane protein region of the coronavirus RNA genome [Ref. 18]. If the "S" gene was not snipped clean from "H-E" before reverse transcription and amplification, there could be a problem. Or, perhaps the "harmless" virus used to deliver the mRNA in the Johnson & Johnson and Astra-Zeneca vaccines is not so harmless after all. Perhaps the viral envelope of these products contains "H-E."

These are, however, just two speculations; only time will tell what the true source of the blood clot problem really is. Although production of the Johnson & Johnson vaccine was temporarily halted while a risk assessment was made [Ref. 16], production later resumed on the grounds that the benefits of the vaccine outweigh its risks [Ref. 19]. In particular, it is a "one-shot" vaccine — a useful feature for transient populations like college students. Also, the vaccination imparts a long-lived immunity, and it can be stored in an ordinary refrigerator longer than other vaccines [Ref. 19].

In this section, the author has tried to convey the flavor, as well as the facts, of how biochemists use enzymes as "tools" to build "designer vaccines" and "designer life" in general. Also, the author has tried to give the reader some insight as to how biochemists troubleshoot problems. In the author's opinion, the new biochemical technology is so astounding and revolutionary that it will someday have a greater impact on daily life than the invention of the computer!

Side-Effects, Effectiveness, and Duration of Immunity

All vaccines have some side effects; if they don't, either they don't work or you're already immune to what was in the vaccination. And sometimes (but rarely) vaccines cause death. These risks must be balanced against the risks of acquiring the wild-type infection.

To put things in perspective, the Varicella (chickenpox, shingles) vaccine kills, on average, 2.1 people per million vaccinated [Ref. 4]. However, most people, as well as health care professionals, consider the benefits of this vaccine to outweigh the risks. Approximately 0.1%of all chickenpox cases are followed by encephalopathy (inflammation of the brain) caused by the virus [Ref. 10]. Women who become infected with chickenpox during the early months of pregnancy are at risk of infecting the fetus. These babies may be born with serious birth defects like missing limbs and cataracts. Furthermore, women who develop chickenpox just before giving birth may pass the infection on to the newborn child resulting in a serious infection. Finally, if chickenpox reemerges later in life as shingles, involvement of cranial nerves can lead to eve inflammation and ocular and facial paralysis [Ref. 10]. So the wild-type varicella infection has its risks also, which are much greater than those posed by the vaccination.

As of April 14, 2021, 98 million doses of the Pfizer vaccine and 85 million doses of the Moderna vaccine have been administered in the U.S. [Ref. 16]. Up to that point in time, there have been no fatalities from these products [Refs. 4 & 16]. These are some of the safest vaccines ever developed. None of the people who experienced blood clots from the Johnson & Johnson vaccine have died, either. Although such clots can be fatal [Ref. 16].

As with varicella discussed earlier, these risks must be balanced against the risks of acquiring the wild-type coronavirus infection. First of all, as of April 26, 2021, in the U.S., 1.8% of all those individuals who contracted COVID-19 had died [Ref. 20]. But the story doesn't end there. COVID-19 symptoms can sometimes persist for months. The virus can damage the lungs, heart, and brain, thereby increasing the risk of long-term health problems (Mayo Clinic Staff, 2021). Older people, and people with serious medical conditions, are most likely to experience lingering effects, but even young, otherwise healthy, people can feel unwell for weeks or months [Ref. 21]. According to the Mayo Clinic, common lingering symptoms include fatigue, shortness of breath or difficulty breathing, cough, joint pain, chest pain, memory or concentration or sleep problems, muscle pain or head-

ache, fast or pounding heartbeat, loss of smell or taste, depression or anxiety, fever, dizziness when you stand, and worsened symptoms after physical or mental activity [Ref. 21]. Furthermore, "eight months after mild COVID-19, one in 10 people still have at least one moderate to severe symptom" [Ref. 22].

In addition to all these symptoms, organ damage can result from COVID-19 infection, including heart damage that may increase the risk of heart failure or other heart complications in the future, scar tissue in the lungs that can lead to long-term breathing problems, blood clots and blood vessel problems leading to heart attacks and strokes, multisystem inflammatory syndrome where some organs and tissues become severely inflamed, and brain problems (including strokes, seizures and Guillain-Barre syndrome — a condition that causes temporary paralysis — as well as a possible increase in the risk of developing Parkinson's disease and Alzheimer's disease).

