COVID-19 Vaccine: How did we get here so quickly?

Jane Kelly, MD
Assistant State Epidemiologist
Division of Acute Disease Epidemiology

How is it possible to develop and get a COVID-19 vaccine to market in record time?

Developing COVID-19 vaccine in record time was possible because of some unprecedented events related to an earlier disease from more than 15 years ago – SARS. The SARS outbreak in 2003 prompted work on vaccine development that was abandoned when the disease was contained. The COVID-19 vaccine developers had that prior work upon which to build.

By January 10, 2020, the SARS-CoV-2 (responsible for COVID-19) genome had been sequenced and released publicly. On January 11, scientists around the world began using that genetic information to create multiple vaccine approaches for COVID-19. Critically, the timetable for vaccine development was shortened for “business case” reasons.

According to the New York Times, the longest periods in a typical vaccine development timeline belong to the Preclinical, Building factories, and Manufacturing phases, and none of the phases overlap (Thompson, 2020). Unlike this usual timeline and because of the federal government’s commitment to purchasing vaccine, companies did not have to proceed sequentially to ensure return on investment. In the COVID-19 vaccine timeline, Academic Research and Preclinical had a head start from previous SARS work and the published genome; Phases I, II, and III trials had some overlap; and Building factories and Manufacturing phases began early on.
No steps have been skipped in COVID-19 vaccine development in the United States but instead have overlapped. Vaccine development acceleration can be done without sacrificing efficacy and short-term safety. Long-term immunity persistence and safety evaluation must continue.


Historical Perspective on Vaccine Hesitancy
Jane Kelly, MD
Assistant State Epidemiologist
Division of Acute Disease Epidemiology

The era of COVID-19 offers a new twist to vaccine hesitancy. Even persons with confidence in the emergency use authorization (EUA) approval process assuring safety and at least 50% efficacy for upcoming vaccines are asking: “Would I recommend taking the first vaccine available or wait to see if a more efficacious one comes out?” This isn’t the first time this scenario has come up in US history.

After World War II, as more Americans moved to crowded urban settings, and, ironically, hygiene improved such that children were not exposed to polio at a young age when they were less likely to be symptomatic, polio incidence began to rise (Table 1). By peak year 1952, there were more than 58,000 cases, 21,000 permanently paralyzed, and 3,000 dead. Two vaccines, inactivated polio vaccine (IPV) and oral polio vaccine (OPV) were under development, but clinical trials for IPV were completed by 1954. Some scientists argued that OPV would offer better vaccine (IPV) and oral polio vaccine (OPV) were under development, but clinical trials for IPV were completed by 1954. Some scientists argued that OPV would offer better protection in prevention and recommended postponing mass vaccination until trials were completed (likely a two-year wait). Americans would not hear of it. People clamored for a vaccine in 1955 because the number of cases and deaths were compelling. Contrast these numbers with COVID-19 (Table 2). The case rate for COVID-19 are more than 210 times higher and deaths/100,00 more than 160 times higher as of this writing in February 2021 than polio was in 1952.

The FDA has assured any vaccine application for EUA will undergo rigorous scrutiny to assure safety and efficacy. COVID-19 has killed more than 10 times as many people in 2020 than influenza has annually the past several years. As public health professionals, we weigh risks and benefits and provide clear information to the public. Comparison to historical experiences offer a sobering perspective.

Table 1. Polio Incidence, US

<table>
<thead>
<tr>
<th>Year</th>
<th>Rate per 100,000 people</th>
</tr>
</thead>
<tbody>
<tr>
<td>1920-1930s</td>
<td>4</td>
</tr>
<tr>
<td>1940-1944</td>
<td>8</td>
</tr>
<tr>
<td>1945-1949</td>
<td>16</td>
</tr>
<tr>
<td>1950-1954</td>
<td>25</td>
</tr>
</tbody>
</table>

We are in a comparable situation qualitatively in that it is likely more than one COVID-19 vaccine will be given EUA status, though some earlier than others. Should we wait to see which one is best? Would you recommend waiting six months to see if a later vaccine might prove more efficacious in the elderly before vaccinating nursing home residents?

People clamored for a vaccine in 1955 because the number of cases and deaths were compelling. Contrast these numbers with COVID-19 (Table 2). The case rate for COVID-19 are more than 210 times higher and deaths/100,00 more than 160 times higher as of this writing in February 2021 than polio was in 1952.

