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THERAPEUTIC DIGEST

VACCINES

INNOVATIONS THROUGHOUT TIME

IN COLLABORATION WITH thinkgen

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The Power of Education in Combating Vaccine Misinformation

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As COVID-19 vaccines roll out around the world, vaccine hesitancy and misinformation have come to the forefront as major threats to public health and virus containment. While these are not new issues (the World Health Organization named vaccine hesitancy as a top 10 health threat in 2019), it is more essential than ever for clinicians to address these matters with their patients. For COVID-19 to be successfully controlled, it is estimated that 55% to 85% of the population will need to be vaccinated,[1] but a recent study of vaccine misinformation during the COVID-19 pandemic suggests that only 38% of the public surveyed in the United Kingdom and 34.2% of the public in the United States would accept a COVID-19 vaccine.[1] Furthermore, this 2021 study found that exposure to misinformation could lower intent to accept the COVID-19 vaccine in both the United States and United Kingdom.[1]

Education Neutralizes Misinformation

Tackling vaccine misinformation is a complex task, but clinicians have a strong tool in their arsenal—education for themselves and their patients.

"It's absolutely essential that clinicians address these concerns with their patients. There is no shortage of misinformation circulating on the Internet and various cable news networks. Clinicians need to combat this head on by addressing uncertainties, and most importantly, educating themselves and their patients on the facts and data surrounding vaccine safety and efficacy." said Doug Kaufman, Group Vice President of Medscape Education.

The power of education in reassuring the public is undisputable. In a 2013 study of pediatric vaccinations, researchers found that addressing vaccine concerns and providing education on vaccine safety increased pediatric vaccine completion rates by 17% in the 9 months following the educational intervention. In addition, influenza vaccination rates increased from 32% to 49%.[2] A 2015 study of adult vaccine patterns found that provider education was an area of focus in improving vaccine coverage, as recommended by the National Vaccine Advisory Committee.[3]

The Need for Clinician Education

In order for clinicians to have productive conversations with their patients and impact these trends, they must first start by educating themselves on the science and social impact.

Since January 2020, Medscape Education delivered impactful education focused on the COVID-19 pandemic through the launch of the COVID-19 Learning Center. This learning center has reached over 2 million healthcare professional learners since its inception, and recently was transformed to meet the current and urgent need of vaccine education. *Advances in Prevention and Management of COVID-19*, launched together with collaborators including the United Nations COVID-19 Communications Response Initiative, an organization also focused on combating misinformation, is a comprehensive curriculum led by a steering committee that includes several vaccine trial investigators. As a continuous professional development platform, the learning center features various types of educational programs including expert interviews, case studies, and other interventions focused on COVID-19 vaccines, treatments, diagnostics, and comorbidities.

"Through this collaborative educational effort, clinicians will have the resources they need to respond to patient questions, combat misinformation, and ease patient fears. All of these steps are critical to improving public health and encouraging community vaccination. We can get there, but we need to work together."

To learn more about the COVID-19 Vaccines Learning Center, visit https://www.medscape.org/sites/advances/covid-19.

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[1] Loomba S, de Figueiredo A, Piatek S, et al. Measuring the impact of COVID-19 vaccine misinformation on vaccination intent in the UK and USA. Nat Hum Behav. 2021;5:337-348.
[2] Suryadevara M, Bonville CA, Ferraioli F, et al. Community-centered education improves vaccination rates in children from low-income households. Pediatrics. 2013;132:319-325.
[3] MacDougall DM, Halperin BA, MacKinnon-Cameron D, et al. The challenge of vaccinating adults: attitudes and beliefs of the Canadian public and healthcare providers. BMJ Open. 2015;5:e009062.

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VACCINES

Innovations Throughout Time and During COVID-19

Vaccination is a powerful method of disease prevention that is relevant to people of all ages and in all countries, as the COVID-19 pandemic illustrates, vaccination can improve people's chances of survival, protect communities from new and reemerging health threats, and enhance societal productivity. But achieving the promise of vaccination requires much more than the vaccines themselves. It requires appropriate incentives to encourage the timely discovery and development of innovative, effective, safe, and affordable products; effective financing and delivery programs; and credible scientific leaders who can provide evidence-based policy recommendations and reassure the public about the value of the vaccines.

