INTERNATIONAL SOCIETY FOR INFECTIOUS DISEASES

GUIDE TO INFECTION CONTROL IN THE HOSPITAL

The 2019 Coronavirus Disease (COVID-19) Vaccines

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KEY ISSUE

COVID-19 disease, caused by the SARS-CoV-2 virus, emerged in Wuhan, China in December 2019 and due to its very rapid global spread, it has been declared a Public Health Emergency of International Concern (PHEIC) [1,2]. Like other coronaviruses, SARS-CoV-1 and MERS-CoV, COVID-19 has attracted major global public health attention due to its novelty, high infectivity, pathogenicity, and lack of effective therapeutic or preventive interventions. Despite all global public health efforts including the implementation of aggressive nonpharmaceutical interventions (NPIs), the novel coronavirus has been able to spread globally causing over 96 million cases and leading to over 2 million deaths in 223 countries, areas, or territories as of mid-January 2021[3]. To date, corticosteroids such as prednisone, hydrocortisone, and dexamethasone, which are relatively inexpensive and readily available drugs have been one of the few drugs shown to be effective in the treatment of COVID-19 patients. In the large multicenter prospective, open-label controlled RECOVERY trials using corticosteroids in patients with COVID-19 infection, in those receiving invasive mechanical ventilation, mortality among those treated with dexamethasone was one-third that in those receiving usual care, and in those receiving oxygen without mechanical ventilation mortality was reduced by one-fifth. In addition, multiple observational studies also suggest that corticosteroids may be helpful in the management of the multisystem inflammatory syndrome, an uncommon but very serious complication of COVID-19 in children. The only hope to halt the spread of SARS-CoV-2 is the development of an effective vaccine that would be able to prevent infection, disease, or death from severe disease with multisystem inflammatory syndrome.

KNOWN FACTS

- Coronaviruses are widespread and are the causative agents of a variety of diseases in mammals, including respiratory, hepatic, enteric, and neurologic pathologies of differing severity in species ranging from humans to domesticated and companion animals (HCoV-229E, -OC43, -NL63, and -HKU1).
- Among the four structural proteins of COVID-19 [spike (S), nucleocapsid (N), membrane (M), and envelope (E)], the S protein is the one responsible for viral entry and pathogenicity and is the target for all vaccine production efforts.
- Coronavirus vaccines induce both humoral and cellular immune responses and both are important for protection from COVID-19.
- The more severe the natural COVID-19 infection, the higher the immune response and the longer the protection[4].
- Multiple studies indicate that neutralizing antibodies decline 6 months after natural infection, and it is not clear if cellular immunity would provide longer protection[5].
- Multiple key platforms for vaccine productions have been used to date for COVID-19 vaccine manufacturing, including nucleic acid (DNA and mRNA), viral vector, virus-like particle and subunit vaccines and inactivated and live attenuated virus vaccines[6].
- Chemically or physically inactivated and live attenuated virus platforms are one of the oldest and well-known vaccine platforms with many years of history of safe use in humans, while nucleic acid (DNA and mRNA) technologies which are based on plasmids or mRNA that encodes vaccine antigens, subunit vaccines, and viral vector vaccines are all considered brand new technologies and no human vaccines using these technologies have been licensed for use before COVID-19.
- Subunit vaccines often require adjuvants to increase their immunogenicity (e.g., MF59, CPG, and aluminum).

- As per data from the US FDA for the last 10 years, it takes an average 8 years to get a vaccine from initial discovery to licensure for human use. With the rapid global unified response against COVID-19, this duration has been reduced to less than 1 year[7].
- As of the first week of January 2021, there are 274 COVID-19 vaccine candidates, 215 candidate vaccines in preclinical trials, 59 in different stages of clinical testing, several licensed[8].
- Current regulatory approval of a new COVID-19 vaccine requires demonstrated safety and clinical benefit in large placebo-controlled efficacy trials.
- Older age, obesity, chronic diseases such as hypertension, cardiovascular disease, diabetes, and underlying immunocompromised state predispose patients to severe COVID-19 disease and these groups should be given priority for vaccination[9].