The FDA has assured any vaccine application for EUA will undergo rigorous scrutiny to assure safety and efficacy. COVID-19 has killed more than 10 times as many people in 2020 than influenza has annually the past several years. As public health professionals, we weigh risks and benefits and provide clear information to the public. Comparison to historical experiences offer a sobering perspective.

Table 2. Polio vs. COVID-19: Cases, Case Rates, and Deaths

<table>
<thead>
<tr>
<th>Disease</th>
<th>Year</th>
<th>Number of Cases</th>
<th>Rate per 100,000</th>
<th>Number of Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Polio</td>
<td>1952</td>
<td>58,000</td>
<td>37</td>
<td>3,000</td>
</tr>
<tr>
<td>COVID-19</td>
<td>2/2020-2/2021</td>
<td>27,669,556°</td>
<td>8,334°</td>
<td>489,067°</td>
</tr>
</tbody>
</table>

As of 2/18/2021, CDC

References:

New mRNA Vaccine Technology
Jane Kelly, MD
Assistant State Epidemiologist
Division of Acute Disease Epidemiology

At this time, it seems likely that one or both mRNA vaccines (made by Pfizer and Moderna) will be the first ones available. These vaccines use a novel platform of delivery. Rather than inactivated or attenuated whole virus, or antigen vaccines presenting protein subunit with or without a vector, the mRNA vaccines deliver a segment of genetic code containing the directions for making the spike protein (which is the virus’s attachment site to enter the cell). The vaccine delivers the mRNA instructions, the cells make spike protein, which is released and induces antibody production and memory T cell activation to the spike protein. Ideally, this dual response of B and T cells will provide a robust response when an individual is exposed to SARS-CoV-2.

There are, however, lots of logistical challenges. Both vaccines require two doses (separated by 21 and 28 days for the Moderna and Pfizer vaccines, respectively) and the booster dose must be consistent with the first vaccine administered. Cold-chain considerations will impact vaccine distribution as the Pfizer vaccine needs to be held in storage of ~94°F and the Moderna vaccine at ~40°F. Although no serious adverse events have been noted in Phase 1-3 trials involving more than 60,000 participants, mRNA vaccine is a new technology and rare events may only arise after many thousands more are vaccinated.

References:

Laboratory Criteria of the Spotted Fever Rickettsiosis and Lyme Disease Case Definitions
Christina Paul, MPH, CPH
Vector-Borne Disease Epidemiologist
Division of Acute Disease Epidemiology

Spotted Fever Rickettsiosis (SFR) and Lyme disease are the two most commonly reported tick-borne diseases in South Carolina. SFR includes cases of Rocky Mountain Spotted Fever (Rickettsia rickettsii), Rickettsia parkeri rickettsiosis, Pacific Coast Tick Fever (Rickettsia species 364D) and other rickettsial species. Between 2006 and 2018, 20 to 95 cases of SFR were reported annually in the state (Division of Acute Disease Epidemiology [DADE], 2019). Between 2006 and 2018, 22 to 77 cases of Lyme disease were reported annually in the state (DADE, 2019). This summary provides information regarding the laboratory criteria used for public health surveillance in the SFR and Lyme disease case definitions, including recent updates to these criteria.

Spotted Fever Rickettsiosis (SFR)
The SFR case definition was updated in 2020 and includes the following changes to the laboratory criteria:

• IgM serology test results are no longer included as part of the laboratory criteria. Previously, positive IgM results by indirect immunofluorescence antibody assays (IFA) were listed as part of the Supportive Laboratory Evidence. However, this has been removed as IgM results may be less specific than IgG results for diagnosing a recent infection (CDC, 2018).
• A category for Presumptive Laboratory Evidence was added to the case definition. This category includes positive IgG serology results >1:128 by IFA.
• The Supportive Laboratory Evidence was amended to include positive IgG serology results >1:128 by IFA.
• Both the Presumptive and Supportive Laboratory Evidence now include a criterion that positive specimens must be collected within 60 days of the patient’s illness onset date to be used for surveillance purposes (CDC, 2020).

Image credit: NIH

mRNA is complexed into liposome
millifolds for viral protein presentation

direct evidence for vaccination

mRNA is incorporated into lipid vesicle
The vaccine triggers production of the spike protein and antibodies specific to it

Reference:
**Lyme Disease**

The current version of the Lyme disease case definition (dated 2017) includes the following criteria for laboratory results for the purposes of public health surveillance. Patients having any of these criteria would be considered to have laboratory evidence of infection for Lyme disease (CDC, 2017).

