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Clinical data to be used as a foundation to combat Covid-19 vaccine hesitancy

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1. Introduction

It has been over a year since the first case of Covid-19 was reported in the United States. Since then, the coronavirus has become the paramount subject in peoples’ lives, affecting and disrupting virtually every aspect of society, as the pandemic casts a shadow over the world. The mental toll of Covid-19 has affected people who had pre-existing mental health issues, low-income individuals, people of color, and those who have suffered the mental stress of persons who died from Covid-19. Covid-19 deaths have accounted for over 745,000 in the United States. Since then, the coronavirus has become the paramount subject in peoples’ lives, affecting and disrupting virtually every aspect of society, as the pandemic casts a shadow over the world. The facts, myths, and conspiracy theories centered on the Covid-19 pandemic have dominated social media accounts, local and national newspapers, as well as television programs. Strategies need to be evolved to counter Covid-19 vaccine hesitancy and mitigate health disparities in at-risk populations. Overcoming misinformation and distrust will require an interdisciplinary approach to deal with Covid-19. The purpose of this review is to offer a factual basis to all healthcare providers to assist in framing strategies to mitigate vaccine hesitancy and achieve herd immunity to combat the deadly Covid-19 pandemic. First an overview of the discovery of the viruses and their molecular structures will be presented. Secondly, a historical perspective is offered, comparing the differences between the 1918 flu pandemic and the current covid-19 pandemic. Lastly, an overview for proposed techniques and methods to counter and or mitigate covid-19 vaccine misinformation that may be used by an interdisciplinary team will be offered narratively and graphically.
2. Viruses

One of the first microbe-hunters was Antonie van Leeuwenhoek, who used handcrafted lenses to identify "little animalcules" in standing rain water, sea water, and human teeth scrapings; their significance to human health and disease was unappreciated at the time.6–10 After Leeuwenhoek’s death, his excellent techniques for observing microorganisms were not passed down, and eventually were forgotten by the scientific community.7 Although he did not write any scientific paper, Leeuwenhoek did write about his observations in many letters addressed to the Royal Society of London. In 1935, the development of the electron microscope enabled Wendell Stanley to be the first scientist to crystallize the structure of the tobacco mosaic virus and discover that it is composed of RNA and protein. Further, in 1943 Stanley was able to isolate the Influenza B virus, which contributed to the development of an influenza vaccine. Stanley was awarded the 1946 Nobel Prize for his discoveries that unlocked the mystery and nature of viruses which had puzzled scientists for over 40 years and advanced the science of virology.6–10

Viruses are the smallest among all microbes.8–10 There are two categories of viruses, based on general composition: viruses formed from only a nucleic acid, either RNA or DNA, and a protein coat known as a capsid. Viruses formed with a nucleic-acid packed capsid surrounded by a lipid layer are called enveloped viruses.8,10 The viral envelope is a small portion of phospholipid membrane obtained as the virion buds from a host cell. The viral envelope may either be intracellular or cytoplasmic in origin.8–10

The interior of the capsid is not filled with cytosol, as in a cell, but instead it contains the bare necessities in terms of genome and enzymes needed to direct the synthesis of new virions. Each capsid is composed of protein subunits called capsomeres made of one or more different types of capsomere proteins that interlock to form the tightly packed capsid. Viruses vary in the shape of their capsids, which can be either helical, polyhedral, or complex. Sometimes the capsid is surrounded by an additional spiky coat called the envelope. A helical capsid forms the shape of the tobacco mosaic virus, which is a naked helical virus, and of the Ebola virus, an enveloped helical virus.8–10

Extending outward and away from the capsid on some naked viruses and enveloped viruses are protein structures called spikes. At the tips of these spikes are structures that allow the virus to attach and enter a cell, like the influenza virus hemagglutinin spikes (H) or enzymes like the neuraminidase (N) influenza virus spikes that allow the virus to detach from the cell surface during release of new virions. Influenza viruses are often identified by their H and N spikes; of particular interest is the H1N1 influenza virus, which was responsible for the pandemics in 1918 and 2009, H2N2 for the pandemic in 1957, and H3N2 for the pandemic in 1968.9,10

