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# **Journal of System Safety**





## The Delta Variant

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#### Keywords

COVID-19, mRNA vaccines, S-protein, binding site,  $\delta$ -variant, rumors

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Received: 05-Mar-2022 Accepted: 06-Aug-2022 Online: 04-Oct-2022

#### Cite As:

Zito R. The Delta Variant. Journal of System Safety. 2022;57(3):7-34. https://doi.org/10.56094/is s.v57i3.204

### **ABSTRACT**

Nothing is harder than to realize when you are living through history. For most of us, each day is pretty much like another. There is nothing historically remarkable about that. Occasionally, however, our lives are punctuated by events, both natural and man-made, that are apocalyptic and often (but not always) beyond our control - natural disasters, war, pestilence, and famine. These are the events that the historian must recognize. At this time, it is the COVID-19 pandemic that demands to be recorded by "his-story" so that posterity will know what we did right, and what we did wrong. This author has taken up the challenge of producing accurate, unbiased, comprehensive, technical annals of the global coronavirus pandemic that began in 2019. "The Delta Variant" is the third publication in this series. We are now near the end of the third year of the pandemic (summer/fall 2021). As predicted by this author, it has been a draconian year. Last year's peak in the number of active cases was not a global maximum for the pandemic in the U.S., since this year the number of active cases has already surpassed it. Without knowing where the global maximum lies, no accurate predictions can be made about the magnitude and duration of this modern plague. The "Delta Variant" (δ-variant) of COVID-19 has greatly complicated efforts to combat the virus. The "anti-vaxxer" movement, uncontrolled migration of people into and within the U.S., and the relaxation of safety measures during the late spring and early summer in the U.S. also contributed difficulties. All of these problems were foreseen by the author and were discussed in the second paper ("Vaccine Safety") of this series on the COVID pandemic. However, our biggest problem in the U.S. was an over confidence born of a natural summertime trough in the daily infection rate. We wanted to believe the infection was past, so we ignored the experience of India, and our administrators fueled our hopes with their words and actions. We believed because we wanted to believe - except for this author. So, what went wrong? What is a  $\delta$ -variant, and why is it so dangerous? That will be the topic of this publication.

### INTRODUCTION

There are so many places where one could begin describing this year's events that it is difficult to choose one. Nevertheless, there is only one terrible ending – the devastating number of new infections this year. So, perhaps the author should tell the  $\delta$  virus

story backwards. Figure 1 shows the number of active cases since the pandemic began.

At this point in time, it is impossible to know what type of statistical model (Gaussian, Rayleigh, Weibull, something else?) to apply to the global (long-term) data set because a global maximum (for the entire data set) has not yet been reached. However, short term predictions based on extrapolation of linear and quintic polynomial trends in the available data

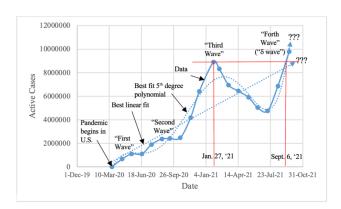


Figure 1: Active cases of COVID in U.S. versus date. From Worldometer, (https://www.worldometer.info) Sept. 28, 2021. Linear and quintic polynomials are the best trend models for the data curve.

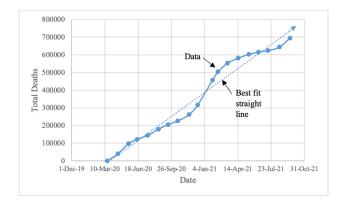
(capturing seasonal trends, behavioral trends, technological trends, etc.) suggest that the number of active cases will continue to rise after Sept. 19, 2021. A series of peaks with decreasing amplitude (active cases vs. time) will be needed before the U.S. can be reasonably confident that the pandemic is waning. And that may take a few years. Once a global maximum has been established after a time tmax from the beginning of the pandemic, it will take another time interval tmax after the maximum before an approximate model can be adopted for active cases. Furthermore, it will take a time interval 2tmax after the maximum before that model can be refined to a reasonably accurate form. Even if this winter's local peak were the global maximum we are all looking for, it will still be 2 more years before approximate projections for active cases can be made. Furthermore, accurate projections will not be available for at least 4 years (Zito, 2020a). The outlook for total deaths is just as discouraging (Figure 2). As of Sept. 19, 2021, it looks like a simple linear increase with no horizontal plateau in sight! Globally, the outlook for daily deaths is considerably brighter due to ongoing vaccination and the use of postinfection therapeutic agents. These statistics and drugs will be covered in detail in another publication of this series.

At this point one might reasonably ask, "How did the author know that this outbreak would happen given that the authorities, including health care authorities, were so confident that an end was near?" The answer is that the opinion of the authorities, although important, does not constitute proof by itself. Only mathematics, and especially experimental evidence, are the arbiters of truth. In this case, all the experimental evidence from the  $\delta$ -variant outbreak in India (Li, Agarwal, 2021) suggested that we were making a *huge* mistake. It must always be remembered that the author's job is to tell the truth. Although the authorities are usually right, it is *not* the author's job to make excuses for them when they are wrong! Even if it's the CDC!

# S-PROTEIN MUTATIONS AND THE $\delta$ -VARIANT

Starting in this section, it would be best for the reader to examine the first two coronavirus papers in this series (Zito. 2020b, 2021). That background information will be invaluable, and it cannot all be repeated here other than to make a few brief statements intended more to reawaken the memory than to be pedagogic.

In Figure 1 of the "COVID-19" paper (Zito, 2020b), the "S-protein (the binding protein) of the coronavirus envelope was depicted schematically as a slender triangular needle. Actually, the S-protein looks more like the "club" in Figure 3 below, and the scale of this cartoon is now 100x smaller than that of Figure 1 in the "COVID-19" paper (Zito, 2020b).<sup>1</sup> Each S-protein is composed of two protein subunits, S1 and S2, each a complete protein in its own right. The two proteins stick together because the amino acid residues (building blocks) that compose these proteins (Zito, 2020b) poses chemically active side chains. These side chains can interact with one another through disulfide bonds (from a sulfur atom in one subunit to a sulfur atom in its neighbor subunit), as well as hydrogen bonding, Van der Walls forces, and other types of non-permanent interactions.



**Figure 2: Total Deaths versus Date for the U.S.** There is no indication of any negative curvature as of Sept. 16, 2021. The author's sobering predictions for this year from "Vaccine Safety" (Zito, 2021) have come true.

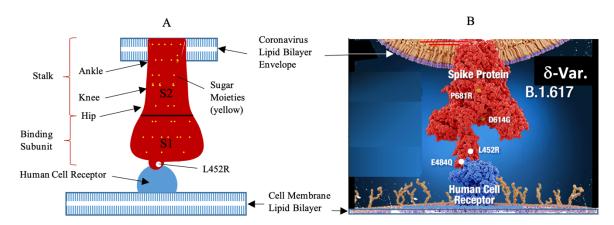


Figure 3: A) Cartoon of a coronavirus spike protein (red) interacting with a cellular binding site, or human cell receptor (blue sphere). The S1 subunit contains the binding site, while S2 is used to support S1 above the viral envelope. The subunit structure of a protein is called its quaternary structure. The yellow dots are sugar moieties while the white dot marks the location of an important amino acid mutation site. B) Computer simulation of a spike protein interacting with a cellular binding site (modified by author from Ayass Biosciences, 2021). Individual atoms can be discerned. The view is about 1000 Å (or  $0.1 \mu$ ) across. Several  $\delta$ -variant (B.1.617) amino acid mutation sites are shown (where L = Leu = Leucine, R = Arg = Arginine, P = Pro = Proline, D = Asp = Aspartic Acid, G = Gly = Glycine, E = Glu = Glutamic Acid, Q = Gln = Glutamine). The things that look like red "weeds" on the cell surface are cellular proteins. The structure of all of these proteins is based on X-ray diffraction studies of these complex biological molecules.

Recall from "Vaccine Safety" (Zito, 2021) that hemoglobin has four such subunits.

The tip of the S1 subunit is responsible for binding, whereas S2 is called a stalk and is used for support. The stalk is broken up, imaginatively, into an ankle, knee, and hip. The ankle anchors the S-protein in the virus's semi-fluid lipid bilayer envelope. And, as the name "ankle" might suggest, some S-protein movement can take place (like the tubes, or spines, on the back of a sea urchin). In the first publication of this series (Zito, 2020b) it was noted that the spike protein (S-protein) was a glycoprotein, meaning that the S-protein has sugar moieties (molecular fragments) attached. These are the yellow spots in the cartoon of Figure 3A. The reason for this can now be explained. Sugar is not normally recognized by the immune system as "not self" because the body needs sugar. So, the dusting of sugar fragments over the surface of the S-protein is an insidious disguise, or cloaking device, to make the coronavirus invisible to antibodies and white blood cells (much more will be said about this later)! Fortunately, the disguise is imperfect, as we will see!

Next, we must increase our magnification by another factor of 10 and focus in on the structure of the S1 subunit. A protein, when first created, is nothing more than a string of various amino acids chemically linked together by polypeptide bonds like

a string of pearls, each with a letter on it that represents a particular amino acid (and there are 20 types) (Zito, 2020b). This linear sequence of amino acids is called the primary structure of a protein. After creation, the protein folds into its secondary (local) and tertiary (long range) structure, which may look, for example, like the S1 protein in Figure 3. Folding occurs for the same reasons (and involves the same types of bonds) that make subunits stick together.<sup>2</sup>

Sometimes, however, a mutation occurs in the primary amino acid sequence, for reasons that will be explained in the next section. When that happens, one letter (label) can change to another. Therefore, to specify a particular mutation it is necessary to specify the original letter, the location of the mutation from the beginning of the amino acid sequence, and the new mutated letter. Hence, L452R means that leucine (denoted by L), the 452<sup>nd</sup> amino acid in the S1 subunit, has changed to the amino acid arginine (denoted by "R"). Similarly, E484Q means that glutamic acid (E), the 484<sup>th</sup> amino acid, has changed to glutamine (Q). To understand why such changes are important, it is necessary to look at the structure of these amino acids (Figure 4).

Figure 4 shows the molecular structure of leucine and arginine. It can be seen that arginine has a much larger side chain than leucine. In fact, arginine is the largest (dimensionally) of all 20 amino acids in its

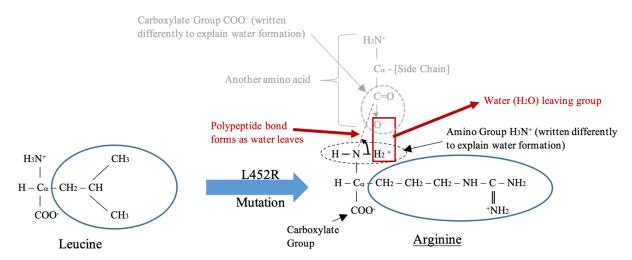


Figure 4: The structure of the amino acids in the  $\delta$  L452R mutation (leucine to arginine). Side chains are encircled in solid blue lines and are attached to what is called the  $\alpha$ -carbon atom of each amino acid. At neutral (~physiological) pH, the carboxylate group will have lost a proton in solution (cellular cytoplasm), and the amino group will have gained a proton from solution. The net result is a structure called a zwitterion, and it is the usual form in which an amino acid is displayed. A Polypeptide bond (shown only for arginine as a dashed red line) forms when the amino group (encircled in dashed black) of one amino acid (arginine) reacts with the carboxylate group (encircled in dashed gray) of another amino acid (in gray) (Mathews, van Holde, 1996). A water molecule is created as a leaving group (a waste product) (boxed in red). When many such reactions (polypeptide bonds) form in sequence, a protein (or polypeptide) is formed. The "backbone" of the protein can be written as  $(-C_{\alpha}$ -N-C-)<sub>n</sub>, and each  $C_{\alpha}$  is associated with a particular side chain structure that is unique to each type of amino acid. This is how the primary structure of a protein polymer is formed. The field of view is now 100 Å across. —At this point the reader should ask, "If the process of polypeptide formation is so complex, how can one amino acid be clipped out of a protein chain and replaced by another?" That will be explained in the next section.

conformation of maximum extent (i.e., when the molecule is all stretched out). Perhaps the steric hindrance (stand-off distance) imposed by this side chain keeps antibodies from binding to this critical contact point of the S1 subunit of the S-protein (see Figure 3). The E484Q mutation is similar, but glutamine (Q) is a smaller molecule than arginine (it looks just like R except that one -CH<sub>2</sub>- moiety is missing in the side chain), and that may explain why this mutation is less important. L452R has turned out to be one of the two most significant mutations that makes the  $\delta$ -variant such a "super-strain". It is worth noting that both L452R and E484Q occur along the edge of the binding domain (area of the S-protein where it makes contact with the cellular binding site - blue sphere in Figure 3) and not in the binding domain. In this way the viral S-protein can still bind to a cell, but it can keep large antibody molecules from binding to, and covering, the binding domain. A virus whose binding domain is protected from antibody attack by further encircling bulky mutations might out-compete one that is not so protected, thereby favoring the generation of resistant strains! So, what can be done to fight it? A new vaccine (a  $\delta$ 

specific booster) needs to be developed. It induces the human immune system to produce an S-protein with the L452R mutation in place. When antibodies are developed against this new (mutated) S-protein, assuming the steric hindrance model is correct, a pocket will be present in the new antibody molecules to accommodate the arginine side chain and allow intimate bonding with the  $\delta$  S-protein. Once the binding domain is capped or blocked by an antibody, an invading coronavirus is neutralized! It is for this reason that a  $\delta$  specific booster is needed. It is of central importance to understand that although the current boosters are NOT  $\delta$  specific, they do boost the waning (weakening) immunity of the original vaccines as a function of time (Neergaard, 2021). Because of the limited advantage of a booster based on the original vaccine, experts at the CDC initially decided to scale down its distribution to the immunity-compromised and those over 65.