By comparison to the litany of horrors outlined in the previous paragraph, vaccine side effects are usually mild. Moderna cites

injection site reactions (pain, swelling, and redness), as well as general reactions like fatigue, headache, muscle pain, joint pain, chills, nausea and vomiting, and fever [Ref. 14]. The fatigue comes from the body trying to marshal its resources to fight an invader; the headache can come from the tris buffer as noted earlier; chills, muscle and joint pain are the body's natural reaction to a "cold." When you get the "chills," it's your body's way of telling you to seek warmth. Raising the body's temperature kills viruses. Shivering also raises body temperature, as does fever. Typically, a vaccinated individual might develop a fever for a few hours after the first shot (Moderna), and for a day after the follow-up booster (second Moderna shot). More threatening than these minor side effects is an allergic reaction to one of the components

It's difficult to understand why the coronavirus vaccine has caused so much backlash when many other vaccines have been on the market for years without complaint. So, there's a problem, possibly political, involving some sort of convoluted reasoning. in the vaccination (like tris, for example). An allergic reaction can be very severe. Signs of such a reaction include difficulty breathing, swelling of your face and throat, a fast heartbeat, a bad rash all over your body, dizziness and weakness [Ref. 14]. Anaphylactic shock (severe reaction) is life threatening, and although vaccination centers only require the vaccinated to wait 15 minutes before leaving, it is better to wait one hour before leaving the center to remove any possibility of developing this condition [Ref. 14]. Anaphylaxis occurs in 2.1 people per million doses of the Moderna vaccine, and 6.3 people per million doses for the Pfizer vaccine [Ref. 4]. But, again, no fatalities as of April 14, 2021. An epinephrine pen is usually nearby at any vaccination center to counteract any anaphylactic shock.

So much for the risks of both wild-type infection and vaccination, but what about vaccination benefits? Even after the first shot, the Moderna vaccine offers 60-85% protection [Ref. 4]. After the second shot, the Moderna and Pfizer vaccine offer 94% and 95% immunity respec-

tively [Ref. 4]. These percentages refer to the *percentage of people* who will develop active immunity, and *not* the percent of infectious insults that are destroyed by the body's immune system. The Astra-Zeneca vaccine offers less protection (69 – 70%), and the Johnson & Johnson vaccine 66.3% [Ref. 4]. Recall from Figure 3 of Reference 1 [Ref. 1], that the immunity gleaned from the wild-type coronavirus infection can last for only a few months. Artificially induced immunity lasts longer — probably a year or more [Ref. 4].

The Rumors: What Some People Believe!

Addressing rumors about the vaccine is the heart of this particular publication. However, it was necessary to understand how vaccines work, how they are made and what they contain, before a response to rumors, charges, and accusations can be made. It's difficult to understand why the coronavirus vaccine has caused so much backlash when many other vaccines have been on the market for years without complaint. So, there's a problem, possibly political, involving some sort of convoluted reasoning. In any case, this section will follow the format of a sequence of statements (rumors), some of which are quotes, and replies.

Rumor #1: This vaccine has been rushed, and because of that, it may not be safe! [Ref. 4]

Response #1: Ever since the Severe Acute Respiratory Syndrome (SARS) outbreak in China in 2002-2004 [Ref. 23], physicians, biochemists and epidemiologists have been expecting further coronavirus outbreaks from mutant strains and subtypes. Another, Middle Eastern Respiratory Syndrome (MERS), occurred in 2012 [Ref. 24]. The basic research began almost 20 years ago — the electron microscopy, sequencing of the coronavirus genome, chemical composition and function of the coronavirus envelope and its proteins, susceptibility to chemical agents, etc. So, these vaccines were not as rushed as one might think [Ref. 4].

Rumor #2: This vaccine employs a new technology. How can we be sure it's safe? [Ref. 4]

Response #2: Although the coronavirus mRNA vaccines are new, they were very well tested on tens of thousands of volunteers before their introduction into the public domain. Furthermore, as of April 14, 2021, about 200 million people have received the Moderna and Pfizer vaccines in the U.S. without significant incident. Finally, mRNA vaccines have been successfully developed for several other diseases as well. These include the Zika virus, influenza, and rabies [Ref. 4].