VACCINES THROUGHOUT HISTORY

It's hard to overstate the benefits that innovative vaccines deployed in the past five decades have had on morbidity and mortality. The incidence of vaccine-preventable diseases among U.S. children has decreased dramatically, an achievement that is attributable in part to high vaccine-coverage rates. By the 2018-2019 school year, coverage rates among kindergarteners exceeded 90% in all but two states, according to data from the Centers for Disease Control and Prevention (CDC). Four vaccine-preventable illnesses have been eliminated from the Americas: smallpox in 1971, poliomyelitis in 1994, and rubella and congenital rubella syndrome in 2015. Moreover, between 2011 and 2020, immunization programs in low-income countries saved an estimated 23.3 million lives[1].

Perhaps the most notable immunization-related accomplishment during the past half century was the eradication of smallpox, which was verified by the World Health Organization (WHO) in 1980. In addition, global cases of paralytic polio have decreased by 99.95% from the estimated 350,000 cases in 1988[2], when the global polio-eradication program was announced, and two of the three wild-type polioviruses, WPV types 2 and 3, have been eradicated.

Other important achievements during this period include the 1986 approval of the first vaccine based on recombinant technology, a hepatitis B vaccine that not only has reduced rates of infection in many countries but was also the first vaccine to reduce cancer risk. In 1987 the first polysaccharide-protein conjugate vaccine was licensed; since then, the incidence of invasive Haemophilus influenzae type b disease among children has fallen dramatically. In 2009, a vaccine for Neisseria meningitidis group A became the first licensed vaccine specifically designed for certain people in low-income countries.

Achieving broad population health benefits associated with vaccination requires effective policies that create incentives for vaccine development, ensure financing of vaccines, and improve access. After a measles outbreak in 1989–1991, the U.S. Vaccines for Children Program was authorized in 1993 to ensure that eligible children would have free access to all CDC-recommended vaccines. To address remaining gaps, the IOM in 2000 issued a landmark report that recommended policy and programmatic improvements to strengthen U.S. immunization programs. One outcome of this effort was the requirement included in the 2010 Affordable Care Act that plans to provide first-dollar coverage (coverage without copayments or other cost sharing) for vaccines recommended by the CDC's Advisory Committee on Immunization Practices for children and adults up to age 26.

Policy advances have also enhanced the effects of vaccination globally.

Policy advances have also enhanced the effects of vaccination globally. The WHO launched the Expanded Program on Immunization in 1974 to increase access to vaccines. Beginning in 2000, the benefits of this program were greatly enhanced by the creation of Gavi, the Vaccine Alliance, an international public–private partnership that provides financial and programmatic support to ensure that children in the poorest countries have access to vaccines. In 2017, with the support of the NAM and other organizations, this model was used as a framework for the creation of the Coalition for Epidemic Preparedness Innovations to fund innovative vaccines and other countermeasures against pathogens that cause devastating public health consequences, such as the Ebola virus and now SARS-CoV-2.

SAFETY AND EFFICACY

Because vaccines are usually administered to healthy people, maintaining the highest safety standards isn't only an ethical imperative but is also essential to sustaining public trust. The story of vaccine progress has been punctuated by both real and misguided safety concerns for as long as vaccines have been in use. Such concerns have included adverse events associated with vaccination itself, quality lapses in the manufacturing process, and false alarms regarding vaccine safety. The potential for financial gain has fueled liability suits related to putative safety concerns. The NAM has conducted ongoing objective assessments of vaccine safety to help address concerns. Between 2000 and 2004, its Immunization Safety Review Committee evaluated evidence pertinent to various vaccine-safety topics and set a new standard for independent scientific review that remains relevant as the NAM contributes to coronavirus-related policies.

Vaccine confidence depends on trust in the safety and efficacy of the products themselves, trust in vaccine manufacturers and the clinicians who administer vaccines, and trust in policymakers who assess the scientific evidence and promulgate vaccination recommendations. Failures in any of these areas can have substantial long-term public health consequences, as was the case with misinformation about measles vaccines[3]. Enduring mistrust stemming from a discredited study that associated childhood vaccination with autism has been linked to recent outbreaks of measles in the United States.

Sustaining both vaccine safety and trust in vaccination will become increasingly complex.