Viruses only exist to make more viruses. Viruses do not metabolize, grow, or respond to stimulus; however, they do reproduce, but only by infecting cells and taking over the host cell’s machinery, which allows for normal replication of DNA or RNA, and this produces proteins. Viruses evolve, like other living organisms. DNA and RNA are molecules whose main function is to carry information in a stable as well as an organized manner to easily enable replication.9,11 The genetic material of a virus tells the cell which proteins to make to produce more viruses and it is duplicated into every individual viral protein produced by an infected cell. Viruses will often evolve along divergent paths and with different strains to become better fits to different environments, such as different host species or cell types.8,10

Viruses can infect every type of host cell, including those of plants, animals, fungi, protists, bacteria, and archaea. Most viruses will only be able to infect the cells of one or a few species of organism. Viruses can be transmitted through direct contact, indirect contact with fomites, or through a vector as illustrated by the example of an animal that transmits a pathogen from one host to another.8,10 In humans, a wide variety of viruses can cause various infections and diseases. Some of the deadliest emerging pathogens in humans are viruses, yet we have few treatments or drugs to deal with viral infections, making them difficult to eradicate. Viruses that can be transmitted from an animal host to a human host can cause zoonoses.5,10

The virus particle attaches to the host cell before penetrating it. The virus then uses the host cell’s machinery to replicate its own genetic material. Once replication has been completed the virus particles leave the host by either budding or bursting out of the cell. As the newly formed viral particle pushes against the host cell’s plasma membrane, a portion adheres to it. The plasma membrane envelopes the virus and becomes the viral envelope.8,10 The virus is released from the cell. This process slowly uses up the host’s cell membrane and usually leads to cell death. The virus particles burst out of the host cell into the extracellular space, resulting in the death of the host cell. Once the virus has escaped from the host cell it is ready to enter a new cell and multiply.8,10

3. H1N1 flu and flu pandemic of 1918

The 1918–1919 influenza pandemic was the most devastating epidemic in modern history.11–23 Although a great deal of evidence indicates that it is unlikely the 1918 (H1N1) influenza virus originated in and spread from Spain, that influenza pandemic will always be known as the Spanish flu. The “Spanish Influenza” pandemic is the infectious disease event associated with the highest mortality burden in recent history, with global mortality burden estimates ranging from 20 to 50 million deaths.11–21 The pandemic was coined “Spanish Influenza” because the Spanish press widely publicized the outbreak in its early stages, as significant increases in respiratory mortality were reported in several Spanish provinces during May–June 1918.11–21 In contrast, the rest of Europe censored all news relating to the pandemic for fear of a decline in troop morale in the midst of World War I.11–21 A characteristic feature of the 1918 influenza pandemic was the disproportionate increase in mortality rates among young adults relative to pre-pandemic years, consistent across populations with different geographic, demographic, and socioeconomic backgrounds.11–21

Swine influenza was first described in the 1918 pandemic and made a resurgence in April 2009 in the form of a triple-reassortant influenza A virus, which was composed of a combination of human, swine, and Eurasian avian strains.25 As evidenced in previous influenza pandemics, young adults and children aged <24 years were the population most affected. Definitive diagnosis has been limited by the inability of conventional influenza testing to distinguish among influenza A subtypes; however, the surge in pandemic cases clearly emerged at the end of the annual influenza season in the northern hemisphere.26

