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Flu or a Bug?

Of late, apart from the four calendar seasons, there is yet another season referred to as the "flu season." During this time of the year, we routinely hear the phrase "the flu is going around." I was surprised last week when I heard my 6-year-old son mention to me that there is some bug going around in his class and that his best friend was sick. I asked him to define the bug and he said it causes stuffy nose. The word "bug" is used so callously by adults that it has been registered wrongly in the minds of the little ones.

What is this so called "bug?" Is it a termite, a spider, or a bee? Nope, it is neither. Flu is caused by a virus; more specifically, an RNA containing virus referred to as the influenza virus. Influenza virus is so small that it cannot be seen even under a light microscope. The size of an influenza virus ranges between 50 and 120 nm which is 10^6 times smaller than a black pepper flake. Isn't it amazing how such a miniscule pathogen can wreak such havoc on the body? As you probably already know, this viral pathogen can cause fever, cough, sore throat, body aches, fatigue, and runny or stuffy nose.

But, here's the million-dollar question raised by the common man: Why does flu occur year after year during the winter months? There are actually quite a few recorded reasons, and they are as follows: (i) Flu virus survives for longer periods indoors in winter; (ii) The virus may stay airborne for prolonged periods and can thus infect others through inhalation; (iii) Less hours of sunshine in the winter may result in diminished immune activity due to a sharp decline in vitamin D; and (iv) In winter, humans tend to be indoors more and thus have closer contact with others, which makes it easier for the

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flu virus to spread. Honestly, neither of these propositions make any sense due to the following reasons:

(i) The virus is relatively stable outside the human body irrespective of the temperature. It can survive outside the human body effectively for a couple of days as tested on banknotes in a recently published work. Now, there are indeed some differences between virus strains, but overall, they can survive at low pH values (pH = 5.5) as well as at drastic short-term temperature fluctuations (between 40 °F or 100 °F). This defies the dogma as influenza virus is an enveloped one. Scientifically, non-enveloped or naked viruses are stable outside the human body or any host as opposed to an enveloped virus, say, a herpesvirus. This is a fine paradox about the virus and the extra envelope coat that some of them wear. When a virus possesses this outer layer called the envelope, it makes it highly sensitive to the environmental conditions, as the envelope is predominantly made up of lipids that are easily degraded by commonly used disinfectants, temperature changes, and pH variations.

(ii) The ability of the virus to be suspended in air does not change drastically through the year. However, it is worth mentioning that the humidity affects the virus particle size which affects its ability to stay suspended in the air. Also, extreme dry conditions may affect the envelope and reduce the virus's ability to survive in the environment.

(iii) Vitamin D does play a role in regulating the innate and adaptive immune response. However, there has been no correlation deciphered between two-to-three-hour shorter days resulting in a sharp vitamin D loss so as to selectively predispose the person to influenza virus alone. Also, there are regions around the globe where there is not a whole lot of difference between the daylight hours during a calendar year. The best example is Chennai (a port city in southern India) where there is no big difference in the hours of a day during a year. In fact, the joke is that Chennai has three seasons in a year: hot, hotter, and hottest!

(iv) In winter months, people tend to be indoors, but this cannot be the major reason for the spread of flu during the winter months because this concept is biased from the start to finish. It is assuming that the whole world has one type of climatic pattern as observed in the Western hemisphere. This is not true; in fact, the weather during the winter months in Southern India is so pleasant (about 70 °F) that people tend to be out and about even more so than in the summer months.

The scientific reasons for why we tend to succumb to the flu during the winter months versus during the other seasons is primarily because the virus replicates better at lower temperatures coupled with the fact that it is best transmitted at a low humidity of 20%. The viral transmission is almost negligible when humidity reaches about 80%. Flu seasons occur during opposing times of the year in the southern and northern hemisphere. With modern day world travel flu can move quickly with the changing season.