The  $\delta$ -variant possesses another important S1 mutation (hence, the appellation "Double Mutant") over its parent called  $\Delta 157\text{-}158$  (not visible in Figure 3). The capital  $\Delta$  (delta) stands for "deletion", while 157-158 stands for the position of the deleted amino

acids from the beginning of the primary chain. These deletions can change the folding of the S1 protein and, therefore, its shape. It's just one more factor that prevents antibodies tuned to the classical COVID strains (Wuhan and  $\alpha$ ) from successfully binding to the  $\delta$ -variant S1 protein. Again, this underscores the need for a  $\delta$  specific booster. Exactly how, mechanically, amino acid deletions, and the previously discussed substitutions, take place will be the topic of the next section.

Eventually, if a  $\delta$  specific booster is not widely distributed, the successful  $\delta$ -strain will continue to mutate further and further out of range of the original two-shot series (it has already bifurcated into B.1.617.1 and B.1.617.2). And, although further mutations may not be that harmful to someone who has received a  $\delta$  specific booster, the consequences for someone who skipped such a booster may be grim, and cumulative deaths (Figure 2) may continue to rise.

Like influenza, annual boosters for the latest coronavirus strains may become a necessary feature of the nation's vaccination program. Until recently (up until Oct. 2021) the prevailing wisdom was to separate any flu and COVID vaccinations by at least one month, and to take the current booster no sooner than 6 to 8 months after the initial series of two injections. However, because the original coronavirus series entered the market so late in the cold and flu season, many people are currently out of synchronization with nature's natural infection cycles.

It may be time to start thinking about migrating one's vaccination schedule so that immunization for both diseases takes place prior to the onset of the cold and flu season; say late August for the current flu vaccine and late September for any coronavirus booster. Although, as of Oct. 2021, many people are taking both shots close together in time, or even simultaneously, since the side effects of the flu vaccine are quite mild. The current booster can be harsher. Typically, for the first 12 hours after vaccination, all you get is tired and a sore arm. Then, for the next 5 hours you might get chills, headache, joint aches, and perhaps a slight fever. Finally, recovery occurs in the last 7 hours. In summary, full recovery can take about a day. Consequently, for vaccines other than flu, the one-month rule should be observed. Furthermore, as discussed in "Vaccine Safety" (Zito, 2021), a time may come in the near

future when an mRNA flu vaccination will be combined with an mRNA coronavirus vaccine. When that happens, people who have successfully modified their vaccination schedule will be in an ideal position to replace the vaccinations for the two diseases with a single "combo" shot. It is unfortunate that these issues have not been fully discussed in the media.

## mRNA, CODONS, tRNA, THE RIBOSOMAL PROTEIN WORKBENCH AND rRNA

This section will be primarily concerned with a detailed look at the translation process (Mathews, van Holde, 1996). Recall from the first report (Zito, 2020b) that the process of producing a protein from the RNA viral code is called translation. That is because the nucleotide language of RNA (with alphabet A, C, G, U) must be translated into the amino acid language of proteins (with alphabet A, R, N, D, C, Q, E, G, H, I, L, K, M, F, P, S, T, W, Y, V – each letter representing one of the 20 amino acids).

So, how is this translation accomplished? First of all, since the nucleotide code consists of only 4 letters, and the amino acid code consists of 20, a one-to-one correspondence between nucleotides and amino acids is impossible. What if two nucleotides corresponded to one amino acid, would that work? No, because two nucleotides can only produce 16 ordered pairs, at most. What about three? Yes, that will work because there are 4x4x4, or 64, possible ordered triplets (e.g., GCA refers to alanine while its reverse ACG refers to threonine - order counts). However, 64 is larger than 20, what about the extra triplets? Well, some amino acids are specified by more than one triplet of nucleotides, and some triplets are signals to start or stop making a protein string. Each triplet of the RNA nucleotide code that specifies an amino acid of a protein's primary structure, or a start/stop signal, is called a codon. The codon for leucine is CUA, but the codon for arginine is CGA! Therefore, a single genetic error (point mutation) that changes a U to a G is enough to direct the cellular protein machinery to replace a leucine with an arginine, thereby turning the old (Wuhan, α strain) S-protein into something that looks more like the new  $\delta$  strain protein.

What about the  $\Delta 157$ -158 mutation? How do you explain that? There are three ways to say STOP in the nucleotide language; UAA, UGA, and UAG. If, for example, the amino acid preceding 157 and 158 were serine (coded by UCA), and if a point

changed the middle C to an A, then the UCA codon would be changed to the UAA STOP codon. In that case, if amino acids 157 and 158 were at the end of a protein chain (for S they are not), they would simply be clipped off the end of the protein chain in the new  $(\delta)$  version of the S-protein during cellular manufacture (Zito, 2021). It is for all these reasons that the probability for a significant mutation in the second paper of this series (Zito, 2021) was set at ~ 2.5 x 10<sup>-8</sup> per year per infected person (~ the product of the probabilities for two point mutations).<sup>3</sup> Once the cell's protein manufacturing centers, called ribosomes, produce all the necessary proteins for the new δ-variant, the pieces self-assemble in the cell's cytoplasm to form new δ-virions that can infect other cells upon release. At this point the reader may say, "All this theory ties up a lot of loose ends from the previous publication, but what exactly do these ribosomes and related protein manufacturing tools look like?"

Figure 5A shows a molecular "stick-figure" (bond) model of the most important tool. It is called transfer RNA, or just tRNA (Anon.a, 2021). Recall from the first publication in this series (Zito, 2020b) that, in the beginning, life was based on RNA. There were no proteins – these came later in evolutionary time. Therefore, all the tools used to make proteins for more modern life forms had to be made of RNA. The tRNA in Figure 5 came from a yeast cell, not a human cell. Human tRNA is a more complex cruciform. However, the author's goal here is to elucidate principles, not obfuscating details.

The reader's first observation should be to note the hairpin turn at the bottom of the stick- figure model. This allows the originally linear strip of RNA to fold in upon itself and form the double helical structure shown below. It suggests that the DNA double helix may have evolved from a structure of this kind, except that RNA contains uracil (U) instead of the thymine (T) of DNA. However, U and T have a very similar molecular structure. In fact, they differ only by the replacement of a hydrogen atom in U with a -CH<sub>3</sub> group in T. It is easy to imagine that such a replacement could have taken place in Earth's early methane (CH<sub>4</sub>) rich atmosphere. Finally, if the strained, chemically reactive, bond at the hair-pin turn should snap due to heat or interaction with its chemical environment - voilà! You have DNA! The story of how cellular life on Earth evolved has been an interest of the author's since he was 15 years old and will be the subject of a future book.

For now, the reader only needs to note that at the site of the hair-pin turn, three open bonding sites are available that match the codons of viral RNA (vRNA). That is to say, the tRNA fits into the vRNA like a plug into a socket. Still more amazing is the fact that the open end of the tRNA double helix is capable of binding an amino acid! And each amino acid has its own type of tRNA. Therefore, tRNA acts like a "taxi", transporting free amino acids to the codons of a vRNA molecule that is trapped on a cellular ribosomal workbench where proteins will be manufactured. The operation of that workbench will be discussed next.

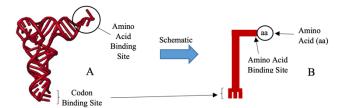
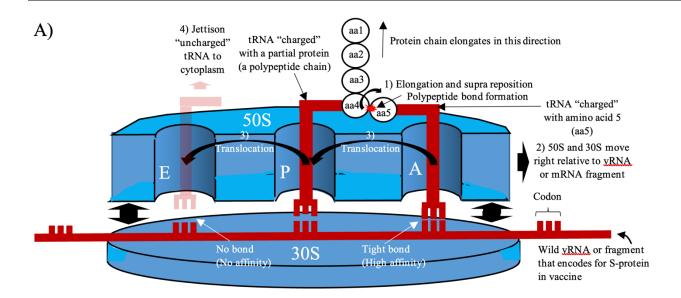


Figure 5: A) "Stick-figure" (bond) model of tRNA showing its codon plug (bottom) and its amino acid binding site (top) (Anon.a, 2021). B) Schematic representation of tRNA binding an amino acid.

Ribosomes are also made of RNA (called rRNA), and each comes in two pieces (subunits); one is called a 30S subunit (or "small" subunit) while the other is called a 50S subunit (or "large" subunit). The 30S and designations called sedimentation 50S are coefficients and refer to how these subunits separate after centrifugation. Together, the two subunits form complete ribosome, whose sedimentation coefficient is 70S, where the sum of the sedimentation coefficients of the parts is not necessarily equal to the sedimentation coefficient of the whole. In solution (cytoplasm) an equilibrium exists between the 30S and 50S subunits, and the 70S ribosome: 30S + 50S  $\leftrightarrow$  70S. Whenever a strand of mRNA (or vRNA) is trapped between the two subunits, protein production can begin. This biological "hammer (50S) and anvil (30S)" is diagramed in Figure 6.

The 50S subunit contains three cavities, or chambers. From right to left, the first is called "A" for "amino acid chamber". The second is "P" for "polypeptide chamber", and the third is called "E" for "exit chamber". It used to be thought that there were only two chambers, but it is now known that there are definitely three. The entire process of protein chain initiation, elongation, and release is very complex. However, the basic steps can be outlined easy enough.



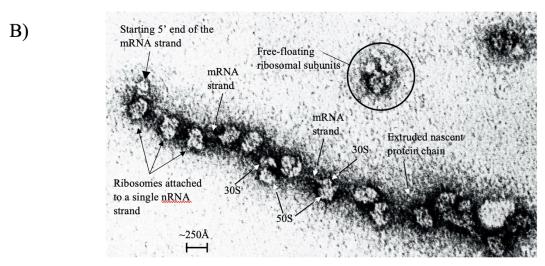


Figure 6: A) Schematic of the 70S ribosomal workbench showing the elongation of a protein chain. "aan" stands for "amino acid n" in a protein chain. This figure ties together Figures 4 and 5 of this publication with figures 1 and 6 of the first publication of this series (Zito, 2020b). Like moving missiles between silos, tRNA (either "charged" or "uncharged") can be moved between chambers A, P, and E. tRNA's can also enter or leave chambers. B) An astounding electron micrograph by Barbara Hamkalo (Mathews, van Holde, 1996), modified by the author, showing sixteen E. coli ribosomes translating a strip of mRNA from its starting end (called the 5' end for technical reasons). About 50 ribosomes can be attached to a single mRNA; a fact that will prove important for the calculations that will follow. All ribosomes are moving to the right as in A. Some ribosomes are floating free, sometimes individual subunits can be discerned. In one case an extruded nascent protein chain can be detected. Although the cartoon in A is not to be taken too literally, it is not too far from the literal truth either!

As the reader might have guessed, the initiation of protein manufacture is signaled by a START codon (AUG). After that, Figure 6 shows the crucial steps in polypeptide (protein) chain elongation. When chambers "P" and "A" are filled, two amino acids, one from the elongating protein chain, and one attached to a tRNA, are close enough to each other that a polypeptide bond can form as depicted in Figure 6A (Step 1).

Therefore, the ribosome acts like a catalyst facilitating bond formation. The entire chain is now transferred to the "A" chamber, and the tRNA in the "P" chamber is now uncharged (i.e., it has lost its polypeptide chain). If 50S and 30S momentarily lose their mutual grip on each other and move to the right one codon relative to the mRNA (or vRNA) (Step 2), two translocations occur (Step 3). That means the uncharged tRNA that is in the "P" chamber moves to

exit chamber "E", where it is eventually released into the cytoplasm too pick-up another amino acid (Step 4). And the tRNA, with its protein chain, that resides in chamber "A" moves to chamber "P". Empty chamber "A" now has a strong affinity for a new tRNA that will match the new codon. Termination and protein chain release occurs when one of the STOP codons is reached, as discussed above. This is how vRNA hijacks the cellular machinery to produce more viral proteins. It is also how vaccine RNA fragments induce the cell to produce the S-proteins that eventually produce the immune response. The vaccine RNA fragments, however, eventually wear out and are cleared from the body in a few hours. The same is *not* true for the complete viral RNA because the proteins that are produced self-assemble into new virions to continue the wild infection. Vaccination and the infection process will be discussed further in the next section, but first there is one detail that demands discussion and one curiosity.