Sustaining both vaccine safety and trust in vaccination will become increasingly complex. Vaccines continue to be approved, and more vaccines have become accessible in resource-limited countries, but safety surveillance systems are less evolved in many low-income regions than in high-income regions. For example, earlier this month Pfizer and BioNTech announced updated topline results from analysis of 927 confirmed symptomatic cases of COVID-19 observed in their pivotal Phase 3 study through March 13, 2021. The results show the Pfizer-BioNTech COVID-19 vaccine, BNT162b2, was 91.3% effective against COVID-19. "These data confirm the favorable efficacy and safety profile of our vaccine and position us to submit a Biologics License Application to the U.S. FDA," says Albert Bourla, chairman and chief executive officer of Pfizer in a press release. "The high vaccine efficacy observed through up to six months following a second dose and against the variant prevalent in South Africa provides further confidence in our vaccine's overall effectiveness[4]."

Similarly, vaccines are being manufactured in regions where regulatory oversight isn't always optimal, and counterfeit vaccines remain a threat. Emerging infections may require rapid availability of new vaccines before comprehensive safety studies are complete. Perhaps most important, the speed and reach of communication on social media platforms have created unprecedented opportunities for users to amplify misinformation and flame the fears of parents and other stakeholders in the immunization ecosystem.

COVID-19 VACCINE DEVELOPMENT

When scientists began seeking a vaccine for the SARS-CoV-2 coronavirus in early 2020, they were careful not to promise quick success. The fastest any vaccine had previously been developed, from viral sampling to approval, was four years, for mumps in the 1960s. To hope for one even by the summer of 2021 seemed highly optimistic.

But by the start of December, the developers of several vaccines had announced excellent results in large trials, with more showing promise. On December 2, a vaccine made by drug giant Pfizer with German biotech firm BioNTech, became the first fully-tested immunization to be approved for emergency use[5]. It's tempting to hope that other vaccines might now be made on a comparable timescale. These are sorely needed: disease such as malaria, tuberculosis, and pneumonia together kill millions of people a year[6], and researchers anticipate further lethal pandemics, too.

The world was able to develop COVID-19 vaccines so quickly because of years of previous research on related viruses and faster ways to manufacture vaccines, enormous funding that allowed firms to run multiple trials in parallel, and regulators moving more quickly than normal. Some of those factors might translate to other vaccine efforts, particularly speedier manufacturing platforms. But there's no guarantee. To repeat such rapid success will require similar massive funding for development, which is likely to come only if there is a comparable sense of social and political urgency. It will depend, too, on the nature of the pathogen. With SARS-CoV-2, a virus that mutates relatively slowly[7] and that happens to belong to a well-studied family, scientists might — strange as it sounds — have got lucky.

Years of Advance Research

The research that helped to develop vaccines against the new coronavirus didn't start last January. For years, researchers had been paying attention to related coronaviruses, which cause SARS (severe acute respiratory syndrome) and MERS (Middle East respiratory syndrome), and some had been working on new kinds of vaccine — an effort that has now paid off spectacularly.

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Conventional vaccines contain viral proteins or disabled forms of the virus itself, which stimulate the body's immune defenses against infection by a live virus. But the first two COVID-19 vaccines for which efficacy was announced in large-scale (phase III) clinical trials used just a string of mRNA inside a lipid coat. The mRNA encodes a key protein of SARS-CoV-2; once the mRNA gets inside our cells, our bodies produce this protein. That acts as the antigen — the foreign molecule that triggers an immune response. The vaccines made by Pfizer and BioNTech and by the US pharmaceutical company Moderna both use mRNA that encodes the spike protein, which docks to human cell membranes and allows the coronavirus to invade the cell. Moderna, in particular, is a biotechnology company pioneering messenger RNA (mRNA) therapeutics and vaccines, announced earlier this month that the first

participants have been dosed in the Phase 2/3 study, called KidCOVE study, of mRNA-1273, the company's vaccine candidate against COVID-19, in children ages 6 months to less than 12 years. "It is humbling to know about 53 million doses have been administered to people in the U.S.," says Stéphane Bancel, chief executive officer of Moderna in a press release earlier this month. "We are encouraged by the primary analysis of the Phase 2 COVE study of mRNA-1273 in adults ages 18 and above and this pediatric study will help us access the potential safety and immunogenicity of our COVID-19 vaccine candidate in this important younger age population[8]."