- **A positive culture for Borrelia burgdorferi**
- **A positive two-tiered test**
  - **A positive two-tiered test is defined as a positive or equivocal variable immunoassay** (EIA) or immunofluorescent assay (IFA) followed by a positive Immunoglobulin M (IgM) or Immunoglobulin G (IgG) western blot (WB) for Lyme disease.
  - An IgM WB is considered positive when at least two of the following three bands are present:
    - 24 kilodalton (kDa) outer surface protein C (OspC)“
    - 39 kDa basic membrane protein A (BmpA)
    - 41 kDa (Fla).
  - Additionally, the specimen of a positive IgM WB result must be collected within 30 days of the patient’s illness onset to be used for surveillance purposes.
  - An IgG WB is considered positive when at least five of the following 10 bands are present:
    - 18 kDa
    - 41 kDa flagellin (Fla)
    - 24 kDa (OspC)“
    - 28 kDa
    - 58 kDa (not GroEL)
    - 30 kDa
    - 66 kDa
    - 39 kDa (BmpA)
    - 93 kDa.
- **A positive single-tier IgG WB test for Lyme disease** (see the details above regarding the band requirements to be considered a positive IgG WB)
- **While a single IgG WB is adequate for surveillance purposes, a two-tier test is still recommended for patient diagnosis.**

- **Parotitis with Mumps and Other Viral Infections**

  Clarissa A. Felima, MPH, CHES
  Vaccine Preventable Disease (VPD) Epidemiologist
  Division of Acute Disease Epidemiology

Parotitis, swelling in one or both parotid glands, has historically been associated with mumps viral infection. However, this symptom has also been reported in individuals who have tested positive for other viral infections, such as influenza and, now, COVID-19.

According to Dr. Mariel Marlow, CDC Epidemiologist on the Mumps, Varicella, and Zoster (MuVZ) Epidemiology Team, as of epi week 46 (November 14, 2020), 42 states had reported 592 mumps cases compared with 50 states and 3,323 mumps cases as of the same time in 2019. Mumps cases continued to be reported throughout the period of COVID lockdowns and other control measures, with 31 states reporting 107 cases from April 2020 through November 14, 2020. Because of this, clinical evaluation of patients with parotitis and consideration of mumps and other viral testing in these patients remain important for clinical and public health management.

**COVID-19 and Parotitis Case Reports**

A case report in the American Journal of Emergency Medicine described a 21-year-old woman who was diagnosed with COVID-19-associated parotitis (Fisher et al., 2020). The patient was not tested for mumps but tested positive for COVID-19 upon evaluation at an emergency department. A study published in Emerging Infectious Diseases reported three patients in France who presented with parotitis-like symptoms as a clinical manifestation of confirmed COVID-19 infection (Lechien et al., 2020). Although the three cases were not tested for mumps, they were fully vaccinated for mumps. All three patients were female, ranging in age from 23 years to 33 years, and all were identified in a short period of time, with illness onsets ranging from March 21, 2020, to April 2, 2020. The patients also exhibited other symptoms consistent with COVID-19 such as loss of smell and taste, myalgia, and headache.

**Mumps and Other Viral Testing**

Based on these reports, it remains important to test for mumps in patients presenting with parotitis, while also considering other diagnostic testing. Testing for influenza should be considered if influenza is known to be circulating in the community. And testing for COVID-19 may also be appropriate, especially if patients present with other symptoms consistent with this condition. Additionally, mumps should not be ruled out based on patients’ age or vaccination status. Most mumps cases in the US are now adults and fully vaccinated (Marlow, 2020). Therefore, patients with these characteristics who present with parotitis should still be tested for mumps.