Recall from the first publication in this series (Zito, 2020b), and from Figure 3A above, that the coronavirus S-protein is dusted with sugar to make it (at least partially) invisible to the human immune system. So, the S-protein is really a glycoprotein (or sugar-protein) and not just a pure protein. How does that happen? That is now easy to explain. Look at Figure 7. Arginine contains an -NH<sub>2</sub> group at the end of its side chain (where the "-" represents a bond), and that group can bind to a number of different sugars by simply forming a water molecule as shown in Figure 7. The process is called glycosylation. Normally, very few proteins manufactured by free floating ribosomes in the cytoplasm are glycosylated, and those that are, usually only have a single N-acetylglucosamine sugar ring added. But the ribosomes bound to the intracellular membrane called the endoplasmic reticulum (ER) are different (Alberts et al, 2002). The ER contains an enzyme called oligosaccharyl transferase that allows an entire block of connected sugar molecules (like the one depicted in Figure 7) to be transferred to the nitrogen atom of an amino acid side chain. Up to a point, the larger the block of sugar molecules, the better the S-protein camouflage. It is for this reason that the ER plays such an indispensable role in coronavirus replication (see Figure 4 of Zito, 2020b).

Finally, it is worth noting that neither tRNA nor rRNA are pure RNA. Each comes with protein attached. It is as if evolution is not satisfied with a pure RNA protein-making-micro-machine and is trying to develop a more versatile protein protein-making-micro-machine. Perhaps an all-protein protein-making-micro-machine will be the future of all life on Earth in another few billion years!

### **DEFINITIONS AND RUMORS**

Before beginning the calculations of the next section, a few definitions are necessary. Some of these precise definitions were devised by the author to clarify paradoxes that arise when a vaccine is not 100% effective. Most are forms of definitions from "Melloni's Illustrated Medical Dictionary" (Dox, 1979), a standard medical reference. Other definitions come directly from the U.S. Center for Disease Control (CDC). As will be demonstrated, a great deal of confusion, acrimony, and misery has been generated by misunderstanding vocabulary.

Infectious Agent = A microbe, such as a coronavirus particle, that is capable of replicating within a host. The existence of such an agent has been proved experimentally and will be taken as axiomatic.

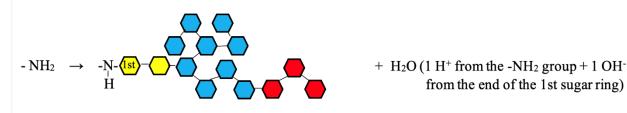


Figure 7: Forming a glycoprotein from a protein by reaction of 6-carbon (hexose) sugar rings with an amino acid side chain. Red rings are glucose, blue are manose, and yellow are N-acetylglucosamine sugars. The network of sugar rings is called an oligosaccharide, and it will contribute significantly to the steric hindrance that an antibody will encounter when trying to block the S-protein binding domain of a  $\delta$ -variant virion. Other amino acids (besides arginine) can also have a sugar network, most notably glutamine (Q) of the  $\delta$ -variant's E484Q mutation, and asparagine (the abundant amino acid found is asparagus), but not leucine! If, however, the S-proteins oligosaccharides becomes too ornate and bizarre, the immune system will recognize it as something foreign and can build an antibody to fit around it like a glove and bind to it. A  $\delta$  specific booster gives the human immune system an opportunity to adapt itself to the arginine and glutamine oligosaccharide networks. Just one more reason why it is so important!

*Infection* = A condition in which an *infectious agent* is actively replicating within a host.

Immune = A condition in which an infectious agent cannot replicate within a host. Note that the intersection of the set of all people with an infection induced by a specific infectious agent with the set of all people immune to that infectious agent is the null set.

Artificial Inoculation = The entry of a live attenuated infectious agent, a killed or inactivated infectious agent, a protein from the infectious agent, or even part of a protein from an infectious agent, into a host via controlled artificial means (injection, ingestion, subcutaneous administration, etc.).

Wild Inoculation = The uncontrolled entry of a viable "wild" (not attenuated) infectious agent from another host (via a sneeze, cough, contact with urine, stool, or epidermal eruptions, etc.).

Infectious = A condition in which the titer of infectious agents within a host is high enough to cause the wild inoculation of another host. Immune and infectious are mutually exclusive conditions by these definitions. (Note that external mechanical transport of an infectious agent by an immune intermediary to another host does not make the intermediary infectious by these definitions, since the agent was never replicating within the intermediary).

Fully Vaccinated = A host that has received all artificial inoculations of a series. See Figure 8.

Partially Vaccinated = A host that has not completed all artificial inoculations of a series (including any required boosters). See Figure 8.

Unvaccinated = A host that has not received any artificial inoculations of a series. See Figure 8.

Successful Vaccination = Antibody levels, induced by full vaccination (only), that are sufficient to render a host immune to any likely wild inoculation by a given subtype, strain, or sub-strain. Successful vaccination status is not necessarily lifelong and must be maintained by periodic artificial inoculations ("boosters"). See Figure 8.

Unsuccessful Vaccination = Antibody levels, induced by full vaccination (only), that are insufficient to render a host immune to any likely wild inoculation by a given subtype, strain, or sub-strain. Unsuccessfully vaccinated hosts do not include the partially vaccinated but are a subset of the fully vaccinated. See Figure 8.

Vaccinated = a nonspecific colloquial term that could mean, successfully vaccinated, unsuccessfully

vaccinated, fully vaccinated, partially vaccinated, or the union of any of these sets, depending on context.

Breakthrough Infection = Infection of a host fully vaccinated against one or more circulating strains (CDC.gov).

Vaccine Effectiveness (VE) = The percent (%) of cases below what would be expected of an unvaccinated population. All data are collected under typical field conditions; not the ideal controlled conditions of a clinical trial (CDC.gov). Therefore, any resistance to infection due to natural immunity (innate and wild acquired), behavior, age, etc. in the unvaccinated population has already been taken into account. VE is defined only in terms of observables.

Potentially Infectious Superset = the union of the unsuccessfully vaccinated, the partially vaccinated and the unvaccinated. People in the potential infectious superset are at risk of infection but, when infected, the symptoms of the unsuccessfully vaccinated and the partially vaccinated will generally be milder than those who are unvaccinated.

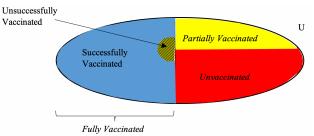


Figure 8: Venn diagram (Meyer, 1970) for a population (blue = safe, yellow and yellow shaded = at risk, red = unsafe). The intersection of any pair of mutually exclusive subsets is the empty (or null) set  $\emptyset$ , while the union of all mutually exclusive sets is the Universal Set (U) equal to the entire population. Furthermore,  $\{Fully\ Vaccinated\} = \{Successfully\ Vaccinated\} \cup \{Unsuccessfully\ Vaccinated\} \}$ Vaccinated}, {Successfully Vaccinated} ∩ {Unsuccessfully Vaccinated =  $\varnothing$ , {Potentially Infectious Superset} = {Unsuccessfully Vaccinated}  $\cup$  {Partially Vaccinated}  $\cup$ {Unvaccinated}, {Unsuccessfully Vaccinated} ∩ {Partially  $Vaccinated \} \cap \{Unvaccinated\} = \emptyset, and \{Potentially Infectious\}$ Superset}  $\cap$  {Successfully Vaccinated} =  $\emptyset$ . Finally, if # represents the number of elements (people) in a given set {...} then, for the Pfizer and Moderna COVID vaccines, #{Successfully Vaccinated} >> #{Unsuccessfully Vaccinated} for all strains from Wuhan to  $\delta$ (Halmos, 1960). Note that the notion of "successful" and "unsuccessful" vaccination has not been extended to the partially vaccinated because the VE is generally low and short lived.

With this ladder of precise definitions, each depending on a previous definition, we can begin to talk. First of all, if vaccines were 100% effective, full vaccination, successful vaccination, and immune

would all be synonymous terms, and the unsuccessfully vaccinated would not exist. However, as Table 1 shows, most common vaccines are *not* 100% effective.

In that case, the definitions above allow the reader to draw several conclusions. First of all, by definition, successfully vaccinated people are unlikely to develop an active infection or spread an infection to others because an infectious agent cannot replicate within these hosts to any significant extent. They are effectively immune. Basically, by the definitions above, the spread of disease is through those who are unsuccessfully vaccinated, partially vaccinated, or unvaccinated, because these are the sets that contain hosts who have insufficient antibody levels to prevent infection (disease) from any likely wild inoculation. Furthermore, breakthrough infections of the fully vaccinated are almost exclusively confined to unsuccessfully vaccinated people, and tend to be milder, involve less hospitalizations, and the period of time during which they are infectious is shorter compared to those who are unvaccinated. The same is true of partially vaccinated people, although little has been said about them in the literature.

The author was asked the following very practical question during his August 2021 live presentation, "How does one know if they have been successfully vaccinated against COVID?" To be assured of successful vaccination, the fully vaccinated must wait two weeks after their last artificial inoculation. Then an S-protein specific antibody titer test must show a level of antibodies high enough to assure effective immunity (numerically, a titer of 100%, or something close like 99%), while a virion test shows a negative result (indicating that the patient has no current asymptomatic active infection that is responsible for

high antibody levels). It goes without saying that antibody levels must be maintained (not allowed to expire) for any circulating strains to stay successfully vaccinated.<sup>5</sup> As a practical matter, if a patient has had a reaction to the required series of injections, including boosters, that is an indication that the patient's immune system has recognized the S-protein produced in cells after vaccination as "not-self" - an essential step for successful vaccination.

What if someone gets no reaction from vaccination? In that case, an S-protein specific antibody test is warranted. If the test is positive after 2 weeks, there is no obvious reason for concern, although a *titer test* would have been more informative. The lack of reaction may have been due to a previous contact with the coronavirus S-protein. But, if the test is negative, then a trip to one's primary care physician is warranted, as this may be an indication of some underlying problem. Such problems may include impaired immune response due to disease, prescription drugs, age, or other factors. There is even the remote possibility of a spoiled batch of vaccine (Paduano, 2021; Chuck, Kesslen, 2020).

A patient's physician is the best person to decide what the next step should be in the vaccination process. But, if an antibody titer is not too low, the attending physician may just suggest another inoculation (with the same composition and strength, or a booster). That has been the common practice recently in cases of both weak immune response and waning immunity (say, less than 60% below peak – a benchmark used by many physicians). Remember, just because you are in a state of unsuccessful vaccination does not mean that you must remain so. Furthermore, some people refuse to be vaccinated because they claim they are allergic to a particular vaccine's ingredients. In that case, switching to

**Table 1: Vaccine vs. Effectiveness.** The word "any" means all infections regardless of severity, whereas "severe" means only the most life-threatening cases. The Moderna vaccine is among the most effective vaccines. Strangely, none of these "imperfect" vaccines, other than that for COVID-19, currently excites even the slightest public passion.

DISEASE	VACCINE	<b>EFFECTIVENESS</b>	REFERENCE
Tuberculosis	BCG Vaccine	70% for children 5-15 yrs	Stulpin, 2019
	(Bacillus Calmette-Guérin)	~30% for adults	Katelaris et al, 2020
Cholera	OCV (Oral Cholera Vac.)	52% (any), 71% (severe)	Firdausi et al, 2018
Varicella (Shingles)	Varivax (1 dose)	82% (any), 100% (severe)	CDC.gov, Oct. 21, 2021
Varicella (Shingles)	Varivax (2 doses)	98% (any), 100% (severe)	CDC.gov, Oct. 21, 2021
COVID-19 (Wuhan, α)	Moderna (mRNA-1273)	~95% (any)	CDC.gov, Oct. 22, 2021
COVID-19 (δ)	Moderna (mRNA-1273)	~80% (any)	CDC.gov, Oct. 22, 2021
Smallpox (Variola)	ACAM2000	95%	CDC.gov, Nov. 11, 2021
Polio	IPV (2 doses)	90%	CDC.gov, Nov. 11, 2021
	(Inactivated Polio Vaccine)		
	IPV (3 doses)	99% → 100%	CDC.gov, Nov. 11, 2021

another type of vaccine with a different composition may help. Many are available (Zito, 2021). An allergist should be consulted.

A less rigid, less definition and logic driven, more analogue, way to understand infections and vaccination dynamics is in terms of antibody titers and infection probabilities as described by D. Bhattacharya, Chairman of the Department of Immunology at the University of Arizona, (Bhattacharya, 2021a). All available evidence to date (using the Moderna and Oxford-AstraZeneca vaccines) suggests that the higher the COVID antibody titer, the lower the probability of infection by a wild inoculation of given dose and strain (Gilbert et al., 2021; Chau, 2021). "Someone who mounted a robust immune response is less likely to get infected in the first place, less likely than an unvaccinated person to develop serious symptoms if they do get infected, and less likely to transmit.", (Bhattacharya, 2021b). When the antibody titer rises to a level that is sufficient to produce immunity against any likely wild inoculation by a given subtype, strain, or sub-strain, breakthrough infections, and therefore transmission, are unlikely. At that point the fully vaccinated host is successfully vaccinated. But what if a successfully vaccinated host receives a massive number of virions through some unusual incident (e.g., having a very sick child or spouse sneeze or cough in their face while not wearing masks). Then, will they get sick? Possibly, if they are that unlucky. However, as we will see, most wild inoculations are much smaller, therefore infection is unlikely. Similarly, some unsuccessfully vaccinated people, with low antibody titers, may escape a marginal wild inoculation. However, on the average the statistics in table 1 must be reproduced because, by definition, VE is measured under typical field conditions (see definitions above).