The next obvious question is: Where does the flu virus take shelter during the summer months only to infect us again during the following winter? Does it stay dormant outside the human host? Does it stay dormant inside the human host? Unlike herpesviruses, influenza virus does not cause latent infections; in other words, the virus does not stay dormant inside or outside the host. To understand this, one needs to understand the viral agent in question. Evolutionarily the flu is one of the most highly-diversified pathogens. There are three major types of the virus: influenza virus types A, B, and C. Human influenza virus types A and B cause the disease year after year in the human population. Influenza virus type C generally causes only a minor form of the illness and is relatively rare compared to the other types. This virus exists in multiple types and strains, making it complicated for the human immune system to thwart it. To add to the misery, influenza A viruses are found in many different animals including birds, pigs, horses, whales, and seals. Though, influenza B virus is largely considered to circulate only among the humans, recent scientific work seems to show its ability to infect pigs and maybe other animals. Thus, these other hosts serve as potential natural reservoirs of infection, fueling the virus through to the next season. In nature, any pathogen that has evolved a means to thrive in multiple hosts is a successful pathogen. For example, swine influenza virus, a common pathogen of pigs worldwide and causes flu in them. Transmission of swine influenza virus from pigs to humans is not all that common. However, such a zoonotic transmission is always possible as it happened in India during the early months of 2015. Swine influenza virus strains include influenza A virus (H1N1, H1N2, H2N1, H3N1, H3N2, and H2N3) and influenza C virus. One of the main factors that enable influenza virus to infect multiple species is that it is an RNA containing virus which accumulates mutations 350 times faster than a DNA virus. Accumulation of mutations results in genetic changes critical for a pathogen's ability to adapt for better infection of new hosts. The ecological mechanisms always ensure that the transmission of pathogens between more than 2 different hosts is more than often bound to be asymmetrical. Such asymmetries in interspecies transmission of viruses, including influenza virus is the key to the emergence of viruses that are antigenically different. People

have little or poor immunity against such mutation-driven antigenically different viruses resulting in a pandemic. Acquiring mutations is a double-edged sword: on one hand, it allows the pathogens to adapt better to different species while on the other hand may result in a virulent form of the virus.

In a way, humans should thank their lucky stars that such a dynamic and sturdy virus as influenza virus that intimidates the population year after year is not nearly as lethal as the Ebola virus. By December of 2014, I was interviewed by a news channel about the threat of Ebola virus on US soil. In fact, right at that time, all the news channels, as always, were making stories of the Ebola outbreak in the triad nations of Africa: Guinea, Sierra Leone, and Liberia. To the dismay of the interviewer, I laughed it off and mentioned that the worries were in vain and that Ebola would not end the world. I was 100% sure of my judgment and 3 years later, the world is still fine. I based my conclusion on the fact that the number of outbreaks outside these three countries were literally negligible in that year and that the Ebola virus, unlike the influenza virus, really has no proven natural animal host. People concluded bats to be a natural reservoir for Ebola virus and that the virus was transmitted to humans by eating bushmeat of bats. Once again, there is no truth to it. There was not even a single case of Ebola from a neighboring country, Ghana, where at least 100,000 or more bats are consumed every year and it is considered a delicacy. As lethal as Ebola virus may seem, for it to be successfully transmitted around the world over a sustained period, the virus must be well adapted to survive in other hosts as well. With respect to Ebola virus, humans seem to serve as a rather dead-end host. As of now, there are only hypothetical theories as to how the Ebola virus could have been transmitted from animals and none said theories have been effectively proven.

The major problem with treating virus causing diseases of the upper respiratory tract is that there are more than a couple of these "bugs" that can cause diseases of the upper respiratory tract. The viruses that can cause infection of the upper respiratory tract are influenza A and B viruses, adenovirus, coronavirus, rhinovirus, metapneumovirus, respiratory syncytial virus (RSV), human parainfluenza virus (HPIV-1, -2, & -3), and Chikungunya virus. Apart from this list, bacteria referred to as *Bordetella pertussis* and *Mycoplasma pneumonia* can also cause infection of respiratory tracts in humans. When so many agents can potentially cause infection of the upper and lower respiratory tract, resulting in clinical manifestations like the common cold, pharyngitis, laryngitis, tracheitis, bronchitis, bronchiolitis, and bronchopneumonia, it makes diagnosis very complicated and difficult. A friend of mine who is a division chief of the department of infectious diseases mentioned in a lighter vein that if a doctor is not sure of the pathogen, she or he calls it a "bug." Diagnosis is

critical only in immune-compromised patients, infants, children under high-risk conditions, and the aged.