Influenza A (H1N1) virus, a genetic reassortment of endemic strain of human flu, avian flu, and swine flu, with an inherent ability to mutate continuously, has developed a subtype which is causing the present flu in humans.22 During May 2009, twenty-nine countries which were affected by H1N1 officially reported 4379 cases, with Mexico accounting for 1626 affected and 45 deaths, United States accounting for 2254 affected (02 deaths), Canada reporting 280 cases with 1 death, and Costa Rica reporting 8 cases with 1 death. The World health Organization declared a Pandemic Alert V on April 29, 2009 and created a reserve of 10,000 million doses of anti-viral drugs as a regional stockpile. Accordingly, stockpiling of ten million doses of anti-viral drugs, surveillance at airports, isolation with strict enforcement of quarantine procedures, sustained supply of respiratory masks and other personal protective equipment, and deployment of rapid response teams were some of the activities that were undertaken proactively by the Indian Government.25–27

da Costa et al. have described the clinical similarities between the H1N1 and COVID-19 cases.28 They pointed out that COVID-19 cases tend to be more severe as they often evolve into SARS, with these patients needing hospital care for several days, mainly because they need mechanical ventilation support.28 They have made the following observations: in H1N1, the incubation period was 1.5–3 days, but
sometimes it extended to 7 days, whereas for COVID-19, the incubation period is usually longer (2–14 days), with an average of 5.2 days. The clinical picture usually tends to start with fever and cough that is sometimes accompanied by a sore throat and myalgia. Lastly, for the laboratory diagnosis of both influenza A and SARS-CoV-2, clinical samples including a swab of the throat or nasopharynx and a saliva sample or aspirate of the lower respiratory system are indicated, with the collections being representative of the acute phase of the disease.

Further, Yin et al. demonstrated that on Computer Tomography significant differences between influenza A (H1N1) pneumonia and COVID-19 pneumonia were the following: findings of linear opacification, crazy-paving sign, vascular enlargement, pleural thickening, and pleural effusion were more common in patients with COVID-19 pneumonia, whereas bronchiectasis and pleural effusion were more common in patients with influenza A (H1N1) pneumonia. Finally, Matta et al. compare and contrast the public mitigating measures between the 1918 Pandemic and the Covid-19 pandemic.

First, they assert that confusion and the public mitigating measures implemented to contain the 1918 Pandemic affected the day-to-day lives of citizens, whereas during the Covid-19 pandemic various businesses have been affected due to the Covid 19 pandemic, especially the tourism/airline/hospitality industries, etc. Matta et al. reveal that the 1918 virus could spread to other tissues beyond the respiratory tract, resulting in more widespread damage. Moreover, the virus had mutations that allowed it to be more easily transmitted between humans. Unlike in 1918, scientists today can evaluate the pandemic potential of new viruses, both in animals and humans.

4. History of vaccines

The four kinds of human immunity result from an individual’s adaptive immune system. For any given disease, an individual may be considered immune or susceptible depending on their ability to mount an effective immune response upon exposure. A given population is likely to have some individuals who are immune and other individuals who are susceptible. If a population has very few susceptible individuals, even those susceptible individuals will be protected by a phenomenon called herd immunity. Herd immunity has nothing to do with an individual’s ability to mount an effective immune response; rather, it occurs because there are too few susceptible individuals in a population for the disease to spread effectively.

Vaccination programs create herd immunity by reducing the number of susceptible individuals in a population. Even if some individuals in the population are not vaccinated, if a certain percentage is immune either naturally or artificially, the few susceptible individuals are unlikely to be exposed to the pathogen. However, because new individuals are constantly entering populations, for example through birth or relocation, continuing vaccination programs are necessary to maintain herd immunity.

The sciences of vaccinology and immunology were created only two centuries ago by Jenner’s scientific studies on the prevention of smallpox through inoculation with cowpox virus. This rudimentary beginning was expanded greatly by the giants of the biomedical sciences in the late 19th- and early 20th-centuries. The period from 1930 to 1950 was a transitional era, with the introduction of chick embryos and minced tissues for propagating viruses and rickettsiae in vitro for vaccines. Modern vaccinology began about 1950 as a continuum following notable advances made during the 1940s and World War II. Its pursuit has been based on breakthroughs in cell culture, bacterial polysaccharide chemistry, molecular biology, and immunology, which have yielded many live and killed viral and bacterial vaccines plus the recombinant-expressed hepatitis B vaccine.