To test patients for mumps, collect buccal swab specimens for RT-PCR testing as soon as mumps infection is suspected. RT-PCR has the greatest diagnostic sensitivity when samples are collected within three days of symptom onset. The buccal swab specimens are obtained by massaging the parotid gland area for 30 seconds prior to swabbing the area around Stensen’s duct. If it has been greater than three days since symptom onset, it is still recommended to collect: 1) a buccal swab specimen for RT-PCR testing; and 2) 7–10 mL of blood in a red-
top or serum-separator tube (SST) for IgM detection. If assistance with mumps testing is needed, please contact the regional health department in your area. Contact information for regional health departments can be found at: https://scdhec.gov/sites/default/files/Library/CR-009025.pdf

References:


4. Centers of Disease Control and Prevention (CDC), Mumps Job-Aid Template for Providers: https://www.cdc.gov/mumps/lab/


7. South Carolina 2021 List of Reportable Conditions

---

**DISEASE PREVENTION AND EPIDEMIOLOGY NEWSLETTER**

**Updates to the List of Reportable Conditions for 2021**

Tahtiena Lane
Data Security Officer/Surveillance System Trainer
Division of Acute Disease Epidemiology

Abdoulaye Diedhiou, MD, MS, PhD
Director
Division of Acute Disease Epidemiology

South Carolina Law 44-29-10 and Regulation 61-20 reporting require conditions on the Official List of Reportable Conditions in the manner prescribed by DHEC. South Carolina Law 44-53-1380 requires reporting by laboratories of all blood lead values in children under 6 years of age. Changes to the LORC for 2021 are listed below.

**Conditions Added**

1. Coronavirus Disease 2019 (COVID-19), has been added to urgently reportable within 24 hours by phone and the following footnote included.

2. Footnote 17: COVID-19 cases, deaths, and multisystem inflammatory syndrome in children are urgently reportable within 24 hours. All COVID-19 test results, including positives, negatives and indeterminates, are required to be reported. For detailed information about reporting COVID-19 test results, please go to: http://www.scdhec.gov/sites/default/files/Library/CR-012859.pdf

   - HIV-exposed infants, has been added to reportable within three business days.
   - HIV 1/2 AB/AG+ and/or detectable viral load with each pregnancy, has been added to reportable within three business days.

**Reporting Updates**

1. What to report:
   - For all suspected and confirmed cases, report the following:
     - Patient’s complete name (first, middle and last)
     - Patient’s complete address, phone number, county, date of birth, race, sex, last five digits of social security number
     - Physician’s name and phone number
     - Name, institution, and phone number of person reporting
   - Disease or condition
   - Date of diagnosis
   - Symptoms
   - Date of onset of symptoms
   - Lab results, specimen site, collection date
   - If female, pregnancy status
   - Patient status: in childcare, food-handler, healthcare worker, childcare worker, in nursing home, prisoner/detainee, travel in last four weeks

2. How to report
   - The “How to Report” section of the LORC has been updated to reflect changes in the mailing address for reporting HIV, AIDS, STDs (excluding Hepatitis) and Lead, and the contact information to establish electronic reporting for Lead.
   - For HIV, AIDS, and STDs (excluding Hepatitis):
     - Do not fax HIV, AIDS, or STD results to DHEC
     - Call 1-800-277-0873; or
     - Submit electronically via DHEC’s web-based reporting system; or
   - Mail to:
     - Division of Surveillance, Assessment & Evaluation
     - Mills/Jarrett Complex
     - 2100 Bull St., Columbia, SC 29201

   - Mail to:
     - Bureau of Population Health Data, Analytics and Informatics, Lead Surveillance
     - Sims-Aycock Building
     - 2600 Bull St., Columbia, SC 29201

   - Fax: (803) 898-3236; or
   - Email: scionlead@dhec.sc.gov to establish electronic reporting

   The “How to Report Other Conditions” section has been updated to reflect the change in the fax numbers for the Pee Dee region (Chesterfield, Clarendon, Darlington, Florence, Lee, Marlboro, Sumter, Williamsburg). The only fax number to use is (843) 915-6506.

   As a reminder, all conditions other than HIV, AIDS, STDs, Lead and TB must be reported to the public health office in the region in which the patient resides. Immediately and urgently reportable conditions must be reported by telephone (for specific information about reporting COVID-19, go to: https://scdhec.gov/sites/default/files/Library/CR-009025.pdf) Conditions which are routinely reportable must be reported via mail, fax or submitted electronically via DHEC’s web-based reporting system.

**Resources for Additional Information**

- Reportable Diseases Page on DHEC website https://scdhec.gov/health-professionals/south-carolina-list-reportable-conditions

**Questions?**

For questions about Disease Reporting or to discuss electronic disease reporting via DHEC’s electronic disease surveillance reporting system, call the Division of Acute Disease Epidemiology in Columbia: (803) 898-0651 (M-F 8:30 a.m. to 5 p.m.). To learn about DHEC’s web-based reporting system, call 1-800-917-2093 (M-F 8:30 a.m. to 5 p.m.).