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Hesitancy to get vaccinated against COVID-19 and how it might be overcome

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One evening, as a young teenager in the 1960s, I watched a televised movie entitled “The Story of Louis Pasteur”. It impressed me so much that I began to seriously consider pursuing a career in medicine or one of the biological sciences. I subsequently chose the latter career path and, several years, later I received my Ph.D. degree in microbiology and immunology. The movie was a classic Hollywood production originally released for public viewing in 1937 and was a “Best Picture” nominee. The lead character was the accomplished and well-known actor, Paul Muni, who won a “Best Actor” award from the motion picture industry for his outstanding performance in his portrayal of Pasteur—considered by many in the medical and scientific community to be one of the founding fathers of modern microbiology and immunology. He was a chemist by training (as well as being a self-made accomplished artist), and he coined the term “microbe”, based on his many discoveries and drawings of what he observed under the microscope often to the displeasure of some of his contemporaries, especially the medical establishment. Many of its members were reluctant initially to go along with some of his experimentally derived ideas and concepts, based in part because they seemed quite radical at the time given the limitations of biomedical science 150+ years ago. Despite possibly putting his career and reputation in jeopardy by occasionally going beyond acceptable medical ethics when his work involved certain types of human studies, which were less restrictive then than they are now, Pasteur persevered working tirelessly and with much conviction to prove his sceptics wrong, and indeed he showed through careful experimentation that things (minute living organisms) not visible to the naked eye can indeed cause disease. By doing so, he debunked the previously held belief, by some of his counterparts, in the theory of “spontaneous generation”, and is credited with
providing us with the germ theory of disease. Eventually, many of his original sceptics started to accept his ground-breaking findings as being true.

While some parts of the movie may have been slight exaggerations and overly dramatic renditions of actual events of those described in Pasteur’s biography (Vallery-Radot, 1929), from which the movie got much of its material, it nonetheless had quite a number of heart-warming and inspiring scenes to go along with scientifically accurate pieces of information. Foremost among Pasteur’s many life-altering achievements was his development of two diverse vaccines—one for preventing anthrax in livestock animals, and the other for preventing/treating human rabies (Fig. 1)—both being dreaded diseases having very high levels of mortality, both then and now, in the absence of appropriate medical intervention. With these historical accounts highlighting some of the key events in Pasteur’s career as the background, it is amazing and at times disturbing to observe how certain aspects of this past scenario from another era is playing out closely today in the wake of the current COVID-19 pandemic. In this regard, many people, mostly outside the medical community, but a significant few within, have refused or remain hesitant to receive any of the available COVID-19 vaccines. Given the seriousness of COVID-19 with its life-threatening potential and the worldwide emergence of multiple highly contagious/virulent mutants, such as the Delta variant, of the etiologic agent SARS-CoV-2,
this reluctance to get vaccinated is very difficult to understand and has led to tragic results. In addition, the vaccine options against COVID-19 are multiple (Table 1) and involve either the use of a purified mRNA component of the virus or a viral vector formulation, with both types having excellent safety and efficacy results based on extensive clinical trials and, as of September 2021, have been approved or are nearing full approval from the FDA for use in the United States. In July 2021, as part of a nationally televised briefing (White House COVID-19 Response Team, 2021), highly regarded public health officials from the U.S. Centers for Disease Control and Prevention (CDC) and the National Institutes of Health provided updates on a new surge nationwide in hospitalizations and deaths due to COVID-19, and have pointed out correctly that we are now entering into a “pandemic of the unvaccinated”. This comment by the director of the CDC is supported by data showing that in some locations >99% of the current wave of victims developing serious disease are among the unvaccinated, leading to the obvious conclusion that these negative outcomes could have been avoided if these victims had chosen to receive the vaccine beforehand. This surge in cases has continued and even increased in many locations in the months that followed.