CONTROVERSIAL ISSUES

- The exact duration of immunity induced by the newly produced COVID-19 vaccines is still unclear and the need for future booster doses is being debated.
- Currently, there are limited data on vaccine efficacy in obese patients. In addition to the higher chance of having other comorbidities, obese patients receiving influenza vaccine seem to be twice as likely as vaccinated lean people to get the flu despite having the same level of antibodies[10].
- The robustness of immune response to the COVID-19 vaccine in the elderly and immunocompromised patients needs careful follow-up to ensure lasting immunity. The efficacy of vaccines in the elderly is suboptimal and in general, is not well studied. With advancing age, there is a general decline in the number and functionality of T cells. Aging also brings a loss of T cell receptor diversity in both CD8 and CD4 cells and

reduces T cell survival. While B cell numbers remain intact, they tend to produce less functional antibodies[11].

- Safety and efficacy data on the COVID-19 vaccine in children less than 16 years of age are still limited. Trials are ongoing to address this age group[12].
- Safety of COVID-19 vaccines in pregnant women is still undetermined and until more data are available, instructions in the vaccine product insert should be followed[13].
- The available data to date on the licensed vaccines indicate the need for 2 doses between 4-12 weeks apart, depending on the vaccine. And people should receive the same second dose as the first dose, and the different available vaccines are not interchangeable.

SUGGESTED PRACTICE

Despite the varying level of implementation of NPIs in different countries worldwide, COVID-19 continues to spread on a global scale. The arrival of effective and safe vaccines against COVID-19 is greatly anticipated as an effective countermeasure to halt the spread of the disease. Large scale vaccination of the whole community will be required to develop the needed herd immunity to prevent future outbreaks with this virus. Herd immunity is a key concept for epidemic control. It works through achieving a threshold immunity at the population level that can theoretically cut the transmission chain of COVID-19, be it obtained through natural infection or through vaccination. According to the WHO, herd immunity only works for contagious diseases and it cannot work for diseases such as tetanus, where anyone who is not vaccinated could easily be infected if exposed to the bacteria, even if everyone else around them is vaccinated and protected. It is the threshold immunity that, when high enough, can protect most if not all in a population in each geographical area for a certain time interval. The coverage rate necessary to stop transmission depends on the basic reproduction number, defined as the average number of

transmissions expected from a single primary case introduced into a susceptible population. The prevalence of transmission will decline if the fraction of susceptible hosts is low. When the proportion of susceptible hosts falls below the threshold needed for transmission; this is known as the immunity threshold.

For COVID-19, a vaccine will be needed before a population can achieve herd immunity. How many vaccine doses are needed for each country to establish herd immunity is dependent on the evidence on efficacy and what can be assumed about the average duration of vaccine protection — it will be an assumption until the findings of phase 4 trials on the duration of both protection against infection and severe disease are reported.

Even with an R0 <1, at least 60% to 72% herd immunity will be needed to interrupt the transmission chain. This is all based on 2 key variables: (1) the vaccine efficacy is 100%, and (2) the vaccine will confer lifelong or long-term immunity. Mass distribution, allocation, and administration of 100 million doses of the COVID-19 vaccine will be a mammoth job and will probably be the largest single vaccination campaign ever carried out. As the regulatory approval of different COVID-19 vaccines continues at a slow pace, with extremely limited supplies, the roll out of vaccines will be accompanied by difficult decisions about who should be prioritized to receive it. Frontline healthcare workers in all settings, long-term care residents, and older adults in other congregate-care facilities, followed by the advanced aged and people with high-risk health conditions will be given the highest priority. Not forgetting those who cannot work virtually such as police and firefighters, and people living in settings where physical distancing and other infection prevention and control measures are challenging and access to health care is reduced, including indigenous communities and people living in refugee camps[14].