Finally, vaccination dynamics can be understood in terms of vaccine dose. Recall from "Vaccine Safety" (Zito, 2021) that each Pfizer dose contains 30 μg (3 x 10<sup>-8</sup> kg) of mRNA, while each Moderna dose contains 100 μg (10<sup>-7</sup> kg). Let's calculate how many molecules of mRNA are in each dose. As discussed in the first publication of this series (Zito, 2021), mRNA is basically made up of four building blocks, or nucleotides (hence, the N in RNA). These are adenine (or "A" with a molecular weight of 134 Daltons), cytosine (C, with a molecular weight of 111 Daltons), guanine (G, 150 Daltons), and uracil (U, 112

Daltons); where a Dalton is the rest mass of a proton, or  $1.67 \times 10^{-27}$  kg.

Therefore, assuming A, C, G, and U occur with equal frequency in the RNA coding for the S-protein, the average weight per nucleotide is 126.75 Daltons. But the nucleotides are not connected directly to one another in RNA. Instead, all of these nucleotides are connected to a "backbone" of alternating sugar and phosphate moieties (fragments) called phosphodiester linkage. And each nucleotide is associated with one sugar moiety and one phosphate - a "vertebra" of the backbone one might say. The sugar moiety is called ribose, hence the R in RNA (ribonucleic acid), with a molecular weight of 68 Daltons. The acidic (hence the A in RNA) phosphate moiety has a weight of 95 Daltons. Since the coding of the S-protein requires about 5000 nucleotides (Zito, 2021), the average weight of each mRNA fragment in the vaccine must be about (5000) (126.75 +68+95) = (5000) (289.75)  $\approx 1.45 \times 10^6$  Daltons, or 2.42 x 10<sup>-21</sup> kg. Therefore, the number of mRNA fragments in each Pfizer dose is about (3 x 10<sup>-8</sup> kg) /  $(2.42 \times 10^{-21} \text{ kg}) = 1.24 \times 10^{13} \text{ mRNA fragments},$ while each Moderna vaccine dose contains 4.13 x 10<sup>13</sup> fragments.

Well, that is certainly a lot of mRNA fragments, but how many S-proteins do these fragments produce? Each fragment is capable of producing about 50 proteins before it "wears-out"; assuming it is used only once after being fully loaded with ribosomes (Mathews, van Holde, 1996; also see Fig. 6B and its caption). Therefore, the human body will produce about 6.2 x 10<sup>14</sup> to 2.1 x 10<sup>15</sup> S-proteins, depending on which vaccine is used. Eventually, all of these S-proteins are neutralized and destroyed as a vaccinated individual rapidly recovers from the immunological challenge posed by a vaccine. Therefore, each S-protein is eventually captured by an antibody molecule generated by the host's immune system.

The S-protein is large, but so is the antibody. The antibody IgG (also known as  $\gamma$ -globulin, a name that may be familiar to some readers) has a molecular weight of 152,000 Daltons. If the antibody attack on an S-protein fails, then it will be assumed that the antibody is free to try again until successful attachment is achieved. In that case, the total number of antibody molecules produced must *at least* be equal to the number of vaccine-induced S-proteins. Realistically, the number of antibody molecules are probably many times greater. But, as a lower bound,

the antibody molecular titer must be up in the  $10^{15}$  range, or about 27 antibody molecules for each of the  $3.72 \times 10^{13}$  cells in the human body (Barth, 2017)!

Recall from the first publication in this series (Zito, 2020b), that the minimal infectious dose (MID) of virions needed for an active COVID infection in an unvaccinated host is in the 10<sup>2</sup> to 10<sup>4</sup> range. Therefore, the total number of antibodies produced about two weeks after vaccination probably exceeds this COVID MID by about 10<sup>11</sup> to 10<sup>13</sup> times, or one hundred billion to ten trillion times. When antibodies bind to an antigen (like an S-protein molecule or complete wild virus) one of two things can happen. Either the antigen is precipitated, or it is marked for destruction (digestion) by cells called Macrophages that move in for the kill (Mathews and van Holde, 1996).

All this may sound like a big advantage for the antibodies, and if this massive patrol could be maintained, immunity would be good from even a single vaccination. However, immunity from a single exposure is not long lived, as we know from Figure 3 of the first report (Zito, 2020b). The *second* vaccination convinces the body to maintain antibody levels while boosting them still further. While the *third* exposure (booster) not only continues boosting antibody levels but can convey  $\delta$ -variant specific immunity if the booster is so designed.

These feats are accomplished by Memory B-cells (created by the first inoculation), which when stimulated by the second (and third) vaccination, begin to divide producing more Memory B-cells, and more Effector B-cells, that then produce much longerlived immunity (from the excess memory cells) and higher antibody levels (excreted from effector B-cell surfaces). All this is a big plus for a booster! Worse still for the coronavirus is the fact that the antibody distribution after vaccination is not uniform throughout the body. For example, antibodies are 100 to 200 times more concentrated in lung tissue than in the tissues of the nasal passages (Bhattacharya, 2021a), giving another two orders of magnitude of protection to the lungs, the prime target of the coronavirus.

Tragically for humanity, the  $\delta$ -variant has learned by mutation to offset this last advantage by multiplying ~1000 times more in the lungs than in other tissues (Ayass Bioscience, 2021)! This reproductive proclivity, in addition to the previously described amino acid changes, is what makes  $\delta$  so dangerous! Nevertheless, given all these numbers,

sustaining viral replication seems unlikely, assuming the host has a normal immune response to the vaccine (and any boosters). It would take a wild inoculation many orders of magnitude above the MID to seriously challenge a successfully vaccinated individual. It is for this reason that Pfizer and Moderna have chosen mRNA doses in the 30 to 100 µg range for their vaccines. Still higher doses would have increased the risk of anaphylactic shock, which is already in the 1 to 10 cases per million vaccinated range (Zito, 2021). More is not always better!

The operation of the immune system and its many types of cells<sup>8</sup> and protein signals (e.g., interleukin-2, to be discussed in a future article) is one of the most fascinating stories in all of science, and it is unfortunate that the author cannot discuss it more deeply in this publication.<sup>9</sup> However, it is hoped that these transparent calculations help explain why  $\delta$  is so dangerous, why the vaccine contains the mRNA doses that it does, and gives the reader a more precise idea of what is meant by the descriptive terms sufficient antibody levels, successfully vaccinated, and unlikely.

In summary, regardless of whether you take the definition/axiomatic logic/set theory view, the titer/probability of infection view, or the direct antibody/virion calculation view, the basic story is the same; viz. breakthrough infections in successfully vaccinated people (the great majority of those who are fully vaccinated) are unlikely. Clinically, it is the small minority of people who were unsuccessfully vaccinated, the larger population of partially vaccinated people with limited and rapidly waning immunity, and most especially the much larger population of unvaccinated people (~90-97% of all those entering hospitals and medical centers) who are "the vast, vast majority" responsible for spreading the coronavirus to the levels that are observed in the U.S. today (Innes, 2021). Anything else you might have heard to the contrary, or read in the media, or seen on the television or the internet, or heard from radio talkshow hosts, is a rumor. The author hopes that any paradoxes concerning vaccination effectiveness and carrier status, that may have arisen due to imprecise language or different points of view, have been completely, and unambiguously, resolved to the satisfaction of all parties involved in this debate.

Now, a pernicious and often repeated rumor cited in the previous publication on "Vaccine Safety" (Zito, 2021) can be revisited. On May 4, 2021, the City and

County of San Francisco (CCSF) posted the following statement on their website (CCSF, 2021):

"We don't know if the vaccine can stop you from spreading the virus"

From the discussion and calculations above, it is clear that the purpose of a vaccine is to prevent viral replication by immunological destruction of infectious agents after a wild inoculation. It is unlikely that any successfully vaccinated individual, with a normal immune response to the vaccine, will spread the virus. Furthermore, the great majority of COVID fully vaccinated, who are challenged by a wild inoculation that would normally develop into an active infection in the unvaccinated, will also prove to be successfully vaccinated (19 out of 20 for the classical Wuhan and  $\alpha$  strains; see Table 1).

Finally, two hundred years of experience with modern vaccination techniques, starting in 1796 with Jenner's first use of Cowpox (as a mild analogue for smallpox) to covey immunity (Zito, 2020b), all suggests that the statement above by the CCSF is problematic. The smallpox vaccine is just about as effective as Moderna's mRNA-1273 (see Table 1). Nevertheless, wild (natural) smallpox no longer exists, although the vaccine is still stockpiled to this day because of the omnipresent risk of bioterrorism (another problem for safety engineers). The specter of wild smallpox was eliminated because the virus cannot replicate within people who are successfully vaccinated. Their antibody titer is too high! Therefore, they are unlikely to develop virion levels high enough to spread the disease.

Eventually, as more and more people are vaccinated, herd immunity is established. At that point, the number N of infected people must approach zero as time t approaches infinity, i.e.,  $N \rightarrow 0$  as  $t \rightarrow$ ∞ (Zito, 2021). Polio offers another example of disease eradication. As Table 1 shows, 3 doses of the vaccine approach 100% effectiveness. Consequently, Polio is almost non-existent in the U.S (except when introduced from abroad) because people who are successfully vaccinated against polio (essentially the same as the fully vaccinated in this case) are unlikely to spread the disease because, again, the virus cannot replicate within their bodies. In general, once herd immunity is established, there aren't enough susceptible hosts left in a population to maintain an infection chain, and the infection must die out! When that happens, even people in the potentially infectious superset are protected. That is how "the vaccine can stop you from spreading the *virus"!* As Oscar Wilde has said, "The truth is rarely pure and never simple." – The Importance of Being Earnest.

So, the naïve statement above by the CCSF is sending the wrong message. A very negative one at that! Normally, the author would not include anecdotal information in a report of this kind, but in this case, since all the facts are directly known to the author, the following tragic story shows how *some* people interpret statements like those of the CCSF.

The author has a colleague who is an ardent "antivaxxer", as is his wife. Both are educated people, neither would wear masks, practice social distancing, or vaccinate. Neither were old nor had any underlying conditions, except that the husband was allergic to airborn pollen. Then, given enough time and contact, it happened. The husband contracted COVID, was hospitalized, and was put on a ventilator, where he remained for some weeks with his life in the balance. His wife was understandably frightened, confused, and angry. It was all someone else's fault. It was the government's fault, it was the CDC's fault, it was Dr. Fauci's fault. She felt her husband's care wasn't good enough. It was the hospital's fault, the doctor's fault, the nurse's fault. Then, finally, she pointed to the author and made the following astounding accusation, "It's vaccinated people like you that are spreading this disease!"

That is how some people interpret ambiguous official statements like the one by the CCSF. The result is suspicion, confusion, fear, superstition, resistance to vaccination, wide-spread public anger against safety rules designed to keep the scourge from spreading, and hostility, threats, and violence against health care professionals (Hollingsworth, Schulte, 2021). Exactly what the public authorities are trying to avoid!

By contrast the CDC website (CDC.a, 2021) currently (Sept. 14, 2021) states "Vaccines are playing a critical role in limiting spread of the virus and minimizing severe disease. Although vaccines are highly effective, they are not perfect, and there will be vaccine breakthrough infections." This is sending the right message. Furthermore, the CDC website goes on to say, "Given what we know about the Delta variant, vaccine effectiveness, and current vaccine coverage, layered prevention strategies, including wearing masks, are needed to reduce the transmission of this variant." This also is a correct statement and is precisely what the author stated under "Rumor #14" of the previous "Vaccine Safety" publication in this

series (Zito, 2021). Now, fortunately, the newspapers are also finally getting onto the right track. On October 2-3, a quote in *The Wall Street Journal* (Kamp, 2021) said,

"Given that by far the vast majority of severe illnesses and deaths is occurring in the unvaccinated, that this really is now a pandemic of the unvaccinated, most of the deaths we have seen in this surge were entirely preventable." – Robert Kim-Farley, epidemiologist and professor at UCLA Fielding School of Public Health.

The authorities and the media now have the formidable task of trying to correct previously

misleading news releases and re-instill public confidence in vaccination science (Figure 9). Precise language is important for public releases if misconceptions are to be avoided. Consider the following simple statement, "You can't give a nuclear reactor too much water." What does that mean?

Again, the reader might reasonably ask how the author knew so soon that some of the "official" statements concerning the spread of infection by vaccinated individuals were misleading? As before, official statements, although important, do not constitute proofs by themselves. The requirements of



Figure 9: "The Cowpock", an 1802 etching (hand colored with aquatint) by James Gillray, was published by "y Ana-Vaccine Society", and now resides in The Morgan Library and Museum, New York, NY (www.Themorgan.org). It vividly portrays the public's nightmarish fears about vaccination, as smallpox ravaged England. The caption sarcastically reads, "The Cow Pock or the Wonderful Effects of the New Inoculation!" A sly looking Edward Jenner, left of center, is about to vaccinate a very worried woman. Jenner is dressed in the best fashion of the day, with coiffured white hair, formal long coat, white hose, and buckled shoes, prosperous from the new pharmaceutical's profits. While his boy-servant remains in tatters. Ghoulish, mutilated, and bovinely transfigured spectators lurk in the background, victims of the new vaccine! One woman in the crowd (right) has been transmogrified into a kind of cow-woman. Hilariously, hanging on the rear wall, is the picture of a multitude worshiping the biblical Golden Calf! - By the end of the 20th century, vaccines (although only 95% effective, similar to mRNA 1273 – Table 1) not only stopped the spread of smallpox, but they completely eliminated that virus from the planet! Although we may all laugh at the anti-vaxxer cartoon above, the movement was just as vociferous in the 1950's during the Polio epidemic in the U.S. and is still with us today! "There is nothing new under the Sun" – Ecclesiastes 1:9.

logic, mathematics, scientific experience, and experimental verification must still be satisfied.