What are the reasons for such hesitancy/resistance or for some of the obstacles to get vaccinated? Here are some major examples (summarized in Table 2):

- Let’s take a wait and see attitude—observe how vaccine recipients respond/react to the vaccine, in terms of making sure that the vaccine is safe and there will not be any negative outcomes, and/or that it really works;
- Fear of needles or being jabbed and having to endure a possibly painful injection—this is mostly a psychological or behavioural reaction that may have been triggered by prior unpleasant experiences when receiving injections for various other medications or from during a routine blood draw;
- Difficulty in gaining access to vaccine sites by the elderly, the severely disabled and impoverished people, or in mobile inoculation units being able to safely reach these home-bound or institutionalized people;
- Exercise our “free will” or constitutional rights—in the United States these claims are often invoked by referring to the first amendment of the US Constitution, and falling in line with not having to be compelled to take the vaccine as a requirement to participate in the activities associated with any organization, location or function, such as a governmental agency, an academic institution, transportation venues, sport teams, sport/recreational, entertainment or indoor dining facilities, places of worship, or an employer;
- Moral beliefs held by members of certain religious groups that are against various forms of medical intervention; and perhaps the most egregious of them all;
- Believing or being swayed by the many forms of misinformation/disinformation or conspiracy theories, such as stating that the science behind the vaccine’s development and success is fake, or not to be trusted, or we are being used as “guinea pigs”, which is being spread over various Internet social media platforms and some cable news networks by mostly unscrupulous individuals, some of whom claim to have expertise on medical matters, but actually don’t.
| Vaccine manufacturer | Type of vaccine | Number of doses | Storage method | Efficacy | Authorized for use in the U.S. | EUA pending final approval | Serious adverse events |
|----------------------|-----------------|-----------------|----------------|----------|-------------------------------|---------------------------|------------------------|
| Moderna              | mRNA            | 2               | 4–10 °C        | >94%     | Yes                           | Yes                       | Rare                   |
| Pfizer               | mRNA            | 2               | −80 °C         | >95%     | Yes                           | Yes                       | Rare                   |
| Janssen              | Viral vector    | 1               | 4–10 °C        | 66.3%    | Yes                           | Yes                       | Yes                    |
| Astra-Zeneca         | Viral vector    | 2               | 4–10 °C        | 63%–84%  | Yes                           | Yes                       | Yes                    |

*aInformation that was available as of August 2021.

*bIn the U.S., an EUA (Emergency Use Authorization) was originally given for these vaccines for people aged >16, which was subsequently expanded to >12 years of age.

*cAs of October 2021, additional booster injections were highly recommended for these vaccines by the FDA and CDC.

*dIn the U.K., an EUA no longer applies for the Pfizer, Moderna and Astra-Zeneca vaccines which now have been granted final approval for use. In the U.S. as of August 2021, the Pfizer vaccine was given FDA approval, while the other 3 are undergoing further evaluation for full approval by the FDA.

*eMilder and temporary forms of myocarditis and pericarditis have occurred in a small number of young adults with these vaccines.

*fBlood clots have been reported in a small number of female vaccine recipients <50 years of age with these vaccines.
It is important to realize that the anti-vaccine sentiment is not limited to the United States, but it is a global problem (Hornsey, Harris, & Fielding, 2018) and had been well established as a recurring theme multiple times prior to the onset of the current pandemic often with devastating consequences. Even certain political leaders and other professionals of varying degrees of influence have joined the anti-vaccine bandwagon. This is reminiscent of what has occurred in the pre-COVID days with certain other infectious diseases (reviewed in Smith, 2017), where “herd immunity” which can develop when a sufficient number of people survive a natural infection, has been invoked as the only mechanism whereby the spread of SARS-Cov-2 can be blocked leading allegedly to its eventual disappearance within the general population. Evidence in support of the pervasiveness and effects of these untenable reasons against the COVID-19 vaccine comes from recently published data put forth by the Kaiser Foundation (Hamel, Kirzinger, Munana, & Brodie, 2021), and these are as follows.

In terms of demographics, 27% of the people in the United States remains vaccine-resistant, saying they probably or definitely would not get a COVID-19 vaccine even if it were available for free and deemed safe by scientists and public health officials. Vaccine hesitancy is highest among those who identify as belonging to a certain political party (42%), those in the 30–49 age group (36%), and rural residents (35%), especially those living in certain parts of the Midwest and Southeast sections of the United States where less than 50% of the population has gotten vaccinated, and where concurrently there has been an alarming new surge (as of July/August 2021) in COVID-19 cases requiring hospitalization. In addition, 35% of African American adults (a group that has had to bear a disproportionate burden of the effects of the pandemic) say they definitely or probably would not get vaccinated, citing as major reasons that they don’t trust vaccines in general (47%) or that they are worried they may get sick with COVID-19 from just the vaccine alone (50%). This situation suggests that messages combatting particular types of misinformation may be especially important for increasing vaccine confidence among this group. Perhaps most astonishingly, are the data showing that as much as one third of those who say they are considered to be essential workers and 29% of those who perform services in a health