Over the course of the modern documented years, science has undergone gradual change in the way it is perceived. The contemplative approach has given way to a more manipulative form. The contemplative approach manifests based on passion for a subject matter while the latter approach manifests based on the desire to gain control or power. In earlier days, science progressed immensely due to the limitless passion that man had for the field. Boundless passion leads to lust or love for everything around us, and in a way, such passion is responsible for all the developments we see in the modern world. Of late, science is being used as only a tool to generate money. Even the approach to fund scientific research is now built on the foundation of networking. The current guardians of science are fully drunk with power and money. The seeking of the truth is quickly and steadily reducing. There is always a court of law for ethics, but no ethics are followed. Science and medicine are important but they pale to insignificance when compared to human bonding, love, and emotion. A scientist must value the human emotions and if his inventions do not in some way benefit the sentiments, it will get disregarded with time. I have deliberately omitted doctors here as their direct role in inventions in biological science is limited, sadly. If this approach continues, the government will fail to make life tolerable.

We humans always miss the crux and put in more efforts on unimportant things. Interestingly, this happens more so willfully by corporate giants and government bodies who care more about churning profit than anything else. Many times, clashes of ideologies impede mankind's progress. Let me give an example where one giant of a personality whom we are all aware put our progress into a retrograde spin. We know of the great American scientist, Thomas Alva Edison. Per the Thomas Edison National Historic Park, Edison held 1093 patents. The first thing that comes to our mind upon the utterance of "Edison" is the bulb and the direct-current (DC) system. However, little do we know of Nikola Tesla, from Serbia, who worked for the famous Edison. Tesla was a genius himself. Among a long list of inventions, Tesla was instrumental in developing the alternating current (AC) technology. The number of patents held by Tesla may seem to be relatively small compared to that of Edison, but far more practical. His contributions to technology include AC, neon lamps, Tesla coil (interesting read if you have time), X-ray, radio (many believe it was invented by Marconi but again, if you have time, read about the controversy surrounding it), remote control, electric motor, robotics, laser, wireless communications, and limitless free energy. Thomas Edison did everything in his power to discredit Tesla's invention of AC to promote his less

efficient DC system. To prove his point, Edison went to the extent of even electrocuting animals like elephants using the AC. Edison's histrionics did not end there, as many believe he was instrumental in having bankers opt out of Tesla's projects. There are even suspicions that Edison had a hand in the U.S. patent office's reversal of its original decision to award Tesla the patent for radio; somehow the patent was awarded to Macaroni instead. Today, the local power grids that supply electricity around the globe are based on Tesla's AC. Tesla's idea powers the whole world. Tesla was a genius and worked to solve the problems of the everyday common man, but the shrewd or for that matter, the less intelligent yet wealthier owners of corporate firms always have the upper hand. Tesla died penniless. My friend, Adi (for Adrian) who wrote the preface for this book considers Tesla vs Edison as his favorite example of using money and power to manipulate science and progress. Unfortunately, the situation continues.