SUGGESTED PRACTICE IN UNDER-RESOURCED SETTINGS

The COVID-19 disease has affected all countries, rich and poor, across the globe in varying degrees. Now that an efficacious vaccine has become available it will be needed urgently by all countries. The allocation of an approved COVID-19 vaccine will be incredibly challenging both globally and nationally. Since there are limited vaccine manufacturing facilities in low- and middle-income countries, fair distribution of extremely limited supplies of COVID-19 vaccine is likely to pose a procurement challenge. Consequently, not all people will be first in line to receive it. The WHO Strategic Advisory Group of Experts on Immunization (SAGE) has developed a values framework for the allocation and prioritization of COVID-19 vaccination. The framework articulates the overall goal of COVID19 vaccine deployment, provides six core principles that should guide distribution, and twelve objectives that further specify these principles (Table 1). To provide recommendations for allocating vaccines between countries and prioritizing groups for vaccination within each country, the Values Framework needs to be complemented with information about specific characteristics of available vaccines, the benefit-risk assessment for different population groups, the amount and pace of vaccine supply, and the current state of the epidemiology, clinical management, and economic and social impact of the pandemic.[15]

SUMMARY

On a global level and within one year of its emergence, the COVID-19 pandemic has already infected close to 100 million people and killed more than 2 million people in 223 countries and territories with no evidence of any significant herd immunity or regression in the speed of disease spread. The only positive thing to date is the rapid development of multiple effective and safe vaccines based on rigorously executed and monitored

clinical trials in multiple countries across the globe. In addition to the usual concerns over vaccine safety and efficacy, other concerns arise, including equitable access to poor and rich countries and how to allocate limited initial doses in the different countries. Substantial concerns are being raised about equity and justice because, historically, disadvantaged and minority groups have had lower vaccination rates and less access to healthcare (including newer vaccines).

There has been a global consensus on the hierarchy of groups and individuals that should be prioritized for COVID-19 vaccines, including those with the critical skills needed for the community during a pandemic, such as HCWs, police, firefighters, and military service members who anchor rapid response; individuals who experience the highest medical benefit, which combines medical need with the likelihood of protective responses to vaccination; the oldest, and those with complex comorbidities. For equity purposes, all governments globally, poor and rich, should have access to enough vaccine doses to vaccinate their healthcare workers and older people before the younger, healthier adults in rich countries are vaccinated. For the past 9 months, WHO and through the ACT (access to COVID-19 tools) Accelerator and the COVAX vaccines pillar have been able to secure 2 billion doses from five producers, with options on more than 1 billion more doses, and they aim to start deliveries in February laying the groundwork for the equitable distribution and deployment of vaccines. It is now the responsibility of governments to ensure equitable and fair distribution of COVID-19 vaccines in their own countries.

REFERENCES

1. ProMED: Undiagnosed pneumonia - China (HU): RFI; https://promedmail.org/promed-post/?id=20191230.6864153.

2. Zhu N, Zhang D, Wang W, et al. A Novel Coronavirus from Patients with Pneumonia in China, 2019. N Engl J Med 2020; 382:727–33.
3. World Health Organization. Weekly epidemiological update - 19 January 2021. https://www.who.int/publications/m/item/weekly-epidemiological-update---19-january-2021.
4. Legros V, Denolly S, Vogrig M, et al. A longitudinal study of SARS-CoV-2-infected patients reveals a high correlation between neutralizing antibodies and COVID-19 severity. Cell Mol Immunol. 2021 Jan 6. doi: 10.1038/s41423-020-00588-2. Online ahead of print. PMID: 33408342.
5. Post N, Eddy D, Huntley C, et al. Antibody Response to SARS-CoV-2 Infection in Humans: A Systematic Review. PLoS One. 2020 Dec 31; 15(12):e0244126. doi: 10.1371/journal.pone.0244126. eCollection 2020.
6. Pollard AJ, Bijker EM. A Guide to Vaccinology: From Basic Principles to New Developments. Nat Rev Immunol. 2020 Dec 22:1-18. doi: 10.1038/s41577-020-00479-7. Online ahead of print. PMID: 33353987.
7. Puthumana J, Egilman AC, Zhang AD, et al. Speed, Evidence, and Safety Characteristics of Vaccine Approvals by the US Food and Drug Administration. JAMA Intern Med. 2020 Nov 10:e207472. doi: 10.1001/jamainternmed.2020.7472. Online ahead of print. PMID: 33170923.
8. London School of Hygiene & Tropical Medicine. COVID-19 Vaccine Tracker; https://vac-lshtm.shinyapps.io/ncov_vaccine_landscape (accessed 4 January 2021).
9. Hodgson SH, Mansatta K, Mallett G, et al. What Defines an Efficacious COVID-19 Vaccine? A Review of the Challenges Assessing the Clinical Efficacy of Vaccines against SARS-CoV-2. Lancet Infect Dis. 2020 Oct 27; S1473-3099(20)30773-8. doi: 10.1016/S1473–3099(20)30773-8. Online ahead of print. PMID: 33125914.