The science of vaccinology was established in the late 18th and early 19th centuries by ‘giants’ of the time, including Jenner, Pasteur, Koch, von Behring, Ehrlich, and Lister. Relatively little technological advance was made in the period leading to World War II, except for yellow fever and influenza vaccines. An expansive view of a modern healthcare provider would infer that the keystone of their training is health science. In public health science, if evidence that something helps, and it is unlikely to do harm there is little excuse for not recommending the act. Usually, this behavior makes sense, healthcare providers do not want to overturn established science based on an assertion or speculation.

5. Covid-19 vaccines

The novel betacoronavirus, SARS-CoV-2 (severe acute respiratory syndrome coronavirus 2), has spread across the globe at an unprecedented rate since its first emergence in Wuhan City, China, in December 2019. The first confirmed instance of person-to-person spread of COVID-19 in the United States was reported on January 30, 2020. Scientific communities around the world have been working rigorously and racing against time to develop a potent vaccine to combat COVID-19, employing conventional and novel vaccine strategies. Common human coronaviruses, including types 229E, NL63, OC43, and HKU1, usually cause mild to moderate upper-respiratory tract illnesses, like the common cold. The new coronavirus was named COVID-19 by the WHO. The 229E (alpha coronavirus) is a common cause of upper/lower respiratory infections. However, coronavirus species have been identified over 50 years ago, including the OC43 (beta coronavirus), a common cause of upper/lower respiratory infections; also identified over 50 years ago was the NL63 (alpha coronavirus), a common cause of upper/lower respiratory infections. The HKU1 (beta coronavirus) was identified after the SARS outbreak of 2003—first detected in Hong Kong in 2005, causing upper respiratory illness, identified after SARS outbreak of 2003 MERS-CoV (the beta coronavirus that causes Middle East Respiratory Syndrome, or MERS), the SARS-CoV (the beta coronavirus that causes severe acute respiratory syndrome, or SARS), and finally the SARS-CoV-2 (the novel coronavirus that causes COVID-19).

A patient may be infected with a common coronavirus (229E, NL63, OC43, or HKU1); however, that does not mean they are infected with the 2019 novel coronavirus. There are different tests to determine if you are infected with the 2019 novel coronavirus. COVID-19 is caused by a betacoronavirus in the same subgenus as the severe acute respiratory syndrome (SARS) virus (as well as several bat coronaviruses), but in a different organism derived from a common ancestor species.

Operation Warp Speed’s goal was to produce and deliver three hundred million doses of safe and effective COVID-19 vaccine by January 2021. The U.S. Health and Human Services has provided massive funding (nearly $10 billion) for development, manufacture, and distribution of COVID-19 vaccines, therapeutics, and diagnostics, with the hope of speeding up the process safely. In May 2020, fourteen vaccine candidates were evaluated and three were selected to receive targeted support and manufacturing preapproval or authorization to have the vaccine available as quickly as possible. A number of COVID-19 vaccines have been approved and are in human clinical trials in the United States as of October 27, 2020. Covid-19 vaccine side effects and warnings are described as short-term side effects that were observed in leading vaccine trials and post marketed vaccine administration and include: Injection site pain and redness 84%, Fatigue 63%, Myalgia, or muscle pain 14.8%, Arthralgia or joint pain 24%, Headache 55%, and Fever 14%. On December 8, 2020, the United Kingdom reported that two patients who were injected with Pfizer’s recently approved coronavirus vaccine had to be treated for serious adverse reactions, which has led to warnings that those with “significant” allergies may not be able to get the vaccine. Both patients had a history of allergic responses, and each carried an adrenaline shot EpiPens.

6. Interprofessional approach to mitigate Covid-19 vaccine hesitancy

The interprofessional team, many who find themselves on the frontline can act as patient educators as well as vaccine administrators...
who may address vaccine hesitancy. This team can implement effective communication strategies by informing patients about the safety and efficacy of the Covid-19 vaccine; while addressing patients concerns and fears, and dispel common myths and misconceptions, allowing patients to make informed decisions.