Rumor #3: The (wild-type) coronavirus infection is not all that bad. So, why bother with vaccination? [Ref. 4]

Response #3: As noted earlier, the death rate in the U.S. is about 1.8% as of this writing. In some other countries, the death rate is higher (e.g., 3% in Italy) [Ref. 25]. However, even if you do not die of COVID, your chances of long-term symptoms are high, 10% or more [Ref. 22]. Of the several people that the author knows who have contracted coronavirus infection, two who recov-

ered suffered a great deal and endured a month or more of hospitalization. A wild-type coronavirus infection is definitely something to avoid.

Rumor #4: COVID-19 is a rare infection. Why bother with vaccination? [Ref. 4]

Response #4: Actually, 1 in 10 people have contracted COVID-19 in the U.S. as of April 28, 2021 [Ref. 2].

Rumor #5: Vaccines cause disease. [Ref. 4]

Response #5: The composition of the most common vaccines available in the U.S. has already been discussed. The Pfizer and Moderna vaccines contain only safe ingredients and cannot cause disease. Incidentally, the mRNA from these vaccinations is cleared from the human body in a matter of hours [Ref. 4].

Rumor #6: Vaccines have side effects — some long term. [Ref. 4]

Response #6: This is not really a rumor. Vaccines do have side effects, but the benefits greatly outweigh the risks. The Pfizer and Moderna vaccines contain only safe ingredients that the human body can cope with, such as sugar, fat and water. The human body even has enzymes to degrade the mRNA fragments. And mRNA is contained in the food we eat [Ref. 9]! Safety is further reassured by the almost 200 million people in the U.S. who have received these vaccines without harm. One would have expected the weakest, most susceptible, individuals out of this huge population to have manifested any long-term effects by now, if there were any. Furthermore, mRNA vaccines have been under development for years and no long-term effects have surfaced to date. However, if you become infected by the live wild-type virus, you have at least a 10% probability of long-term effects of varying severity, even if your initial infection was mild.

Rumor #7: If these COVID-19 vaccines are safe, then why hasn't the (U.S.) Food and Drug Administration (FDA) approved them? [Ref. 14]

Response #7: Although mRNA vaccines have a history, the COVID-19 vaccine is the first one to be manufactured and distributed on such a large scale. Consequently, the FDA is being understandably cautious. However, it should be noted that food and drug authorities in other countries *have* approved the vaccine. As of December 21, 2020, many countries of the European Union have authorized or approved the Pfizer/BioNTech COVID-19 vaccine [Ref. 26]. Furthermore, as of April 2021, 13 vaccines have been authorized by at least one national regulatory authority (of some country or country's state) for public use; two RNA vaccines (the Pfizer/BioNTech

vaccine and the Moderna vaccine), five conventional inactivated vaccines (BBIBP-CorV, CoronaVac, Covaxin, WIBP-CorV, and CoviVac), four viral vector vaccines (SputnikV, the Oxford/AstraZeneca vaccine, Convidecia, and the Johnson & Johnson vaccine), and two protein subunit vaccines (EpiVacCorona and RBD-Dimer) [Ref. 26]. (Editor's Note: As of October 28, 2021, the FDA has approved the Pfizer/BioNTech and has authorized the Moderna and Johnson & Johnson vaccines for emergency use, pending final approval).

Rumor #8: Vaccines don't need preservatives because they are kept cold. [Ref. 4]

Response #8: Vaccines in deep storage are kept at -70°C. However, as soon as they are warmed to the liquid state, they can lose water by evaporation. Loss of water can damage the micelles that carry the mRNA. Furthermore, the lipids (fats) in the vaccine are food for bacteria, molds and yeast.

Rumor #9: "There was no possibility *at all*, based on all of the variants that are in the public domain — 4000 or so of them — none of them are going to escape immunity (i.e., become more dangerous)." [Ref. 5]

Response #9: The Delaney reference [Ref. 5] is a mixture of fact and fiction that is going to have to be picked apart. The short answer is that coronavirus immunity, from either vaccination or previous exposure, *can be* variant dependent. Furthermore, a strain does not have to "escape immunity." A strain can be *partially resistant* to the immunity induced by vaccination and still be a public health problem. The same is true for the influenza virus; hence, annual revaccination.