Table 2 Characteristics of the anti-COVID vaccine phenomenon.

| Reason                                | Basis or source                                                      |
|---------------------------------------|----------------------------------------------------------------------|
| Delay in getting vaccinated           | Vaccine must be fully approved                                       |
| Fear of adverse events                | Some serious side effects have been reported                        |
| Anxiety/fear of inoculations          | Behavioural/psychological reaction                                  |
| Inaccessibility to vaccine sites      | Problem with logistics or infrastructure                             |
| Freedom of choice/expressions         | Political convictions or posture                                     |
| Moral or religious objections         | Misguided religious teachings or upbringing                          |
| Vaccine is not safe or effective      | Misinformation/conspiracy theories spread mostly by disreputable, non-scientific/non-medical people |
| Experimental data is fake             |                                                                      |
care delivery setting will not take the vaccine. The resistance of people to receive COVID-19 vaccines is even more perplexing given the excellent track record of other vaccines, some of which have been with us for nearly 100 years as part of routine preventive care. These have been designed to protect us against smallpox, tuberculosis (with BCG) and polio, followed, more recently, with the DPT (diphtheria, pertussis, tetanus), MMR (measles, mumps, rubella), and chickenpox vaccines. It should be noted that, in most jurisdictions, the latter three childhood vaccine combinations are required before young children can start school at the elementary level.

So, in light of the foregoing, how would a modern-day Pasteur react to the relatively high level of resistance to get vaccinated against COVID-19, and what might be a solution to this problem? Given his personality for scientific rigour combined with the overwhelming evidence showing the vaccine’s safety (with few exceptions) and efficacy, he probably would be highly disappointed with the overall public response to getting vaccinated, especially by those who remain unconvinced on why the vaccine is so important from a public health perspective, and why there is such lack of confidence given the many advances made in medicine over the past 100+ years. He would also be very outspoken and adamant against the sceptics who perpetuate false or misleading information about the vaccine. If requested (and this would seem highly likely given his prestige), he would probably be making frequent public appearances on various news programs similar to what the current wave of public health medical experts are doing now. He might even have his own podcast where he could dispense valuable information to the misinformed or uninformed public and reinforce the importance of getting vaccinated. He would probably find it amusing and perhaps a bit misguided that incentives, such as monetary and other rewards, are being offered in certain parts of the United States to try to get people vaccinated, even though vaccines are being administered free of charge in most, if not all, locations. To him, it would seem like deja vu in terms of what he experienced with the obstacles that he had to face in dealing with his disbelieving scientific and medical contemporaries, when he was making his groundbreaking and life-changing discoveries in the late 1800s, at a time when complex biomedical processes were still poorly understood, and initially underappreciated.

Another variable that awaits more clarity is whether and/or when patients, who may have acquired some form of natural immunity after recovering from COVID-19, should get vaccinated, if at all. This provokes the following question: are they no longer susceptible, or are less vulnerable, to serious disease, after re-exposure to SARS-CoV-2, that getting vaccinated would be unnecessary? It is believed, however, that solid immunity against COVID-19 may gradually wane (Centers for Disease Control and Prevention, 2021a), and thus booster injections with one of the available vaccines may still be necessary in order to provide optimal protection against re-infection. A somewhat related recommendation, also coming from the CDC, states that, starting in September 2021, another or third booster shot will have to be given to earlier vaccines to maximize vaccine-induced protection and prolong its durability, and that these booster shots will be offered for all Americans, who had
received their last (second) dose or had recovered from a prior infection with SARS-CoV-2 at least 8 months previously.

Beyond what a contemporary Pasteur might be inclined to do, what else could be done? Various organizations have made numerous suggestions, along these lines, including several promoted and offered by the CDC (Centers for Disease Control and Prevention, 2021b), and a few more that this author will offer. They include the following services that could be implemented. A large number of healthcare professionals and qualified scientists (primarily microbiologists and immunologists) are needed to support COVID-19 vaccination efforts nationwide. It is important they receive the necessary training to effectively meet the demands of their roles. Training must be ongoing as new COVID-19 vaccines become available and as vaccine recommendations evolve and more is learned about the vaccines and how to improve and maintain the vaccination process. In terms of educating the lay public, they are essential to ensuring that the American population is vaccinated safely as soon as possible, based on a true understanding on why this is an important undertaking. Furthermore, as parents’ most trusted source of information on vaccines, paediatric healthcare professionals play a critical role in helping parents and guardians understand the importance of COVID-19 vaccination and assuring them that COVID-19 vaccines are safe and effective, and that they are important steps in protecting their children’s health (both physical and mental). Parents need to be reminded that fully vaccinated people are less likely to spread the virus that causes COVID-19. Getting all family members 12 years and older (and when recommended, children less than 12 years of age) vaccinated can protect other family members around you, including people at increased risk for severe illness from COVID-19. Students also need to be reminded that, after they are fully vaccinated, they will be able to resume many activities with family and friends, such as going to parties, weddings, graduation exercises, and other social gatherings that they have missed due to prior restrictions that were imposed on everyone at the height of the pandemic.