On the same note, I would like to talk about this whole idea of vaccinating against this "bug" called flu. Why do we need a vaccine for flu? If you take medicine, it will last 7 days and without medicine it is going to last a week. All these so-called vaccines are made by different private companies in the USA and are approved by the U.S. FDA. It is a well-known fact as admitted by the Centers for Disease Control & Prevention (CDC) itself that it is not possible to predict with certainty which influenza virus will predominate during a given season. Influenza viruses are constantly changing. The strains that are chosen for the Northern hemisphere is the predominant strain circulating in the Southern hemisphere and *vice versa*. They can change from one season to the next and even transform during the same season. Given all these variables, the so-called "experts" must pick the correct combination of the virus well ahead of the start of the "flu season" to manufacture the custom designed vaccine for that particular season. It is like searching for a needle that ain't in the haystack. The act of "experts" picking the correct combination of the virus is like a 6 year old rolling a dice and waiting for it to land exactly on the number 6. The only difference being that the child plays for fun while the so-called 'experts' play with time, money, and hope of poor citizens. There is absolutely no guarantee that the flu vaccination will be effective. Even the companies do not stand by their product. So, this is one of the greatest jokes of the era, along the same lines of how corporate firms played around with Tesla's inventions to fatten their own pockets. Within the last 2 years I had no other alternatives provided but to have the flu vaccination and it has been no different than the several years prior to it when I chose not to be vaccinated. In fact, last year I felt cheated as I had caught "the bug" (flu) a week after my vaccination.

Scientifically speaking, there has been no benefit from this sort of black-magic flu vaccination, and I am convinced it is not going to have any perks in the future. However, have you ever wondered who pays for this no-guarantee vaccine?

In my opinion, you can load the population with either dead or live virus (vaccinate) if it has a guarantee of preventing the disease in the vaccinated individuals without any untoward effects. The best example is poliovirus vaccination which has almost dramatically reduced polio virus-induced paralysis to negligible incidences around the globe. Poliomyelitis is a debilitating disease that can paralyze young children worldwide. Polio can also cause death in about 2–5% children and in up to 15–30% adults. In the US, live attenuated Sabin oral vaccine was administered to effectively bring down the number of polio cases. Live vaccine was being used in the US while the rest of the world was using the killed vaccine. However, we (US) had to change to the killed Salk vaccine in 2000 to avoid what is called Vaccine-Associated Poliomyelitis (VAP). VAP occurs in every 1 out of 2–3 million doses. In other words, every 1 out of 2–3 million children who received this vaccine succumbed to the disease. Morally and ethically, we changed from the use of the live vaccine to the killed version in an effort to make it foolproof, guarantying the individual an effective treatment. In the case of flu, it is a fun ride for companies to generate the ineffective vaccine and benefit immensely out of this sham business. Such vaccination practices can help medical offices make a beautiful pie chart over the years to fodder statistical data analysis about what can be attained. These statistics that describe the outcome of a vaccination program towards a non-lethal disease like the flu are routinely a farce. If the disease is not life-threatening, a common man seldom visits a doctor. I would not be surprised if there is a drive in the near future to make this world rid of flu by vaccination. It is not a far-stretched imagination as it will immensely boost the American economy.

If the government and corporate world are really looking for the magic bullet to combat the flu, vaccination is a mute effort. Vaccination policy will definitely fill in the coffers of the rich corporate governing bodies, but it does not alleviate the situation for the common man. What then is the alternative situation? There are alternative methods to treat the virus, however, to do that, we should understand the biology of influenza virus. It is a segmented RNA virus that accumulates mutations at a high rate. Making vaccinations based on prediction models will fail miserably. It is like shooting in the dark. The restructuring of approach to treat the flu is as follows:

(i) We need to understand that the flu by influenza virus is not a life-threatening disease on the same level as tuberculosis, malaria, HIV, or heart diseases. Let me give you an analogy to explain this fact. Pneumonia is an inflammatory condition of the lung affecting the alveoli and can be life-threatening. Pneumonia can be caused by a variety of pathogens like bacteria (*Haemophilus influenza, Chlamydophila pneumonia, Mycoplasma pnumoniae, Staphylococcus aureus, Moraxella catarrhalis, Legionella pneumophila*, and gram-negative bacilli), viruses (influenza A and B viruses, adenovirus, coronavirus, rhinovirus, metapneumovirus, RSV, HPIV, and Chikungunya virus, cytomegalovirus), fungi, parasites, and idiopathic of nature. Pneumonia (that can be caused by any one of the above long list of pathogens) can cause death almost during each and every period of human life; an exception being between ages 45 to 64 when the death due to this is at a recorded minimum. A death rate of 1.9% (ages 1–9), 0.7% (ages 10–24), 1.0% (ages 25–44), 0% (ages 45–64), 2.4% (ages 65 and over), and 3.1% (ages 85 and over) due to influenza and pneumonia has been reported by national vital statistics reports (dated December 20, 2013).