The basic research on DNA vaccines began at least 25 years ago, and RNA vaccines have benefited from 10–15 years of strong research, some aimed at developing cancer vaccines[9]. The approach has matured just at the right time; five years ago, the RNA technology would not have been ready. For instance, researchers at the US National Institute of Allergy and Infectious Diseases (NIAID) in Bethesda, Maryland, knew from their research on MERS and SARS that it was best to tune the RNA sequence to stabilize the resulting spike protein in the form it adopts before it docks with a host cell. That work gave the NIAID team, which worked with Moderna, a head start once SARS-CoV-2 was sequenced in January 2020.

The third vaccine to show efficacy in phase III clinical trials in November 2020, made by the pharmaceutical firm AstraZeneca with the University of Oxford, UK, does not use mRNA. Instead, a viral vector (or carrier) holds extra genetic material that codes for the SARS-CoV-2 spike protein. This, too, benefited from years of research to select the vector; in this case, the firm chose a modified form of adenovirus isolated from chimpanzee stool. Advances in conventional vaccines such as these have also come from research on SARS, MERS, Ebola and malaria, and such approaches remain cheaper than using mRNA.

Vaccine researchers were fortunate with SARS-CoV-2 in many respects, the virus doesn't mutate a lot or have effective strategies for foiling the human immune system, unlike HIV, herpes or even influenza. The herpes virus, by contrast, has more evasion capability — it actively blocks antibodies from binding, which makes it harder to find an effective agent against it. And the fast mutation of flu viruses requires a different vaccine formulation for every flu season.

THE FUTURE OF VACCINES

Moving forward, vaccines against a range of infectious agents will need to be developed. New and reemerging pathogens, such as SARS-CoV-2 and new influenza strains, regularly appear. Viruses

More than 1.5 million as yet unknown viruses are estimated to exist in animals worldwide, and 38 to 50% of them are candidates to spread to humans.

that are capable of spreading by vector or airborne routes — one of the most important pandemic threats — continue to emerge. More than 1.5 million as yet unknown viruses are estimated to exist in animals worldwide, and 38 to 50% of them are candidates to spread to humans[10]. Global-surveillance and virus-discovery programs are therefore important, and they may be able to predict pandemics. In 2011, the IOM commissioned the development of a strategic multi-attribute ranking tool for vaccines to facilitate evaluation of new vaccine targets and help guide decisions about prioritizing vaccine-development efforts.

When pandemics emerge, rapid responses are necessary. Vaccines aren't the only available tool: passive administration of antibodies for prevention or treatment of infectious diseases has been used for many years. The Pandemic Prevention Platform program of the Defense Advanced Research Projects Agency aims to develop a new form of passive antibody protection that can slow viral epidemics starting within 60 days after identification of the pathogen and until a vaccine can be made. Thanks to new technology, the vaccine-development process is also being condensed. Experimental vaccines were developed and ready for phase 1 clinical trials in 20 months for SARS after the epidemic began in 2003 and in slightly more than 3 months for Zika virus in 2016.

The response to the COVID-19 pandemic is a prime example of how rapidly new vaccines can now be designed. By the time the WHO declared COVID-19 a pandemic on March 11, 2020, at least 37 groups from biotechnology companies and academic institutions were working on vaccine candidates[11]. These candidates include live attenuated, inactivated, DNA, messenger RNA, viral vector, and spike-protein–based vaccines. Less than 1 year later, the first COVID-19 vaccine-efficacy trials have now been completed, and the first vaccines are authorized for emergency use.

Many approved vaccines, such as those against measles and polio, were made using attenuated or killed versions of the virus without detailed knowledge of viral pathogenesis. In contrast, current strategies for vaccine design rely on new technologies that lead to a deeper understanding of the immune system and of host–pathogen interactions. For new experimental HIV and respiratory syncytial virus (RSV) vaccines, a detailed structural understanding of antibody interactions with the HIV envelope or the RSV prefusion form of the fusion (F) protein is needed.