Delaney did not specify precisely what he meant by "more dangerous." He could mean either *more lethal* or *more transmissible*. The notable variants are *definitely* more transmittable than the original strain [Ref. 27]. In that sense, they are "more dangerous" and will continue to wreak havoc within an infected population, especially among the unvaccinated. As more people are infected, more will die. So mortality can be increased by more than one route. Pfizer has already developed the next vaccination in the coronavirus series [Ref. 28]. The new "booster" will reinforce immunity to the old strains, and may defeat any partial resistance acquired by the Delta strain before further genetic modifications evolve an even more resistant strain. In fact, delta has already bifurcated into two sub-strains. Here is the whole story.

Four *significant* coronavirus variants have been detected this year, all of which have evolved from the original Wuhan strain. These include the U.K. variant (α

variant, or B.1.1.7), the South American variant (β variant, or B.1.351), the Brazil variant (γ variant, or P.1), and a new India variant ("Delta" variant, or B.1.617.2) [Refs. 29 & 30]. To understand why this is so, let's do an approximate back-of-the-envelope calculation. Recall from Reference 1 that a nucleotide of an RNA virus (like coronavirus) has a probability of 10⁻⁴ of being copied incorrectly during viral replication. These are called *point mutations*, and they are by far the most common type of mutation. The "S" protein is encoded by about 5,000 RNA nucleotides. Therefore, the probability for a point mutation in the "S" coding region of the viral RNA (which will be called a "gene" here) is the product of these last two figures, or about 0.5 per "S" gene replication.

Most mutations, however, are either neutral (about half), or harmful (perhaps 99.9% of the remaining half) to the virus [Ref. 31] . Therefore, at the genome level, only about five in 10,000 mutations (half of one in 1,000 mutations) are beneficial to the virus. If infection starts from only one coronavirus infecting a single cell, then the probability of a beneficial mutation occurring after the first replication would be (0.5) (5x10⁻⁴) = $2.5x10^{-4}$.

Once an infection has been established by a strain possessing improved viability, it will be assumed that this strain becomes genetically *fixed* in the infected individual as it out-competes less-fit mutants that may arise [Refs. 31 & 32]. But 150 million people have been infected worldwide. Therefore, theoretically the number of point mutations beneficial to the virus might be about (2.5×10^{-4}) $(1.5 \times 10^{8}) = 3.75 \times 10^{4}$. However, single point mutations (although there really may be thousands of them) are usually not enough to create a significantly improved variant. However, point mutations can accumulate with time. Even if the number of significant mutations per gene (over time) beneficial to the virus was 10,000 times smaller than the rate of beneficial mutations per gene per replication, the number of *significant* variants would still be 3.75 from the start of the pandemic to the present time (April 30, 2021).

Is it any wonder that four major pathogenic variants (which will be called *strains* here) have been identified so far! The new fourth mutant, dubbed the "double mutant," has sharply increased the number of COVID-19 cases observed in India [Ref. 30]. As one virologist working in India noted, "We let our guard down when the variants were appearing. It was the worst time to do so" [Ref. 30].

We may be making a similar mistake in the U.S. as more and more states lower their masks and we plan to greatly increase legal immigration by an order

Figure 3 — Surface of N95 mask material. The synthetic fibers look like randomly oriented glassy rods as light from the point source penetrates the mesh. Note the scale. Although the smallest droplets of saliva (10 μ in diameter) can penetrate the surface of such a barrier, they will soon be entangled in the mesh. Micrographs of this kind have very little depth of field, so most of the fibers within this ply are out of focus. The mask as a whole is three-ply. The synthetic fibers can also be electrets; polymer fibers that can electrostatically trap even the smallest particles via their permanent electrostatic fields created by heating the polymer in the presence of a powerful external electrostatic field and then cooling it to room temperature. This micrograph by author was an 8 sec. exposure on Kodak Ultramax ISO 400 speed film at an objective x eyepiece magnification of 3 x 10.

of magnitude, while 70,000 cases of the U.K. variant were present in the U.S. [Ref. 33] and spreading fast as of April 14, 2021. As the U.S. imports more people, we also import the variants that they may be carrying as well. The pandemic is *not* over! As of April 29, 2021, the global coronavirus cases per day have reached a new high of 824,304 [Ref. 34]. Are we at the top of this last global peak? Unknown! Will there be even bigger peaks in the future? Unknown! When will the pandemic end? Unknown! When successive infection peaks (called *local maxima*) begin to shrink in size, that will be a mathematical indication that the pandemic is beginning to wind down.