Before concluding this section, the author would like to make one last comment concerning public release of information. The Chinese authorities have received a great deal of criticism in the western press concerning their purported withholding information in the initial days of the pandemic. However, when one considers the behavior of people in the U.S. during the first 9 months of the outbreak here – the artificial shortages created by the hording of basic commodities (canned food, toilet paper, sanitary supplies, cleaning agents, etc.) and the potential violence created by a run on weapons and ammunition by survivalists - it is clear that the potential for public panic is very great indeed.

One must also remember that China has four times the U.S. population. That doesn't just mean their problems are four times greater. Not at all! Consider a population of just two people. Clearly, there is only one way for them to interact – directly with each other. Now, consider a population that is four times greater (8 people). The number of two person interactions is now 7 + 6 + 5 + 4 + 3 + 2 + 1, or 28. That is to say, there are now 28 ways for a dispute to arise among two people (perhaps over a roll of toilet paper in a supermarket)!

This calculation gives the reader some idea of what the Chinese authorities are really up against. They needed to be sure before making an unretractable public statement to a population of 1.3 billion people. Remember, not all infections spread out of control. If the lethality of an infectious agent is sufficiently high, and its transmission sufficiently low, it may kill off its hosts before a disease can spread very far.

### INFECTION CALCULATIONS

### **VAERS:**

Before the number crunching begins, the reader needs to understand what the Vaccine Adverse Event Reporting System (VAERS) is. VAERS tracks post vaccination side effects (including death) for many different vaccines. It is a joint effort by the U.S. CDC and the FDA (Food and Drug Administration). Although anyone can report an incident, there are usually specific rules. For example, consider influenza. Anaphylaxis (discussed above) can only be reported for 7 days after vaccination by Influenza-IIV, IIV3, IIV4, RIV3, ccIIV3, or LAIV4 vaccines

(VAERS, 2021). However, VAERS has also been a source of pandemic misunderstandings.

In a July 21, 2021 page-update, the U.S. Centers for Disease Control and Prevention (CDC) said "VAERS received 6,207 reports of death (corrected downward from 12,313) among people who received a COVID-19 vaccine between Dec. 14, 2020 and July 19, 2021" (CDC.b, 2021; Reuters, 2021) - the parenthetical inserts added by the author. This misleading statement has been interpreted by some anti-vaxxers as meaning that the COVID-19 vaccine has *caused* the death of thousands of people. After all, isn't it VAERS' job to track side-effects and deaths?

The current (Oct. 18, 2021) CDC web site also contains several disclaimers separated from the CDC/VAERS claim above. One states, "The FDA requires health care providers to report any death after COVID-19 vaccination to VAERS, even if it's unclear whether the vaccine was the cause". Another states, "Reports of adverse events to VAERS following vaccination, including deaths, do not necessarily mean that a vaccine caused a health problem. A review of available clinical information including death certificates, autopsy, and medical records, has not established a causal link to COVID-19 vaccines. However, recent reports indicate a plausible causal link between the J&J/Janssen COVID-19 Vaccine and TTS, a rare and serious adverse event – blood clots with low platelets - which has caused deaths" (bold-face, underline, and blue highlight, used by the CDC for emphasis). Finally, VAERS "reports may include incomplete, inaccurate, coincidental, and unverifiable information" (wonder.cdc.gov). The only "wonder" is that the CDC/VAERS would allow such "hear-say" evidence (not admissible in court) into a public database!

In order to reconcile all these conflicting statements, implications, and accusations, the author deemed it necessary to call the CDC and VAERS directly on Oct. 19, 2021 (1-800-822-7967) to ask for clarification and guidance. However, after being shuttled around to various departments, the author could discover nothing, other than excessive confusion and uncertainty, concerning the hodge-podge of statements above. Furthermore, a CDC phone representative promised to send the author an explanatory email from a staff "expert". On Oct. 20, 2021, the author did get an email from the CDC, but it contained nothing more than what was on the CDC website. So, where does the truth lie? Can a COVID-19 vaccine cause death?

As far as is known to date (Oct. 19, 2021), there are only a few possibilities. The first is anaphylactic shock discussed above and in "Vaccine Safety" (Zito, 2021). This risk is on the order of a few cases per million people vaccinated. Death is rare due to adrenaline (epinephrine) intervention (no U.S. deaths, 1 death in India).

The second is blood clots (thrombosis). This also occurs at the level of a few cases per million, and it can be life threatening. Thrombosis is only a risk with the Johnson & Johnson vaccine (47 confirmed cases reported total, but only 3 U.S. deaths according to the CDC; 10/18/21) as discussed in "Vaccine Safety" (Zito, 2021).

The third risk is myocarditis, inflammation of the heart, discussed in the author's August 2021 lecture for the ISSC (926 cases reported total, but no deaths; 10/19/21). It is primarily a problem for young men under 30 and involves the Pfizer and Moderna vaccines. The risks are again a few cases per million vaccinated (less than for the smallpox vaccine). Death would be a rare event.

The fourth risk is Guillain-Barre Syndrome (GBS). This disorder involves the Johnson & Johnson vaccine (a total of 228 preliminary cases reported (no U.S. deaths, 1 death globally reported by the European Medical Agency- EMA, 10/19/21), and occurs at the level of about 10 cases per million vaccinated (CDC, 10/19/21). GBS involves damage to nerve cells by the body's own immune system causing muscular weakness and sometimes paralysis. Most people fully recover from GBS, but sometimes the nerve damage is permanent. As far as the author knows, no deaths have yet occurred from vaccine induced GBS. Clearly, all four of these risks together (3 U.S. deaths; J&J vaccine only) account for 0.048% of the VAERS deaths reported on July 21, 2021. So, what accounts for the other 99.952% of VAERS reports?

Several factors are probably involved. First of all, excluding malicious lying, death after vaccination could have been coincidental after distribution of about 400 million doses (10/19/21). Death could have been from an accident (e.g., a plane crash)<sup>10</sup>, old age, cancer, or any number of pre-existing conditions. It is only necessary that the death be *after* receiving a COVID vaccine and within the stated time interval to enter the VAERS database. Just because you were vaccinated does not mean you will never die!

VAERS deaths can also be related to waning immunity (the loss of immunity as a function of time),

"too-late" vaccination, weak partial vaccination, unsuccessful full vaccination, or (rarely) spoiled vaccine. Undoubtedly, some people will call into VAERS claiming that the vaccine gave someone an active case of COVID that killed them. As discussed in "Vaccine Safety" (Zito, 2021), this is impossible. However, many people believe this rumor, and will enter a datum with VAERS. The belief is particularly tenacious when a person already has a latent infection and then receives the vaccine within the 5-day incubation carrier window. In this case, vaccination was too late. A few days later, the vaccinated person becomes sick, and may even die. No one can convince the surviving family and friends that the moribund was already infected before vaccination! There is also the very remote possibility of being vaccinated with a spoiled batch of vaccine (rare). Anyone vaccinated with mishandled or expired vaccine is still unvaccinated. However, even if a person is healthy when partially or fully vaccinated, they may not develop sufficient antibodies to prevent disease. Calculation of the total number of people who develop a COVID-19 infection after vaccination, and who die of that infection, will be next.

During most of the time interval cited by VAERS (Dec 14, 2020 – July 19, 2021),  $\delta$  infections were not an important factor in the U.S., and as of July 27, 2021, about half the U.S. population (49.1%) were fully vaccinated (Anon.b, 2021; CDC.c, 2021) while 17.9% of the population were partially vaccinated (Kirzinger et al, 2021). That leaves about one third of the population (33.0%) unvaccinated (Kirzinger et al, 2021). On July 25, 2021, the total (cumulative) number of COVID cases (T) was ~34,600,000 in the U.S. (Johns Hopkins, 2022). If  $n_{uv}$ ,  $n_{pv}$ , and  $n_{fv}$  are the total number of unvaccinated, partially vaccinated, and fully vaccinated cases respectively, then:

$$T = n_{uv} + n_{pv} + n_{fv}.$$
 Eq 1

Let  $e_{pv}$  be the vaccine effectiveness (in decimal) of a single dose of Moderna or Pfizer vaccine. These are the partially vaccinated, and from "Vaccine Safety" (Zito, 2021) the reader knows that  $e_{pv}$  usually lies in the 60 to 85% range. For this report,  $e_{pv}$  will be set to 0.6 (or 60%), the lower end of its range, because partial vaccination results in rapidly waning immunity, and because some estimates of  $e_{pv}$  are even lower than 60% as will be cited below. Furthermore, for the classical Wuhan and  $\alpha$  strains,  $e_{fv} \approx 0.95$  after full vaccination (see Table 1). Since vaccine

effectiveness (see the above definitions in the section "Definitions and Rumors") is defined as a (percent) decrease in cases relative to the number of cases in an equally large unvaccinated population ( $n_{uv}$ ), it is clear that  $n_{pv}$ , the number of infections following weak partial vaccination is proportional to  $(1-e_{pv})$   $n_{uv}$ . But wait, the set of partially vaccinated people is smaller than the set of unvaccinated people by a factor of (0.17/0.330). Therefore, the partially vaccinated will contribute proportionally less cases to the total T. Therefore,

$$n_{pv} = (0.179 / 0.330) (1-e_{pv}) n_{uv}$$
  
=  $(0.542) (1-0.6) n_{uv} = 0.2168 n_{uv}$  Eq 2

Similarly,

$$n_{fv} = (0.491 / 0.330) (1-e_{fv}) n_{uv}$$
  
= (1.49) (0.05)  $n_{uv} = (0.0745) n_{uv}$  Eq 3

This is the number of unsuccessfully vaccinated of the fully vaccinated, essentially equal to the number of breakthrough infections by CDC definition. When the results for  $n_{pv}$ , and  $n_{fv}$  are plugged into the basic expression for T, the following equation results:

$$T = n_{uv} + 0.2168 n_{uv} + 0.0745 n_{uv}$$
  
=  $(1 + 0.2168 + 0.0745) n_{uv} = 1.2913 n_{uv}$  Eq 4

Therefore,  $n_{uv}=26,794,703$  cases. Therefore, the unvaccinated contribute 26,794,703 / T=26,794,703 / 34,600,000=0.7744 or 77.44% to the total case load. The partially vaccinated contribute  $n_{pv}=5,809,092$  cases or 16.79%, while the fully vaccinated contribute  $n_{fv}=1,996,205$  or 5.77% (these are the breakthrough infections by CDC definition). Note that 77.44%+16.79%+5.77%=100.00%, as it should. It is also important to recognize that  $n_{uv}>>n_{pv}>n_{fv}$ , as stated in the section on "Definitions and Rumors". The next task is to translate infection figures into death figures.

On the average, an American who is infected by COVID has a 1.26% chance of dying (worldometers, 2022). Let  $\%_{uv}$ ,  $\%_{pv}$ , and  $\%_{fv}$ , be the post-infection death rates (in percent) of the unvaccinated, partially vaccinated, and fully vaccinated respectively. It is certainly true that

$$1.26\% = (0.330)(\%_{uv}) + (0.179)(\%_{pv}) + (0.491)(\%_{fv})$$
 Eq 5

where each percentage is weighted by the fraction of the population it represents. It is also known that (Mathieu, Roser, 2021):

$$\%_{fv} = (0.155)(\%_{un})$$
 Eq 6

Now comes a real problem. There is very little data on the partially vaccinated, in spite of the fact that they form an important part of the population. Therefore, an assumption will have to be made. It will be assumed that  $\%_{pv}$  lies between  $\%_{un}$  and  $\%_{fv}$ , so that

$$\%_{pv} = [(0.155 + 1)/2]\%_{uv} = (0.577)(\%_{uv})$$
 Eq 7

Therefore, putting equations 6 and 7 into 5 yields:

$$1.26\% = [(0.330) + (0.179)(0.577) + (0.491)(0.155)](\%_{uv}).$$
  
= (0.5094)(\%\_{uv}). Eq 8

Therefore,  $\%_{uv} = 2.473$ ; that is to say, the unvaccinated have a 2.473 percent chance of dying from an active COVID-19 infection. While  $\%_{pv} = (0.577)(2.473) = 1.427$  percent, and  $\%_{fv} = (0.155)(2.473) = 0.383$  percent. Note that  $\%_{pv} = (\%_{un} + \%_{fv})/2 = (2.473 + 0.383)/2 = 1.428$ , as it should aside from a round-off error in the fourth significant digit. Also note that (0.330)(2.473) + (0.179)(1.427) + (0.491)(0.383) = 1.26%, as it should.