CONCLUSION

Vaccines remain the most effective tool for preventing infectious diseases and improving global health. Remarkable progress has been made with the use of vaccines, including the eradication of smallpox and the control of childhood diseases such as measles, mumps, rubella, and polio. New insights into the functioning of the immune system on a cellular and molecular level have made possible the rapid development of new vaccines. Difficulties facing vaccinologists include predicting the type and timing of the next pandemic; developing vaccines to combat rapidly changing pathogens such as HIV-1, influenza, and multidrug-resistant bacteria; and establishing rapid-response strategies to control emerging and reemerging infectious diseases. The future holds great promise for vaccine-mediated control of global pathogens, but providing affordable access to effective vaccines for everyone who could benefit from them remains an important challenge.

NOTES

[1] Lee LA, et al. "The estimated mortality impact of vaccinations forecast to be administered during 2011-2020 in 73 countries supported by the GAVI Alliance. Vaccine. 2013.

[2] Greene SA, et al. "Progress toward polio eradication — worldwide, January 2017 – March 2019." Morbidity and Mortality Weekly Report. 2019.

[3] Benecke O, DeYoung SE. "Anti-vaccine decision-making and measles resurgence in the United States." Global Pediatric Health. 2019.

[4] "Pfizer and BioNTech confirm high efficacy and no serious safety concerns through up to six months following second dose in updated topline analysis of landmark COVID-19 vaccine study." BusinessWire. April 1, 2021.

[5] Ledford H, et al. "The UK has approved a COVID vaccine — what scientists now want to know." Nature. December 2020.

[6] Kaslow D, et al. "Vaccine candidates for poor nations are going to waste." Nature. December 2018.

[7] Callaway E. "The coronavirus is mutating — does it matter?" Nature. September 2020.

[8] "Moderna announces first participants dosed in phase 2/3 study of COVID-19 vaccine candidate in pediatric population." Moderna News Release. March 16, 2021.

[9] Dolgin E. "Unlocking the potential of vaccines built on messenger RNA." Nature. October 2019.

[10] Carroll D, et al. "The global virome project." Science. 2018.

[11] Usdin S. "WHO mapping out COVID-19 vaccines." Biocentury. 2020.

RESOURCES

Ball P. "The lightning-fast quest for COVID vaccines — and what it means for other diseases." Nature. December 2020.

Benecke O, DeYoung SE. "Anti-vaccine decision-making and measles resurgence in the United States." Global Pediatric Health. 2019.

Calina D, et al. "Recent advances, approaches and challenges in targeting pathways for potential COVID-19 vaccines development." Immunologic Research. October 2020.

Callaway E. "The coronavirus is mutating — does it matter?" Nature. September 2020.

Carroll D, et al. "The global virome project." Science. 2018.

D'Amore T, Yang YP. "Advances and challenges in vaccine development and manufacture." BioProcess International. September 2019.

Dolgin E. "Unlocking the potential of vaccines built on messenger RNA." Nature. October 2019.

Dutchen S. "One year in: vaccines." Harvard Medical School. January 2021.

Gerbering J, Haynes B. "Vaccine innovations — past and future." New England Journal of Medicine. February 2021.

Green D. "SARS-CoV2 vaccines: slow is fast." Science. May 2020.

Greene SA, et al. "Progress toward polio eradication — worldwide, January 2017 – March 2019." Morbidity and Mortality Weekly Report. 2019.

Kaslow D, et al. "Vaccine candidates for poor nations are going to waste." Nature. December 2018.

Krammer F. "SARA-CoV2 vaccines in development." Nature. September 2020.

Leask J. "Vaccines — lessons from three centuries of protest." Nature. September 2020.

Ledford H, et al. "The UK has approved a COVID vaccine — what scientists now want to know." Nature. December 2020.

Lee LA, et al. "The estimated mortality impact of vaccinations forecast to be administered during 2011-2020 in 73 countries supported by the GAVI Alliance. Vaccine. 2013.

"Moderna announces first participants dosed in phase 2/3 study of COVID-19 vaccine candidate in pediatric population." Moderna News Release. March 16, 2021.

"Pfizer and BioNTech confirm high efficacy and no serious safety concerns through up to six months following second dose in updated topline analysis of landmark COVID-19 vaccine study." BusinessWire. April 1, 2021.

Rabaan A, et al. "Recent advances in vaccine and immunotherapy for COVID-19." Taylor and Francis Online. November 2020.

Usdin S. "WHO mapping out COVID-19 vaccines." Biocentury. 2020.

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