The current vaccines are thought to give the recipient some protection against the major variants (strains). But that level of protection is uncertain and will depend on the exact nature of the mutations that have occurred in the structure of variant "S" proteins. To completely understand the situation, consider the Influenza A virus. Immunity to this virus can be strain-specific (as it can be for the coronavirus). Significant strains (e.g. strains SW30 and SW31 of the "swine flu") can differ by as little as two or three nucleotides out of 18, 000 (or 0.01%), although it usually takes more than that [Ref. 18].

The continuing appearance of new strains arises from antigenic drift as described in Reference 1. Typically, like the current coronavirus, two or three (*prominent*) strains of influenza A are circulating in the population at any one time. As people travel, the strains spread around the globe as they arise. These strains are *partially resistant* to the host immunity induced by previous infections or vaccination [Ref. 18]. As a strain is passed from person to person, mutations can accumulate due to natural immune selection (hence, India's "double mutant" coronavirus). After a few years of drift, a new *resistant* strain can arise.

Influenza A, however, has an added trick. The outer envelope of influenza A contains two proteins that act as antigens, call them H (*hemagglutinin* — does that name sound familiar?) and N (neuraminidase). At present, due to antigenic drift, there are 15 kinds of H proteins and nine kinds of N proteins known. Therefore, mathematically, there are $15 \ge 9 = 135$ types of influenza A at present. Not all of these are compatible with human infection and epidemic spread [Ref. 18]. Only three kinds of H (called H1, H2 and H3) and two kinds of N (called N1 and N2) are important for human disease. Unfortunately for humanity, the gene segments of influenza A have an unpleasant habit of *reassorting* in their animal and human hosts by a process called antigenic shift. Each combination of HX and NY is called a *subtype*, where X and Y are integers. Immunity to influenza A is definitely subtype dependent, where each subtype can potentially cause a pandemic.

Typically, devastating influenza A pandemics occur about once every 10 to 20 years. Therefore, the globe has seen H1N1 (1918 "swine flu" pandemic), H2N2 (epidemic of 1957), H3N2 (1968), and again H1N1 (another strain of the H1N1 subtype called the Russian Flu that appeared in northern China in 1977) [Ref. 18]. Remarkably, all 135 H and N combinations have been found somewhere in the animal kingdom! *Because of antigenic drift and antigenic shift, annual revaccination is required for influenza*.

Undoubtedly, more significant coronavirus variants (strains), and possibly coronavirus subtypes (SARS, MERS, COVID-19), will evolve in the future. Therefore, it would not be surprising if an annual coronavirus shot is required to maintain peak immunity, just as it is for the flu. This is another reason for the development of a "one-shot" coronavirus vaccine of the Johnson & Johnson type. Perhaps the coronavirus and flu vaccinations will be combined into a single convenient shot in the future, the way measles, mumps and rubella are combined today. An mRNA influenza vaccine has already been developed [Ref. 4]. This will fit in nicely with the storage and delivery requirements of the most popular coronavirus vaccines used in the U.S. today.

Rumor #10: The coronavirus vaccine is associated with prion disease ("mad cow disease"). [Ref. 4]

Response #10: This particularly pernicious piece of misinformation appeared on social media [Refs. 4 & 35]. Not only have no such cases been reported after almost 200,000 mRNA vaccinations in the U.S., nor by any other country using a variety of strategies invented by companies all over the globe, but there is scientific evidence against such claims.

Recall from Reference 1 that a prion is a misfolded protein that can be used as a template to misfold other proteins similar to itself. Protein similarity is very important. How important? Hemoglobin is composed of four molecules: two molecules of α hemoglobin with 141 residues (amino acids, [Ref. 1]), and two molecules of β hemoglobin with 146 residues [Ref. 9 & 36]. So, by residue sequence, the two types of hemoglobin proteins are 96.5% similar. Yet neither of these proteins normally interferes with the other. By contrast, the human proteins share only 0.6% of their residue sequence with "S" [Ref. 4]. So there is really no chance of template misfolding. The rumor may have had its early origin in a newspaper article from 2001 [Ref. 37] in which some vaccines were made with serum or gelatin obtained from cows in England. At that time, cattle in the U.K. were experiencing an outbreak of "mad cow disease." No coronavirus vaccine used in the U.S. employs animal serums.