The members of the healthcare interprofessional team may include doctors, specialists, nurses, pharmacists, social workers, and veterinarians remain significant influencers on vaccine decisions especially when the team is in a primary care role. Each member of this team can overcome vaccine hesitancy by providing facts about the Covid-19 vaccine, including efficacy and safety data. Most importantly this team can also help dispel common myths and misconceptions about the Covid-19 vaccine and address the patient concerns and fears. The interprofessional team should appreciate that a patient’s family is the most powerful motivator for vaccine acceptance as opposed to moralizing or lecturing Americans.5,25

When the members of the team has a conversation about Covid-19 vaccine hesitancy, they need to include a conversation about vaccine need and the threat and seriousness of the disease, to include the long-term effects, long after the immediate risk of serious illness and death that far exceeds influenza. The members of the team while working together must acknowledge and understand that a person’s risk assessment does not come from fact but from their experience. Further, the members of the team can assist each other by allowing for developing a structure to allow more people to share their experience with Covid-19 to allow for the disease to become real for the unvaccinated patient.

Members of the interprofessional team working as one may be able to: (1) Tailor messages for a specific audience (population), (2) Explain the benefits of getting the vaccine, not just the consequences of not taking the vaccine, (3) Focus on the need to return to normal and reopening the economy, (4) Avoid judgmental language when talking about or to people who are worried about taking the Covid-19 vaccine, and (5) Acknowledge the person’s concern or skepticism and offer to answer their questions.5,54 Moreover, the team members can connect with both vaccine-hesitant and pro-vaccine individuals through storytelling in the examination room or pharmacy.55 The team can encourage patients who are already confident about their choice to vaccinate to speak up about their decision and be a part of trusted online communities.56 Also, the members of the team can work collaboratively with local religious and community leaders within the context of healthcare professional societies, academia, global agencies and others who support religious and community leaders within the context of healthcare professionals.33,57

As a team the members can accentuate their counter to vaccine hesitancy information systems.58 A final avenue members of the interprofessional healthcare team may use to influence the barriers to Covid-19 vaccine hesitancy is to appreciate, acknowledge, and realize both the “5C” and “5A” models of factors influencing vaccine hesitancy and utilize these models to break-through the barriers to covid-19 vaccinations.55,56,57 (Table 1) An observation the members of the interprofessional team may glean form reviewing these two models is that given the seriousness of the Covid-19 pandemic; that the majority of these factors have been mitigated by the federal government.55,56,57 The ability for individuals to access the vaccine is enhanced by federal stakeholders. The Covid-19 vaccine as well as boosters are free and therefore affordable. Over the last year, media campaigns have allowed for the patient’s ability to understand the need for and availability of Covid-19 vaccines.

Targeted campaigns have been initiated and continue to increase uptake through trusted healthcare services such as primary care and local pharmacies.54,59,60 A major barrier for the Covid-19 vaccine has been social media platforms. It is essential that the public needs to be empowered to report misinformation despite national news networks who allow for entertainment to dominate facts. Federal stakeholders have launched cultural competent, multilingual, visually appealing messages in communities with high vaccine hesitancy. Finally, the prioritizing of healthcare professionals from ethnic minorities has taken place to increase the community’s trust in the Covid-19 vaccine.

7. Conclusion

This review offers a factual foundation to healthcare providers to assist in framing strategies to mitigate vaccine hesitancy and achieve herd immunity to combat the deadly Covid-19 pandemic. Overcoming miscommunication and polarization will require an interdisciplinary approach to mitigate Covid-19, grounded in historical factual and objective data. In this paper, an overview of the discovery of viruses and their molecular structures was first presented. Second, a historical perspective was offered, comparing the differences between the 1918 flu pandemic and the current Covid-19 pandemic. Lastly, an overview for proposed techniques and methods to counter and mitigate covid-19 vaccine misinformation that may be used by an interdisciplinary team will be offered narratively and graphically.

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