Finally, according to these calculations, the death rate for the unvaccinated after infection is six and a half times higher than the death rate for the fully vaccinated after infection (i.e., 2.473/0.383 = 6.457)<sup>11</sup> – another reason why full vaccination is important even if you have been unsuccessfully vaccinated. Now, these VAERS calculations can be finished because the number of deaths following unsuccessful (low titer) full vaccination is

(%<sub>fv</sub>; in decimal)(
$$n_{fv}$$
) = (0.00383)(1,996,205)  
=7645 Eq 9

The number of deaths following weak partial vaccination is

$$(\%_{pv}; in \ decimal)(n_{pv}) = (0.01427)(5,809,092)$$
  
=82,896 Eq.10

Finally, the number of deaths due to lack of vaccination is:

$$(0.02473)(n_{uv}) = (0.02473)(26,794,703)$$
  
= 662,633 Eq 11

The total as of July 27 should be about 7645 + 82,896 + 662,633 = 753,174 dead. But wait, the graph in Figure 2 shows that the total deaths on July 19 to be about 630,000. So, the calculated value is 19.6% larger than the actual value. Why? It is primarily because theory calculated all the deaths that will eventually result from the total number of infections as of July 27. In reality, some of those who were infected near the end of the VAERS time interval, may not have died yet! Also, it has been tacitly assumed that the percentage of unvaccinated, partially vaccinated, and fully vaccinated remained the same from Dec. 14, 2020 to July 19, 2021. This is clearly not true for the first month after vaccination began, but there were also relatively few cases at that time. Therefore, the calculated number of people who died due to unsuccessful full vaccination should be downwardly revised by 19.6% to 6,147 deaths. This figure differs by only 1% from the VAERS figure of 6,207 deaths! Therefore, enough unsuccessfully vaccinated people died to explain the VAERS data. Actual deaths from the vaccine are negligible! What about the partially vaccinated, those who were vaccinated "too-late", coincidental preexisting conditions, malicious lying, etc.? Those were probably contained in the original VAERS figure of 12,313 deaths but were removed prior to downward revision. Until the CDC/VAERS is more transparent about how they select, filter, and revise data for the VAERS database, nothing more can be said. Finally, the reader may reasonably ask, "Wouldn't it have been easier to have started from total deaths rather than total infections?" Yes, but then how would you partition the dead into those who were unvaccinated, partially vaccinated, and vaccinated?

Although VAERS data may be useful to experts looking for potential vaccine trends, these complex data are just confusing to the general public and lead to rumors, misunderstanding, and *resistance* to vaccination. Just the opposite of what the authorities are trying to accomplish! The reader can now understand why imprecise and confused language and thoughts have caused so much bickering and prevented calculations! The readers may also wish to compare these more precise VAERS calculations to

the approximate calculations presented at the August 2021 annual meeting of the ISSS (conference video available from ISSS). Those calculations were performed in a different, simpler, but less precise way. However, the results were similar.

# CASES ENTERING HOSPITALS AND MEDICAL CENTERS (AUG. 2021):

On July 21, 2021, the total number of active COVID cases (T') was about 5,000,000 in the U.S. (see Figure 1). If  $n_{uv}$ ,  $n_{pv}$ , and  $n_{fv}$  are the number of unvaccinated, partially vaccinated, and fully vaccinated active cases respectively, then

$$T' = n_{uv}' + n_{pv}' + n_{fv}'$$
 Eq 12

As before, let  $e_{pv}$  be the vaccine effectiveness (in decimal) of a single dose of Moderna or Pfizer vaccine;  $e_{pv} \approx 0.6$ . Again, let  $e_{fv} \approx 0.95$  for the classical strains after full vaccination (see Table 1). Therefore, in analogy to the previous calculations, the number of infections following weak partial vaccination is  $n_{pv}' = (0.179 \ / \ 0.330) \ (1-e_{pv}) \ n_{uv}' = (0.542) \ (1-0.6) n_{uv}' = 0.2168 \ n_{uv}'$ . Similarly,  $n_{fv}' = (0.491 \ / \ 0.330) (1-e_{fv}) \ n_{uv}' = (1.49) \ (0.05) \ n_{uv}' = (0.0745) \ n_{uv}'$ ; this is the unsuccessfully vaccinated subset of the fully vaccinated set for the active cases circa July 21, 2021. Substituting these results for  $n_{pv}'$ , and  $n_{fv}'$  into the basic expression (equation 12) for T' yields:

$$T' = n_{uv}' + 0.2168 \ n_{uv}' + 0.0745 \ n_{uv}'$$

$$= (1 + 0.2168 + 0.0745) \ n_{uv}'$$

$$= 1.2913 \ n_{uv}'$$
Eq 13

Note that equation 13 has the same form as equation 4, except that unprimed variables have now been replaced by those that are primed. That is because both equations are dealing with cases, not deaths. Therefore,  $n_{uv}' = 3,872,067$  cases. Therefore, by the end of July, the unvaccinated contribute 3,872,067 / T = 3,872,067 / 5,000,000 = 0.7744 or 77.44% to the total active case load. The partially vaccinated contribute  $n_{pv} = 839,464$  cases or 16.79%, while the *fully vaccinated* contribute  $n_{fv} = 288,469$  or 5.77% (these are the breakthrough infections by CDC definition).<sup>12</sup> The USA Today article cited above (Innes, 2021) did not discuss the partially vaccinated. They may have been considered part of their population. However, by the "unvaccinated" definitions used here, the union of the unvaccinated

and the partially vaccinated would account for 94.3% of all cases. A figure that is close to the center of the ~90 to 97% range for their so-called "unvaccinated" (probably meaning not fully vaccinated, or the complement of the fully vaccinated set; Halmos, 1960) entering hospitals and medical centers during the month of August 2021 (Innes, 2021). Furthermore, it is precisely the unvaccinated (no vaccinations at all) who are most likely to be hospitalized with life-threatening infection, as demonstrated by the previous VAERS calculations. Now the reader can understand why Dr. Kim-Farley called the current situation in the U.S. "a pandemic of the unvaccinated". Mathematics has a way of exposing the truth, and sharpening understanding, in a way that verbal arguments never can!

### THE δ-VARIANT AND HERD IMMUNITY:

On Sept. 9, the *Arizona Republic* (2018 Pulitzer Prize winner) reported a breakthrough infection rate of approximately 15% for Aug. 9 to Sept. 9, 2021, in Arizona, the author's home state (Innes, 2021). Whereas the *Arizona Daily Star* reported 25% breakthrough infections for October in Pima County (Machelor, 2021). How can this be if the Moderna and Pfizer vaccines had a 5% breakthrough rate during testing? That is to say, these vaccines were about 95% effective during trials.

Are successfully vaccinated people spreading the infection? No! Two factors are involved. One is the lower vaccine effectiveness of the two popular vaccines against the  $\delta$  variant. The other is waning immunity. Let's consider each of these in turn.

A recent article in Medical Life Science, although claiming vaccine effectiveness was "barely affected" by the  $\delta$  variant, also stated that the average vaccine effectiveness (e) of the two common vaccines used in the U.S. was only 84.1% for the  $\delta$  virus (Solis-Moreira, 2021). That is approximately a 10% drop from test results involving the classical strains. However, it should also be noted that the data points had a large standard deviation and were scattered over the 70 to 95% range. The study involved the following U.S. populations: Washington D.C., Contra Costa Co. CA, DuPage Co. IL, King Co. WA, San Diego Co. CA, Santa Clara Co. CA, Connecticut, Massachusetts, New York State, Oregon, South Carolina, Utah, and Virginia. So, quite a lot of the U.S. was involved in the study. Another study in the New England Journal of Medicine cited a vaccine effectiveness figure of 30.7% after the first dose, and

79.6% after the second dose (Bernal, et al. 2021). So, although the results of these studies are reassuringly close, they are not exactly the same due to differences in experimental procedure and populations. It is also known that by Aug. 2021, almost all COVID infections in the U.S. were  $\delta$  variant ( $\sim 100\%$ ; Bhattacharya, 2021c). Therefore, the number of breakthrough infections among fully vaccinated people must be in the range of 15.9% to 20.4% (the compliment of the effectiveness; 100% - e in %). These are the unsuccessfully vaccinated. As one would expect, this range overlaps nicely with what has been reported in the press.

The other important factor to consider with regard to breakthrough infections is waning immunity. That is to say, immunity does not last forever after vaccination. "Two weeks to four months after a patient received their second dose, the Pfizer vaccine was 91% effective at preventing δ variant hospitalizations. After 120 days (four months) the effectiveness fell to 77%. Moderna's vaccine showed much less of a decrease in protection over the same time interval (LaFraniere, Weiland, 2021). We must always remember that, like the story of Lazarus (John 11:1-44), just because the successfully vaccinated have been saved from the Grim Reaper for a while, does not mean that such protection lasts forever!

With the precise definitions established in the previous section, the general requirements of herd immunity can be established. Recall from "Vaccine Safety" (Zito. 2021), that the multiplicity factor m is the number of people that each infected person will infect in turn before they are quarantined. For the classical Wuhan and  $\alpha$  strains, the average is about 3, in rural communities close to 1, and in an urban setting perhaps 5. However, the  $\delta$ -variant is 2 to 4 times more infectious, depending on which researcher you ask (Innes, 2021). Therefore, in the city, we might expect m = 10 to 20 for  $\delta$ . Let f be the fraction of people in a population that are members of the potentially infectious superset and, for the moment, consider a vaccine that is 100% effective (so that there are no unsuccessfully vaccinated). Then herd immunity is established if  $mf \le 1$ . That is to say, the multiplicity is offset by the scarcity of potential hosts (who are members of the potentially infectious superset) so that a vector can only infect no more than one other person, maximum. For example, consider a  $\delta$  infection with m = 10. If 90% of the population is fully vaccinated (in this case, synonymous with being

successfully vaccinated), then 10% remain in the potentially infectious superset; i.e., f = 0.1 in decimal. Then mf = (10)(0.1) = 1. That is to say, in this case, an infected person can only infect one other person before they are removed from the population. The infection can be maintained, but it cannot spread. If mf < 1, the infection will eventually die out as time approaches infinity. Now, define F as the fraction of people who are successfully vaccinated, then for the ideal 100% effective vaccine f = 1 - F, and the condition for herd immunity becomes  $m(1 - F) \le 1$ . What if a vaccine is not 100% effective, but has effectiveness e (expressed as a decimal fraction)? By CDC definition, the fraction F of successfully vaccinated is eF, where F is the fraction of a population that is fully vaccinated. That is to say, the set of successfuly vaccinated will be smaller than the set of fully vaccinated by a factor of e. Therefore, the condition for herd immunity becomes  $m(1 - e\mathcal{F}) \leq 1$ . Solving for F yields,

$$\mathcal{F} \ge (1/e) \left[ 1 - (1/m) \right]$$
 Eq 14

This simple, but powerful, equation will expose the difficulties that the  $\delta$ -variant presents to public health officials.

First, however, equation 14 must pass the test of logic. Suppose  $m \rightarrow 1$ . That means an infected individual cannot pass their infection on to more than one other person. Such a disease can maintain itself, but it cannot spread. Therefore, vaccination is unnecessary for containment. What does equation 14 have to say about this situation? Substituting unity for the value of m in equation 14 yields  $\mathcal{F} \geq 0$  for any positive non-zero value of e. That is to say, the fraction of people who need to be fully vaccinated can be zero, as expected. Of course, if some people are vaccinated, that will do no harm. Suppose  $m \to \infty$ . That means we are dealing with an infinitely contagious disease (say, as an approximation, a germ weapon genetically optimized to be exquisitely infectious). In that case,  $\mathcal{F} \geq (1/e)$ . Therefore, if  $e \to 1$ (i.e., a vaccine approaches 100% effectiveness, like 3 doses of the IPV – see Table 1), then  $\mathfrak{F} \geq 1$ . That is to say, the spread of such an artificial infection can be stopped only if everyone is fully vaccinated with a perfect vaccine - common sense! However, if e < 1, then  $\mathcal{F} > 1$ , and the infection cannot be stopped because § can never be greater than unity (or 100%). What if  $m \rightarrow 0$ ? That means an infected person cannot

infect anyone else (e.g. tetanus). Substituting a limiting value of zero for m in equation 14 yields  $\Im \to -\infty$ . Therefore, not only is vaccination unnecessary, but the disease cannot spread even if you artificially introduce it into a population (the negative of full vaccination). Suppose m > 1, but e  $\to$  0. That means a vaccine is totally ineffective (e.g. gonorrhea; VE  $\to$  0 for trial vaccines). In that case,  $\Im \to +\infty$ , and heard immunity is impossible since  $\Im$  can never be greater than unity. Finally, if e  $\to$  1, then  $\Im \ge 1 - (1/m)$ . Hence, equation 14 has desirable properties and passes the logic test.

Now, let's consider a few practical examples. Suppose the  $\delta$ -variant is three times more infectious than the classical COVID strains so that each infected city dweller can infect 15 other people before they are quarantined. This is easy to do in a crowded rush-hour subway car in New York. And suppose a δ specific booster is available that is 95% effective against  $\delta$ . What fraction F of the population needs to be fully vaccinated to achieve herd immunity? Setting m = 15, and e = 0.95, in equation 14 yields  $\mathfrak{F} \geq 98.24\%$ . Sometime about Sept. 30, 2021, the author heard an official of the Pima County Health Department (Tucson, Arizona) on KUAT (PBS) radio declare that, at that time, virtually the entire population of the county would have to be fully vaccinated to achieve herd immunity. Amazingly, as these numbers show, this statement is completely accurate for the City of Tucson – provided such a  $\delta$  specific booster is available! The good doctor was probably severely reprimanded by her supervisor for candor.