Rumor #11: The "S" protein might affect women's fertility. [Ref. 4]

Response #11: Once again, this rumor is completely false [Ref. 39]. Confusion arose when a false report appeared on social media. The report claimed that the "S" protein was the same as another spike protein called syncitin-1 that is involved in the growth and attachment of the placenta during pregnancy. The false report claimed that the vaccine would cause a woman's body to fight this other spike protein and affect her fertility. The amino acid residue similarity between the two spike proteins is only 1.3% [Ref. 4]. The two proteins are really quite different and have nothing to do with each other.

Rumor #12: "We don't know if the vaccine can stop you from spreading the virus" [Ref. 39]

Response #12: This statement, or some variation of it, continues to circulate. The most authoritative source that the author could find for this problematic concern has been cited. The difficulty is understanding the "carrier" mechanism. The purpose of a vaccine is to *stop replication* of the wild-type virus in a human host. Without replication, a virus cannot be passed on to others by, say, a sneeze.

A vaccine is *not* an analgesic (pain killer) intended to reduce symptoms (as does aspirin or ibuprofen) while the wild-type infection runs its course and can be spread to others. Once a person is vaccinated, *antibodies* begin to develop. For example, large amounts of the antibody *IgG* are produced by the human body two weeks after vaccination [Ref. 18]. Hence, the waiting period after vaccination to reach full immunity. Antibodies then circulate widely within the body through the bloodstream. Their high concentration, and the anamnestic effect (i.e., the further boosting of antibody production) that occurs after secondary exposure gives a virion little chance of survival. Antibodies in the blood bind to the virions, surround them, and neutralize them. When visualized by fluorescence microscopy, such neutralized assemblies look like irregular clumps [Ref. 9].

So, how does transmission of the virion take place? Furthermore, if vaccination doesn't stop the spread of a viral infection, then how was smallpox eradicated? Vaccination doesn't just turn the vaccinated into walking asymptomatic carriers; it actually stops the person-to-person spread of disease. Eventually, after enough people are vaccinated, herd immunity is established and the disease dies out. Those who weren't vaccinated are safe because no one can infect them. Until there is scientific evidence to the contrary, this author must consider the above quote to be a "rumor," in spite of its source. Convincing evidence would be a demonstration that a population of successfully vaccinated individuals (as judged by an adequate antibody titer, maintained against circulating strains, and a "-" viral titer two or three weeks after their second vaccination) later possessed a wild-type *viral* titer high enough for transmission – *unlikely*!

Rumor #13: The coronavirus vaccine changes your DNA. [Ref. 38]

Response #13: The coronavirus vaccine cannot change your DNA because it contains no retroviruses, reverse transcriptase or even DNA. It operates in the usual direction of the Central Dogma (blue path of Figure 1). That is the natural direction of information flow in your body: mRNA \rightarrow proteins.

Rumor #14: Masks don't work because a virion is much smaller than the spacing between mask fibers. The scale is totally different. [Ref. 40]

Response #14: It is true that the mean diameter of a virion lies in the $0.12 - 0.16 \mu$ range, as discussed in Reference 1 (see Figure 1 of Reference 1). It is also true that the spacing in the weave of various fabrics is three orders of magnitude larger. However, virions are not transmitted as free particles, but rather in droplets of saliva and mucus. Otherwise, they would be very quickly destroyed by dehydration, oxygen (O₂), heat, sunlight, and even air pollution (ozone; O₃).

Recall from the earlier discussion how much care is required to keep micelles intact in a vaccine (a micelle is similar to a coronavirus envelope). Typically, infectious droplets lie in the 10 - 1,000 microns range [Ref. 41], with a geometric mean of about 100 microns (i.e., a tenth of a mm, or about $1/250^{\text{th}}$ of an inch). Therefore, most particles jettisoned in the forward direction during a sneeze will be trapped by mask fibers (Figure 3).

Of course, a mask is not hermetically sealed to your face, so a small amount of "blow by" will occur around the mask perimeter. However, one has to ask how dangerous an escape is that moves perpendicular, or to the rear, of the direction that the source is facing.

It's difficult to understand public resistance to masks. Of course, you don't need to wear a mask if you are jogging alone in the desert, or are safely ensconced in the privacy of your car. But people should ask themselves if they would allow a surgeon to operate on them without a mask, or a dentist to extract a tooth without some kind of facial barrier? It should always be remembered that vaccination is not a substitute for wearing a mask. No vaccine in 100% effective and, as discussed earlier, strain and subtypes do exist that might evade the defenses of a vaccine. Vaccination and masks should be thought of as *working together* to lower a person's overall risk of infection. Even though fully vaccinated, the author wears a double mask in high-risk situations: a cone mask under a flexible N95 mask that loops over the ears.