As part of the education process, students should be contacted and encouraged to learn more from reliable sources derived from rigorously peer-reviewed articles, especially those found on medically-based Internet sites, such as PubMed, reputable blog and social media posts, properly mentored student-driven publications and social groups. A feedback mechanism should be created in order for students to ask questions and get a meaningful response quickly about COVID-19 vaccination, such as by using either e-mail, online video conferences (via Zoom, Skype, Facetime or any other similar provider), or by phone number. Any student concerns or questions should be proactively addressed and the spread and harm of misinformation should be countered by sharing credible and accurate information. Students, as well as other participants, should be warned about relying on unregulated or non-scientifically based sources of information that are circulating on the Internet or other similar platforms. Students should be warned about the dangers caused by misinformation and disinformation, and health literacy should be promoted as a means to be fully informed in understanding the benefits of being vaccinated as well as the negative outcomes that could arise if the vaccine is not received.
Although much of the preceding suggestions pertain mostly to the adolescent age group, similar interventions should also be considered for those attending colleges and universities after completing high school, to reinforce and update what students had learned previously about vaccines. Hopefully, as this younger and now well-informed generation matures into adulthood, they will be representative of a population having much greater acceptance and less resistance to getting vaccinated when deemed necessary by experts in the health care community for both now and, just as important, later on, when other future serious outbreaks may arise.

As an additional approach, schools, at both the elementary and high school level, can also take the initiative by recruiting the suitably trained medical professionals or scientists to come to their classrooms, when this becomes allowable, and supplement the curriculum by providing a better understanding of the vaccine process. In order to accomplish this task more effectively, local health departments, especially those within the jurisdiction of the schools, should provide the schools with a registry of trained personnel who would be willing to come to the schools and share their knowledge and expertise pertaining to the COVID-19 vaccines with the students, along with the teachers and administrators, as well as answering any questions or concerns that students may have on this topic, preferably at no additional cost to the school district.

Another possible program worth considering would be for medical schools to offer a short course on the vaccine process to be attended by elementary and high school teachers to better educate them on this topic with all of its subtle nuances. Upon completion of the course, the teachers would receive a certificate of recognition (similar to CME credits) showing that they had participated successfully in this learning exercise. As such, they would be well equipped to return to their respective schools with what they had learned about vaccines and share this information with their students, during one of their standard classroom sessions or remotely (typically when the subject of “Biology” is being taught or during “Health Class”). Presumably, the best time to give this course would be during the summertime when most medical schools are less active with their didactic responsibilities as part of the regular pre-clinical curriculum, and where most of the first- and second-year medical students are not on campus due to being on an extended break for their summer vacation. In so doing, this would not impose an undue burden on the school’s infrastructure or their faculty who would be providing this pertinent information to the participants in this program.

In conclusion, people should not be fearful of receiving any of the available anti-COVID-19 vaccines. The benefits of getting jabbed far outweigh the minimal risks of having an adverse or serious outcome. Historically, vaccines have had an excellent track record in terms of saving lives, reducing morbidity caused by a wide variety of infectious agents, and easing the burden of the health care community and infrastructure. In addition, the various and somewhat innovative interventions put forth in this chapter, that are designed to educate people about the COVID-19 vaccines, with the goal of getting as many people vaccinated, especially towards dealing with the existing anti-vaccine trend, may be seen as a daunting task. Accordingly, it will require a
well-organized and coordinated effort, a well-equipped infrastructure and co-operative interactions among all parties involved in order to make these interventions a success and not just wishful thinking. Such opportunities to try to gain much wider vaccine acceptance would perhaps be in keeping with the often-quoted comment by the legendary Pasteur of: “dans les champs de l’observation, le hasard ne favorise que les esprits préparés” (“in the field of observation, chance favours only the prepared mind”) (Pasteur, 1939), in honour of him as we approach in the coming year of 2022 the bicentennial of his birth.

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