One more specific example is instructive. Suppose the  $\delta$ -variant is only twice as infectious as the classical strains so that m = 10. Also suppose that a  $\delta$ specific booster is *not* available, so that the population can only rely on the protection given by the original formulation as discussed in "Vaccine Safety" (e = 0.8). In that case  $\mathcal{F} \geq 1.125$ . How can that be? This figure for 3 implies that 112.5% of the population would have to be fully vaccinated in order to achieve herd immunity. In other words, herd immunity is impossible for the given conditions (see Figure 10)! This is still one more reason why a new  $\delta$  specific booster is necessary. If  $\delta$  is only twice as infectious as the classical COVID strains (optimistic), and if e = 95% for a  $\delta$  specific booster, then  $\Im \geq 94.7\%$  in the cities to establish herd immunity (see Figure 10). Vaccination levels of 95.5% have been reached

among the hospital staff of the Strong Memorial Hospital in Rochester, New York (Otterman, Goldstein, 2021), but it is uncertain if they can be reached in the general population given the observed resistance in the U.S. to vaccination.

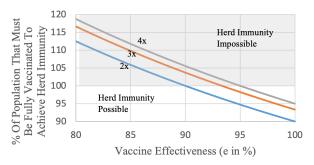


Figure 10: The requirements for herd immunity. Only (Vaccine Effectiveness, population %) ordered pairs that lie in the unshaded part of the diagram are achievable. Infectiousness levels are labeled 2x, 3x, and 4x, over the classical COVID strains (Wuhan and  $\alpha$ ). Urban crowding has been assumed. For  $\delta$ ,  $e \approx 0.8$  for the current vaccine. Therefore, herd immunity is not possible, but fully vaccinated individuals will receive partial to full protection.

The Biden Administration proposed vaccination of the adult population in the U.S. with a  $\delta$  non-specific booster, based on the formulation used to combat the original COVID strains, 8 months after the initial 2-shot series. However, the plan was insufficiently convincing to "experts" at the FDA and CDC (16 to 2 against; LaFraniere, Weiland, 2021). It was claimed that the old vaccine series is still good enough for most people to prevent "severe disease"; actually, you don't want any disease at all! Others argued that reducing the spread of the disease is also important. In the end, the original proposal was scaled down to only cover people with certain medical conditions and those 65 and older. These limitations were another CDC faux pas.

Pima county, Arizona, along the southern border of the U.S., a major corridor for medically unscreened illegal entry into the U.S., has opened booster shots to all adults "because of the high transmission rate" there (Machelor, 2021). Some other states and counties in the U.S. have done the same (Machelor, 2021). As of Nov. 15, 2021, the U.S. government was on the verge of making all those 18 and older eligible for the booster (Walker, Holder, 2021), as the administration originally wanted. However, in the author's *opinion*, eligibility for the current  $\delta$  nonspecific booster should also have been extended to

anyone who received the Pfizer vaccine more than 4 months ago because this is the vaccine for which waning immunity has been most pronounced in the U.S. (Walker, Holder, 2021). A 6-month rule (current) is alright for the Moderna vaccine.

This CDC comedy of errors highlights a very important fact. Some of the "experts" named in the *New York Times* article by LaFraniere and Weiland seemed, after an internet search, to be primarily career administrators, not active researchers, or practitioners at the top of their profession. The result was that the CDC was overwhelmingly *wrong*, in spite of early Israeli experience with waning immunity (Walker, Holder, 2021). Perhaps there is a problem at the CDC, or friction with the administration (LaFraniere, Weiland, 2021). However, if the CDC and the FDA aren't informing the American administration, then who is?

### **CALCULATIONS SUMMARIZED:**

The author hopes that these paragraphs bring some order to the tangled mélange of conflicting and misleading information found in the public domain concerning the vaccine. All aspects of the vaccine's performance can be mathematically understood, and it is doing just what it is supposed to do. What is important is the *statistical* behavior of the vaccine, not individual cases unless ALL the relevant facts are known (e.g., age, occupation, underlying conditions, exposure levels, vaccination dates, antibody levels prior to infection, etc.). The latter is what VAERS attempted to do – how successfully is a matter of debate

It must always be remembered that the pandemic has become heavily politicized, and there are a great many people in the U.S. who wish to find something - anything - wrong with the COVID vaccines that they can. The anti-vaxxers come from all frequencies of the political spectrum. Some claim that former President Donald Trump is trying to poison them. Others claim that the Biden Administration is trying to control them with microchips in the vaccine. Still others claim that the global pandemic is a hoax, and that the vaccine doesn't work. Finally, there are those who claim that COVID-19 is just another common cold. What Rubbish! The author has heard it all! Furthermore, vague ambiguous statements from the authorities, and the publication of statistics having a complex or uncertain interpretation, just exacerbates the misinformation problem (Wichner, 2021).

Some will complain that this article is too detailed. However, it must be detailed if endless verbal arguments are to be avoided! It's all part of the interminable American cacophony of vitriolic political vituperation that stinks in the ear! The antivaxxers should remember that, given a pandermic of sufficient duration, almost all the unvaccinated will contract COVID!

### THE BOOSTER: AN ETHICAL DILEMMA

The author struggled with the question of whether or not to include this section on the ethical difficulties posed by the current  $\delta$  non-specific booster. This is not science, and the author is certainly not a theologian, philosopher, or lawyer (although an attorney was consulted). Nevertheless, if this narrative is to be comprehensive, as purported by the abstract, the author has no choice but to walk were even angels dare not tread.

On the surface, the distribution of a booster seems to be only positive. However, how does one answer Dr. Tlaleng Mofokeng, a South African expert advising the UN, when he says that the booster will have the effect of "advancing and deepening the existing inequalities" when "there are people who are yet to receive a single shot" (Miller, Perrone, 2021)? Or that "[Moderna] has been shipping its shots almost exclusively to wealthy nations, keeping poor countries waiting [...]" (Robbins, 2021). Moderna says they are a small company, with only one product, and cannot possibly produce enough vaccines for the whole world. Furthermore, Moderna claims that they have tried to get governments to invest in expanding their scant production capabilities but have failed.

The basic issues are old, but also complex. By implication, racially diverse America and American pharmaceutical companies will be accused of discrimination, greed, and profiteering; all emotional "hot-button" words. It must be remembered that many other countries, like vaccine powerhouse India, produce COVID vaccines as well (Zito, 2020b). Although they may not be as effective as Moderna's vaccine, they are certainly better than going unvaccinated!

So, beyond all these inveterate emotional accusations and corresponding retorts, is there any common ground that everyone can agree upon? The author thinks there is, especially at the personal level. First and foremost, all COVID vaccine doses that have been produced (regardless of manufacturer)

should be used. Few would question the morality of distributing (giving away) unused doses to third world countries before they spoil. Here in the U.S., there are some people who believe that COVID vaccination violates their religious rights (Otterman, Goldstein, 2021)! Whether such people truly believe what they say, or whether it is just an excuse not to take the vaccine is a matter of conjecture. Nevertheless, their resistance to vaccination is based on freedom of religion, so it is unlikely that they can be compelled to cooperate. In such cases, remitting their doses to someone in another country seems both prudent and ethical.

What about people who refuse to be vaccinated? Some Americans, amazingly, are using counterfeit CDC cards to evade vaccination mandates. Such people are so spoiled and ungrateful that they simply don't realize how lucky they are! In such a case, there is no way to know if a person is compliant, so their doses will either be used by another person or be given away de facto before they spoil.

What about people who voluntarily wish to donate their dose to someone in another country? Shouldn't they be allowed to do so? After all, as the Hindu's would say, our own life is the only life we truly own! The practical answer to this question depends on whether vaccination is legally voluntary or compulsory. If voluntary, their doses can be given away. If compulsory, then refusal, without constitutional exemption, could be fined and their doses given away before they spoil. The fine money can be used to purchase a new dose should they later decide to comply. Nothing is truly free, and the object here is to *persuade* rather than punish!

On a national level, the author would be remiss if he did not raise the controversial question, "Can an employer in the U.S. 'persuade' an employee to be vaccinated by using the threat of dismissal, given that vaccination is *not* the law of the land?" Is this disease control, or "threats and intimidation"? What about the risk to other employees? Who has the liability if someone gets infected? According to current U.S. law, an employer has the right to make vaccination a condition of employment. Thereby mitigating the risk to other employees and reducing an employer's liability. However, as a practical matter, the risk of losing essential employees needs to be balanced against the risk of infection. Furthermore, it is not clear if a government agency has the right to "mandate" vaccination for all companies having more than 100 employees, essentially making

vaccination law. It is an issue that is currently before the U.S. Supreme Court. The government will undoubtedly argue that the mandate is an Occupational Safety and Health Administration (OSHA) rule. The opposition will undoubtedly argue that the pandemic is not occupation related, and that only legislative approval can make vaccination law. What the justices will decide is anyone's guess.

What about on an international level? Should the U.S., or any other country, that manufactures vaccines, distribute them to other nations before vaccinating their own people, who paid for the technology through their taxes?

Regardless of where COVID may have originated, the U.S. is now the most infected country in the world by a very substantial 11.3 million more total cases, 61% more total deaths, and a shocking 45 times more active cases than the runner-up (sorted by total cases), India as of Oct. 11, 2021 according to Worldometers (worldometers, 2021). These figures are all the more appalling when one considers that India has four times the population of the U.S.! On September 27, 2021, Medical Life Sciences (Solis-Moreira, 2021) declared that "The United States remains the country with the highest number of cases and deaths from coronavirus infection 19 (COVID-19)", and that makes the U.S. the primary source of COVID disease for the rest of the world, by far. Clearly, we are doing something very wrong!

Our inability to vaccinate the population (especially minorities) in a timely fashion, and to achieve herd immunity, has taken its toll. Our politicians do a splendid job of manipulating every media outlet when they want to win an election, but where is the corresponding commitment to public education about vaccination? Why doesn't every billboard in the land say, "Uncle Sam Wants You To Get Vaccinated!"?

Furthermore, our inability to control the flow of infected people across our international and interstate borders (Jervis, 2021), complacency and over confidence born between waves of infection, and the current political civil cold-war with its concomitant lack of public cooperation over everything from wearing masks and social distancing to the mitigation of stock-piling behavior, have all exacerbated America's problems. Additionally, governmental internecine battles over whether or not to deploy the  $\delta$  non-specific booster, didn't help matters either. Our efforts were too little, too late, not to mention the fact that we still do not have a *truly*  $\delta$  specific booster that

would maximize our ability to fight that strain. The U.S. needs to put in place, and fund, an infrastructure capable of developing and distributing vaccines for the new COVID strains on an annual basis – perhaps even faster. Perhaps *this* country should be the focus of the global effort to stamp out the pandemic, not South Africa (17<sup>th</sup> for total cases). These are all issues and questions to stir the passions and, undoubtedly, we will all be arguing about their answers for many years to come. For now, each reader will have to decide for themselves what constitutes ethical national and international public health behavior.

### **CONCLUSION**

"May you live in interesting times" is purported to be an ancient Chinese curse. Actually, it is a modern paraphrase of a Chinese lament from a collection of short stories published in Suzhou in 1627 (Anon.c. 2015). The words may have been different, but the sentiment is the same. Well, these certainly are interesting times, but like so many interesting periods of history, it is filled with a great many tribulations. The current "hot-buttons" of controversy seem to center around the definitions used for infection calculations and how to ethically distribute vaccine doses. Can a vaccine stop the spread of an infection? Should we get vaccinated? If so, who should get vaccinated? These questions all have clear answers as discussed above. So, why are we still fighting about them? Well, this *imbroglio* clearly has nothing to do with the facts. It is emotional, but not without parallel in history. Something similar was going on in the Italian city states starting from the very earliest days of the Renaissance ("re-birth"). It is a story wellknown to the Italian members of the ISSS. In 1300 you were either Ghibelline (yielding political allegiance to the Holy Roman Empire), or you were Guelf (yielding political allegiance to the Pope). But rather than the author retelling the story, let's read the words of the eminent historian Will Durant (Durant, 1953):

"Partisans of the popes and partisans of the emperors not only divided Italy, they split almost every city into Guelf and Ghibelline, and even when that strife subsided the old labels were used by new rivalries, and the lava of hate flowed into all the avenues of life. If Ghibellines wore feathers on one side of their caps, Guelfs wore them on the other; if Ghibellines cut fruit crosswise, Guelfs cut it straight down; if Ghibellines wore white roses, Guelfs wore

red. In Crema the Ghibellines of Milan tore a statue of Christ from a church altar and burned it because its face was turned in what was considered a Guelf direction; in Ghibelline Bergamo some Calabrians were murdered by their hosts, who discovered from their way of eating garlic that they were Guelfs. The timid weakness of individuals, the insecurity of groups, and the delusion of superiority generated perpetual fear, suspicion, dislike, and contempt of the different, the alien, and the strange." – Will Durant

Does this story sound familiar? Although the passage above may seem comical to modern readers far removed from the passions of that time, the character of man has not really changed in 700 years. Today, we fight over masks, vaccinations, and postinfection therapeutics. These, however, are not the real reasons for animosity any more than the way they ate their garlic in Renaissance Italy. No! These are little more than excuses for a confrontation, as each side turns a faccia tosta (a hard or impudent face) toward the other. This author doubts very much that the modern American "Ghibellines" and "Guelfs" in Washington know, or even care, about the science and the public health issues of the day. It's going to take a lot more than how we cut our fruit to put an end to the pandemic in the U.S. In the end, Americans are going to have to get control of their borders to stop the flow of medically unscreened, possibly infected, undocumented immigrants into the U.S. In the end, the government will have to institute mandatory adult vaccination for all circulating strains (including  $\delta$  and now Omicron). And in the end, public health measures are going to have to be enforced with fines. All very unpopular "hot-button" issues that will offend both the "Ghibellines" and the "Guelfs". But until these controversial measures are implemented, total deaths in the U.S. may continue to mount with each cold and flu season at a frightening rate as we approach 1 million deaths in the U.S. (about 20% of the global total). Equally as important, our infected travelers will continue to be a source of disease vectors for the rest of the world! - Stay Well.