Beyond these sometimes ridiculous, and sometimes vitriolic, rumors there is one other important — and tragic — belief that needs to be discussed. One-fifth of all Black Americans say they have been treated unfairly because of race when receiving health care. Furthermore, 50% of Black Americans and 62% of Hispanic Americans say they don't trust their local hospital [Refs. 4 & 42]. These figures underscore the difficulty that public health officials have trying to gain people's confidence in a national vaccination effort. We are simply going to have to do a better job of reaching out to minorities and other groups expressing concerns about the vaccinations if we expect to vaccinate the entire U.S. population and establish herd immunity.

Corporate safety engineers have an important role to play in this regard as vaccinations become more routine and are administered to employees at large companies [Ref. 43]. As the most broadly educated of corporate personnel, it is our job to supply accurate information to supervisors and employees who have been frightened into hesitation by irresponsible rumors. In the end, however, mandatory vaccination may be required in the workplace, schools, churches, etc. It is important to note that mandatory vaccination has been successfully carried out previously, even in the U.S. [Ref. 43].

⁴ The American administration has recently (May 20, 2021), and prudently, extended its border crossing restrictions. It is a fluid situation, but the border between the U.S. and its neighbors to the north and south is "restricted" through at least June 21, 2021. Only trade and essential travel will be allowed until then [Ref. 51].

Once a rumor starts, it often spreads via a chain reaction, much like the coronavirus itself. If each person who believes a rumor convinces, even fractionally, more than one other person on average, an isolated falsehood can become a popular belief. Indeed, such 'beliefs' can cause the needless death of thousands of people.

Why do people start such rumors? Assuming the originator is sane, which may or may not be true, there can be many reasons. Anger at a previous employer, the misunderstanding of facts, petty political rivalries, or the desire for attention are just a few human motivations.

Conclusion

In the U.S., the confluence of resistance to vaccination [Ref. 44], excessive and uncontrolled immigration⁴, new coronavirus strains [Ref. 27], and resistance to basic public health measures such as wearing masks and maintaining social distancing, do not paint an auspicious picture for the coming 2021/2022 cold and flu season [Refs. 6, 45 & 47].

Inaccurate rumors concerning vaccination just frighten the public and exacerbate the problem. The internet is a wonderful thing, and by its "open" nature, it is resistant to government censorship. However, there is also a downside — namely, the publication of irresponsible or false information. There is an old Asian proverb, "You cannot un-ring a bell!" Once a rumor starts, it often spreads via a chain reaction, much like the coronavirus itself. If each person who believes a rumor convinces, even fractionally, more than one other person on average, an isolated falsehood can become a popular belief. Indeed, such "beliefs" can cause the needless death of thousands of people.

Why do people believe, and repeat, "eye-popping" falsehoods, rich in accusations, but unsupported by experiments, facts, mathematics, or authoritative references? Several factors are probably involved, and the psychological literature is full of explanations. This author will only confine himself to a couple of historical references since the phenomenon is not new. Julius Caesar, himself an historian of the first rank, provides some insight into this ancient human fault: "We are both ready to believe the things we want to believe, and also hope other people feel what we feel ourselves" [Ref. 46]. Beyond this, it seems that people would rather believe an interesting fabrication than the plain unvarnished truth.

Apparently, for many people, it is easier to believe that a major pharmaceutical company ("big pharma") is cooperating in a government scheme that could "lead to your death" [Ref. 5] than it is to believe in an electrostatically accelerated spherical gold micro-bullet that can inject foreign genetic material into a single microscopic cell (and that was the "old" technology)! The first sounds like an *interesting* conspiracy theory that someone may *wish* to believe; the latter may sound like a science fiction fantasy.

Modern science is what the popular imagination considers *unbelievable*! To conclude, the eminent historians Will and Ariel Durant summed up the current situation nicely in "The Age of Reason Begins," volume seven of their encyclopedic *Story of Civilization*" [Ref. 48]:

"To the poor in body and mind superstition is a treasured element in the poetry of life."

Stay well!

About the Author

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