(ii) We need to cut down millions of dollars being funded to generate vaccines for flu and instead focus on attempting to develop a combination drug regimen targeting the virus entry and replication process.

(iii) We need to develop better management of the influenza virus-induced symptoms.

(iv) We need to mobilize money to effectively provide the infected general population with good and affordable supportive hospital care. Most people who die around the globe are above 65 years of age coupled with poor lifestyle. Honestly, you need a reason to die or else find medical methods to increase the productive lifespan of humans.

Harping on those lines, I strongly believe that the manufacturing of vaccines must be strictly regulated. Currently, it is poorly regulated and is in a pathetic state in the US. The minute a new 'bug' is described, a bunch of scientists whom I often refer to as the vaccine-jockeys start working on developing vaccines. The best example is the severe acute respiratory syndrome (SARS) outbreak in China. It was in November of 2002 when the first outbreak of SARS was reported in the Guangdong province of China. It was immediately declared a global disease; though the number of cases was miniscule compared to any disease we know. Immediately, labs in the US started working on developing a vaccine to this so-called deadly (mockingly) disease. There is nothing wrong with pouring in ideas to develop a vaccine against a

potential threat but things should always follow a rationale. The following questions must be addressed before actually proceeding to invest money in developing vaccines:

(i) What is the etiology for the said disease?
(ii) What is the impact of the pathogen on humans?
(iii) Is the disease zoonotic?
(iv) What is the lifecycle of the pathogen?
(v) What is the epidemiology of the disease?
(vi) Has the pathogen been sequenced?
(vii) Has the structural and non-structural proteins of the pathogen been thoroughly analyzed? and
(viii) What is/are the protein(s) in the pathogen that is immunogenic or more importantly neutralizing?
(ix) The most important of them all: Vaccines are meant for preventing a disease. But, as seen in the case of the flu, even after vaccination if there are approximately 31.4 million outpatient visits, 200,000 hospitalization, and about 5000 deaths, the vaccine is just a futile attempt. It is just a way to boost the revenue for the healthcare division at the behest of the poor citizens. Flu vaccines have not changed the scenario at all. It is essentially a placebo to the patients and a money maker for the doctors. As in many cases, the highly worshipped vaccine pushing doctors are either just ignorant or they pretend to be believers. I can tell you with 100% honesty that I have had such discussions with scientists who are directly involved in the design and development of this and other vaccines, and admittedly they all know the flu vaccine is not a magic bullet as in the case of the poliovirus vaccine.

It is crucial to understand the biology of a pathogen. What is the purpose or rationale behind initiating the development of a vaccine before you understand the pathogen that its being designed to rid? That is like going to a war without any strategy. Can you imagine that the first scientific paper on vaccine for SARS was published only a year after the outbreak? With such little time lapse, not a whole lot was known about the pathogen itself. Goodness gracious! This pathogen turned out to be a dummy or a pseudo-pathogen, at best. All the panic and mass media coverage for less than 1000 deaths in a handful of countries to date. I am sure that my point-of-view regarding the matter is not music to the ears of vaccine developers. Believe me, I am not being heartless but rather trying to present my case against the commonly

peddled flu vaccine. There are so many other pathogens that are not only debilitating but can cause huge loss in terms of mortality year after year. I am NOT against treating flu, but I am advocating scientists to pour money into developing alternate methods of treatment as opposed to holding on to a preventive approach of vaccination that has no guarantee. Why waste money on a burger gone bad?