### **FOOTNOTES**

- 1) There is an interesting and instructive piece of video (with a companion booklet) worth examining at this point called "Powers of Ten" by Charles and Ray Eames (Eames, 1989, 1982).
- 2) There is an interesting piece of experimental music called "Dance Folding" by Augusta Read

Thomas (augustareadthomas.com) that debuted on PBS radio (KUAT – Tucson, AZ). It aired on Friday evening, September 3, 2021, and was from the BBC Proms Concert. It is an acoustic rendering of what happens when a protein folds. Each "click" might be interpreted as the contact of two amino acid side chains. It's worth listening to!

- 3) If the probability for a significant mutation per year per infected individual (2.5 x 10<sup>-8</sup>) is multiplied by 1.8 years (the duration of the pandemic as of Oct. 30, 2021), you get a probability of significant mutation of 4.5 x 10<sup>-8</sup> per infected person. However, the global number of infected people is 246,000,000 as of Oct. 30, 2021 (Wikipedia). Therefore, the total number of significant strains worldwide should be about  $(4.5 \times 10^{-8}) (2.46 \times 10^{8}) \approx 11$ . In fact, the number of significant strains is 7 as of Oct. 30, 2021 (Wuhan,  $\alpha$ ,  $\beta$ ,  $\gamma$ ,  $\delta$ 1,  $\delta$ 2,  $\lambda$ ). This actual number of significant strains implies a probability of 1.6 x 10<sup>-8</sup> per year per infected individual. Therefore, the error between theory and experiment relative to the theoretical value is  $100 \times (2.5 - 1.6)/2.5 = +36\%$ , where the "+" sign means that theory has overestimated the observed number of significant strains. So, the virus is mutating with mathematical precision. The coronavirus is just a machine. An unconscious, parasitic, biological killing machine. As such, it is subject to the rules of mathematics. Like smallpox, the sooner COVID is wiped off the face of the Earth (if that is even possible - it may not be since the virus is mutating faster than the rate at which vaccines are currently being developed and distributed), the better off, and safer, humanity will be. Just one more reason why a δ specific booster is needed and should be widely distributed!
- 4) The units used for titer vary, but typically a successfully vaccinated person should have a titer of 1, or 100%, or 1000, depending on where you wish to put the decimal point. Unsuccessfully vaccinated people will have a titer well below these figures, say, 0.6, 60%, or 600. While a few people who have just received a booster or have just recovered from a wild infection may have a titer of almost 2, 200%, or 2000.

An experimental understanding of successful vaccination begins with an understanding of titer (from the word titrate). Antibody titer is a measure of antibody level relative to the mean antibody levels found in unvaccinated patients convalescing from the wild infection. This latter group has enormous antibody levels because they have just destroyed a full-blown infection, and the concomitant temporarily

uncontrolled proliferation of virions within their bodies. Therefore, these are the antibody levels capable of destroying any likely initial wild inoculation that has not yet started to proliferate in the receptive host. The base-line titer of 1 (or 100% or 1000) refers to this enormous antibody level and it is visualized by a biochemical tool called ELISA (Enzyme Linked ImmunoSorbent Assay) (Khoury et al., 2021). There are many variations on the basic ELISA scheme (Mathews, van Holde, 1996), but the most direct procedure for an antibody analysis would be to create a titrant by covalently linking an antigen (like the S-protein) to a (colored) dye molecule. Note that copious amounts of antigen can be produced by a yeast using the methods outlined in the first report of this series (Zito, 2020b). Now, if a standard amount of blood serum is taken from a convalescing COVID patient, and it is mixed with an excess of titrant, the antigen-antibody conjugate will also be colored. The intensity of that color, after removal of any interfering unreacted titrant, is defined as a unit standard titer (or 100%, or 1000). All other titers are measured relative to this baseline. Therefore, if a patient has a blood serum displaying half the color saturation of the standard (as measured by a photodensitometer or visual inspection after serial dilution), then the patient has a titer of 0.5 (or 50%). It is essential to understand that the titrant will not conjugate with just any antibody, but only the S-protein specific antibody (or antibodies if there are more than one). A variation on the ELISA procedure involves the use of a fluorescent dye (usually fluorescein) covalently bonded to the Sprotein (Mathews, van Holde, 1996). In either case, the trick is to remove any excess titrant. There are many ways to do this. However, since the S-protein is small compared to an antibody, it is probably best to simply pour the mixture through an appropriate chromatographic column; a glass cylinder containing beads (usually made of polystyrene) coated with permanently bonded S-protein specific antibodies. The liquid that is eluted (comes out of the bottom of column) the is the solution he spectrophotometrically analyzed (the analyte).

Clearly, it is important to keep personal immunity as high as possible (Read, 2021) because massive infections can occur (e.g., if a seriously infected person coughs in your unprotected face). However, baring such unlikely circumstances, a wild inoculation will not be able to seriously challenge a successfully vaccinated person. Experiment, clinical experience, logic and set theory arguments, infection

probabilities vs. titer, and calculations of antibody levels, all tell the same story: viz, healthy successfully vaccinated people are unlikely to contract or spread disease!

Naturally, there will always be rumors. An amusing "hear-say" story was related to the author about a wine tasting event attended by 11 supposedly fully vaccinated people. Shortly thereafter, it was claimed that 9 of these got the COVID. As usual, there was no proof of any of this. Cognoscenti must patiently smile at such fables. Their purpose, like that of Aesop's fables or any religious parable, is not to convey facts, but to preach a sermon. In this case, the erroneous anti-vaxxer sermon that "vaccination is futile". Furthermore, such stories are elaborated upon as time progresses through the natural processes of storytelling. So, why do some people believe such rumors? Perhaps one of Oscar Wilde's witticisms captures their sentiment, "I'll believe anything, so long as it's absolutely incredible!" There are no limits to human gullibility!

- 5) Waning immunity was suspected to be a problem with the BNT162b2 vaccine used in Israel, the first country vaccinated, and has resulted in a sharp increase in COVID cases (Levin et al., 2021). It is for this reason that a booster was prepared for the American population. Because its formula was unchanged (not  $\delta$  specific), rapid production was possible, vs. a booster with  $\delta$  specific activity and a longer development time. Finally, it should be noted that waning immunity is a necessary natural process. Very few artificial or wild inoculations convey lifelong immunity. Otherwise, the energy cost to the human body required to maintain a standing army of antibodies at maximum strength against every occasional biological invader would be so great when summed over the years that either premature death would result from the complete exhaustion of the body's energy currency, or species extinction would result from "eating-out" our food supply to furnish the necessary ever-increasing energy Strangely, on a macroscopic scale, the nations of the world are doing the same thing today with their money, their military expenditures, and their everincreasing populations and energy consumption. Guess what the result will be!
- 6) This statement assumes the antibody test yielded a "true" positive. Real tests, however, are imperfect. Nevertheless, test repetition is a valid way of removing doubts as described in the first paper of this series (Zito, 2020b). It should also be noted that

an antibody test will only turn positive when the antibody levels reach the levels seen in a person about two and a half days after a wild type infection begins. Therefore, any verified "+" antibody test following vaccination of a healthy person means that the vaccinated has at least a 60-hr. head start in combating the establishment of a new infection. Realistically, it is probably a lot more than that!

- 7) Anaphylactic shock involves still other types of immune system cells called basophils and mast cells (Wessells, Hopson, 1988; Cowan, Talaro, 2006). Both of these cell types have a similar structure. In particular they contain granules filled with chemicals like histamine, the agent responsible for many unpleasant allergies. In fact, these two cell types were once considered the same. However, we now know that they are quite different. Basophils are a line of immune system cells (0.5% of all white blood cells) that originate from the bone marrow, and, like all such cells, they are mobile in the blood. By contrast mast cells are immobile cells bound to connective tissue around blood vessels, nerves, and epithelia. If the immune system is overstimulated, these cells (especially mast cells) will release their granule contents all at once. If that happens, anaphylaxis is the result. It is a condition that can kill in just 15 minutes from complete airway blockage (Cowan, Talaro, 2006). It should be noted that more health care authorities are moving toward the author's more conservative recommendation of waiting 30 minutes after vaccination before departure to reduce the possibility of anaphylactic shock.
- 8) The human immune system is very complex. It contains cells for clotting, cells for phagocytosis (digesting foreign substances), cells for inflammatory response, cells to destroy worm and fungal infections, cells to produce antibodies, and cells that produce chemical messages to induce other immune system cells to replicate. The whole menagerie starts from hematopoietic stem cells in the bone marrow ("hem" is Greek for blood, and "poietic" is also from the Greek meaning "having the character of"). Some of these stem cells develop into erythroblasts and then into erythrocytes, or red blood cells. However, it is the remainder that are of interest to us here; megakaryoblasts, myeloblasts, monoblasts. monocytes, macrophages, dendritic cells. megakaryocytes, granulocytes, platelets, neutrophils, basophils, eosinophils, natural killer (NK) cells, lymphoid stem cells, lymphoblasts, and lymphocytes (types T and B) (Cowan, Talaro, 2006). Mast cells are

also part of the human immune system, but they are part of another cell line.

- 9) At this point one might reasonably ask, "Why doesn't the immune system normally attack one's own body?" When immature B-cells in a fetus encounters substances that bind to their surface antibodies, they are not stimulated to replicate. Instead, these cells are destroyed. Therefore, cells producing antibodies against all potential "self" antigens to which we might react are eliminated before birth! The only B-cells that mature are those that produce antibodies against "non-self" substances (Mathews, van Holde, 1996). Welcome to the astounding worlds of biochemistry, cellular and molecular biology, immunology, and modern medicine.
- 10) Some have speculated that a small aircraft might crash because the pilot suffered heart failure during flight after vaccination. It seems improbable, but any excuse will do for the anti-vaxxers. Presumably some coincidental deaths are eliminated from the data base by postmortem investigation. However, the author has not yet been able to get anyone at the CDC to admit to that (CDC.d, 2021).
- 11) Although a factor of 6.5 may be reasonable for the entire (pre-δ) VAERS period when only the twoshot basic vaccination series was available, it is too conservative for the δ-predominance period that followed in the U.S. Statistics for October -November 2021 show deaths were 12.7 times higher for the unvaccinated relative to those who had received the basic two-shot series (Johnnson et al., 2022). The increased lethality of the  $\delta$ -variant among the unvaccinated probably accounts for the factor of 2 difference in deaths since the vaccinations were the same. Furthermore, there were 53.2 times more deaths among the unvaccinated relative to those who received the basic series plus the booster (Johnson et al., 2022). As previously discussed, the booster produced such a massive increase in antibody levels that the death rate among the boosted fell by almost half an order of magnitude compared to those who only received the basic series!
- 12) Note that the ratio of unvaccinated cases to fully vaccinated cases is 13.4; a figure close to the truth. Statistically, the incidence rate ratio (IRR) was 13.9 at the end of the pre- $\delta$  period. The error between theory and experiment is only 3.6%.

### ADDENDUM (JAN. 2022)

This report primarily covers the narrow time interval from mid-August 2021 to the end of October Since then, the Omicron strain has been detected. That will be the subject of a separate publication. There is simply too much to say in a single publication! It should also be noted that active COVID cases in the U.S. (Figure 1) stand at 15,288,098 cases as of Jan. 4, 2022 (Worldometers). This case figure is 8.4% above what is projected by an updated 5<sup>th</sup> degree polynomial fit to the total data set, and a very substantial 28% above an updated linear model. Furthermore, total deaths in the U.S. are still rising at a linear rate as of Jan. 4 (Worldometers). Although the best fit 5<sup>th</sup> degree polynomial was a good short-term predictor, it says nothing about when the current surge in cases might reach its peak or, on an even longer time scale, when the pandemic might end. It is likely, however, that cases in the U.S. will ameliorate as the northern hemisphere reaches the warmer spring and summer months.

Also significant is that The Wall Street Journal ran an article entitled "CDC Aims to Revamp Covid

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Moves" (Schwartz, 2022). Although the article is not completely fair to the CDC, and contains one important error in its science, it does highlight the fact that "Confusion has further undermined faith in the nation's public-health system at a critical moment", just "before the  $\delta$  variant emerged", when the CDC "suggested people stop wearing masks". It was a replay of what happened in India!

Finally, on Jan 13 the Supreme Court declared the Biden Administration's "vaccine or test" mandate for private companies having more than 100 employees exceeds the authority of the Occupational Safety and Health Administration (Totenberg, 2022).

### **COMPETING INTERESTS**

The author declares that from July 1, 2021 to January 31, 2022 he had no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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