10. Ledford H. How Obesity Could Create Problems for a COVID Vaccine. Nature. 2020 Oct; 586(7830):488–489. doi: 10.1038/d41586-020-02946-6.PMID: 33082543.
11. Soiza RL, Scicluna C, Thomson EC. Efficacy and Safety of COVID-19 Vaccines in Older people. Age Ageing. 2020 Dec 2:afaa274. doi: 10.1093/ageing/afaa274. Online ahead of print. PMID: 33320183.
12. Kamidani S, Rostad CA, Anderson EJ. COVID-19 Vaccine Development: A Pediatric Perspective. Curr Opin Pediatr. 2021 Feb 1; 33(1):144–151. doi: 10.1097/MOP.0000000000000978. PMID: 33278108.
13. Rasmussen SA, Kelley CF, Horton JP, Jamieson DJ. Coronavirus Disease 2019 (COVID-19) Vaccines and Pregnancy: What Obstetricians Need to Know. Obstet Gynecol. 2020 Dec 23; doi: 10.1097/AOG.0000000000004290. Online ahead of print. PMID: 33370015
14. Ismail SJ, Zhao L, Tunis MC, et al; National Advisory Committee on Immunization. Key Populations for Early COVID-19 Immunization: Preliminary Guidance for Policy. CMAJ. 2020 Nov 30; 192(48):E1620–E1632. doi: 10.1503/cmaj.202353. Epub 2020 Nov 3. PMID: 33144317.
15. WHO SAGE Roadmap for Prioritizing Uses of COVID-19 Vaccines in the Context of Limited Supply. An approach to inform planning and subsequent recommendations based upon epidemiologic setting and vaccine supply scenarios; 14 September 2020. https://apps.who.int/iris/bitstream/handle/10665/334299/WHO-2019-nCoV-SAGE_Framework-Allocation_and_prioritization-2020.1-eng.pdf.

Table 1. Values Framework[15]

Goal Statement	COVID-19 vaccines must be a global public good. The overarching goal is for COVID-19 vaccines to contribute significantly to the equitable protection and promotion of human well- being among all people of the world.
Principles	**Objectives**
Human Well-Being	Reduce deaths and disease burden from the COVID-19 pandemic;
	Reduce societal and economic disruption by containing transmission, reducing severe disease and death, or a combination of these strategies;
	Protect the continuing functioning of essential services, including health services.
Equal Respect	Treat the interests of all individuals and groups with equal consideration as allocation and priority-setting decisions are being taken and implemented;
	Offer a meaningful opportunity to be vaccinated to all individuals and groups who qualify under prioritization criteria.
Global Equity	Ensure that vaccine allocation takes into account the special epidemic risks and needs of all countries; particularly low-and middle-income countries;
	Ensure that all countries commit to meeting the needs of people living in countries that cannot secure vaccine for their populations on their own, particularly low- and middle-income countries.
National Equity	Ensure that vaccine prioritization within countries takes into account the vulnerabilities, risks, and needs of groups who, because of underlying societal, geographic, or biomedical factors, are at risk of experiencing greater burdens from the COVID-19 pandemic;
	Develop the immunization delivery systems and infrastructure required to ensure COVID-19 vaccines access to priority populations and take proactive action to ensure equal access to everyone who qualifies under a priority group, particularly socially disadvantaged populations.
Reciprocity	Protect those who bear significant additional risks and burdens of COVID-19 to safeguard the welfare of others, including health and other essential workers.
Legitimacy	Engage all countries in a transparent consultation process for determining what scientific, public health, and values criteria should be used to make decisions about vaccine allocation between countries;
	Employ best available scientific evidence, expertise, and significant engagement with relevant stakeholders for vaccine prioritization between various groups within each country, using transparent, accountable, unbiased processes, to engender deserved trust in prioritization decisions.