



## Measles in 2019 — Going Backward

Catharine I. Paules, M.D., Hilary D. Marston, M.D., M.P.H., and Anthony S. Fauci, M.D.

In 2000, the United States achieved a historic public health goal: the elimination of measles, defined by the absence of sustained transmission of the virus for more than 12 months. This

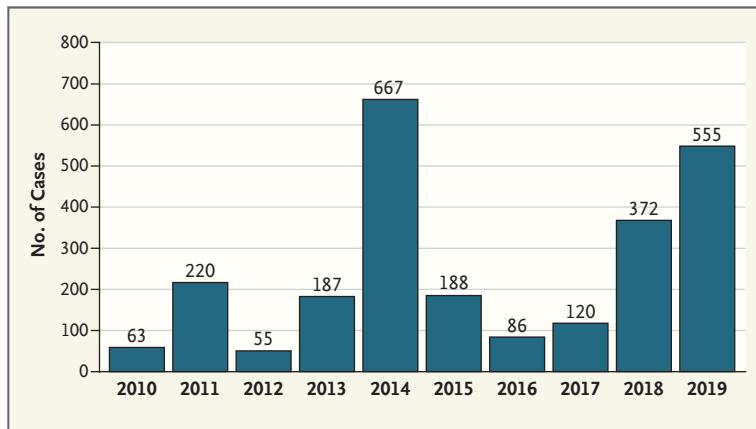
achievement resulted from a concerted effort by health care practitioners and families alike, working to protect the population through widespread immunization. Unfortunately, that momentous achievement was short-lived, and localized measles outbreaks have recently been triggered by travel-related introductions of the virus by infected persons, with subsequent spread through under-vaccinated subpopulations. According to the Centers for Disease Control and Prevention, 555 cases of measles in 20 states had already been confirmed from January 1 through April 11, 2019 (see graph). The increase in measles cases in the United States mirrors patterns elsewhere: several other countries that had eliminat-

ed measles are now seeing resurgences.

Measles is a highly contagious cause of febrile illness typically seen in young children.<sup>1</sup> It is transmitted primarily by means of respiratory droplets and small-particle aerosols and can remain viable in the air for up to 2 hours. Exposed people who are not immune have up to a 90% chance of contracting the disease, and each person with measles may go on to infect 9 to 18 others in a susceptible population.<sup>2</sup>

Most people with measles recover uneventfully after approximately 1 week of illness characterized by fever, malaise, coryza, conjunctivitis, cough, and a maculopapular rash. However, measles is by no means a trivial disease;

before widespread vaccination, the virus caused 2 million to 3 million deaths globally per year.<sup>1</sup> Even today, it remains a leading cause of vaccine-preventable illness and death worldwide, claiming more than 100,000 lives each year.<sup>2</sup> Common complications include secondary infections related to measles-induced immunosuppression, diarrhea, keratoconjunctivitis (which may lead to blindness, particularly in vitamin A-deficient populations), otitis media, and pneumonia (the leading cause of measles-related deaths). In approximately 1 in 1000 cases of measles, serious and often fatal neurologic complications such as acute disseminated encephalomyelitis and measles inclusion-body encephalitis occur, and most patients who survive these complications have long-term neurologic sequelae. In addition, a rare neurologic complication (affecting approximately 1 in 10,000 patients) called subacute scleros-



**Measles Cases in the United States since 2010.**

The number of reported cases through April 11, 2019, has already surpassed all years except 2014 (according to the Centers for Disease Control and Prevention). The number for 2018 represents all cases as of December 29, 2018.

ing panencephalitis (SSPE) can occur years after measles virus infection, with a severe, progressive, and fatal course.

If the potential danger posed by measles is clear, so is the solution. Live-attenuated measles vaccines are among the most highly effective vaccines available (providing 97% protection with two doses, given at 12 to 15 months and 4 to 6 years of age), with a proven safety record.<sup>1</sup> The most common side effects of the measles vaccine are a sore arm and fever. A small proportion of vaccinees (about 5%) will develop a rash; an even smaller proportion will have a febrile seizure or transient decrease in platelet counts. A very rare complication, meningoencephalitis, has been described, almost always in immunocompromised vaccinees.

Measles vaccination has prevented an estimated 21 million deaths worldwide since 2000.<sup>3</sup> Despite these substantial gains, global elimination goals have not been met, and previous strides are now being threatened by a 31% increase in the number of

measles cases reported globally between 2016 and 2017.<sup>3</sup> The growing number of travel-related infections and local outbreaks in the United States reflects this alarming trend, yet the U.S. situation is dwarfed by outbreaks elsewhere in the world. For example, the World Health Organization (WHO) reported 117,075 measles cases and 1205 deaths in Madagascar between early October 2018 and early April 2019. Venezuela is also experiencing a large-scale epidemic, with endemic measles transmission now reestablished in a country where it had previously been eliminated.<sup>3</sup> In Europe, the number of reported cases in 2018 was triple that in 2017 and 15 times that in 2016.<sup>4</sup> In addition, it is likely that endemic measles has now been reestablished in several European countries where transmission had previously been interrupted.<sup>3</sup>

The resurgence in measles cases is all the more frustrating since the disease is entirely preventable through vaccination. Measles has all the components of an eradicable disease: there is a safe

and highly effective vaccine, it has a readily diagnosable clinical syndrome, and it has no animal reservoir to maintain circulation.<sup>1</sup> But because of the highly contagious nature of the virus, near-perfect vaccination coverage (herd immunity of 93 to 95%) is needed to effectively protect against a measles resurgence. Although there are valid reasons why some people might not be vaccinated, such as a medical contraindication due to marked immunosuppression, the failure to vaccinate too often stems from misconceptions about vaccine safety, especially those resulting from a now-debunked claim that posited a connection between the vaccine and autism. The growing anti-vaccination movement, based heavily on philosophical objections to vaccinations, poses a threat to public health. Vaccine hesitancy has been identified by the WHO as one of the top 10 threats to global health and is a serious hurdle to the global elimination and eradication of measles.

If we continue to lose ground on measles prevention through vaccination, we face the reemergence of measles into new populations, which will pose new and varied challenges. Historically, measles has been a disease of children, with severe disease seen primarily in children younger than 5 and those with poor nutritional status, particularly if they have vitamin A deficiency. The successful implementation of measles vaccination programs is changing the epidemiology of measles from seasonal epidemics in young children to sporadic cases in older children and adults, including pregnant women. Data assessing the effects of measles infection in these latter populations are sparse

but are suggestive of increased morbidity and mortality.<sup>2</sup>

The greatest risk of measles-related complications occurs in immunosuppressed people. This population may have atypical presentations with severe complications that have not been documented in immunocompetent patients, such as giant-cell pneumonia and measles inclusion-body encephalitis. Exposure to measles in people with HIV infection has led to serious complications and even death. Higher rates of measles complications and deaths have also been reported in patients with cancer, patients with solid organ transplants, people receiving high-dose glucocorticoids, and those receiving immunomodulatory therapy for rheumatologic disease. People with profound immunosuppression cannot be safely vaccinated with the live-attenuated vaccine and must rely on herd immunity to protect them from measles infection.

Exposure to measles in the community certainly represents a

danger to high-risk persons during a local outbreak; however, nosocomial transmission may pose an even greater threat and has been reported throughout the world. For example, during a measles outbreak in Shanghai in 2015, a single child with measles in a pediatric oncology clinic infected 23 other children, more than 50% of whom ended up with severe complications, and the case fatality rate was 21%.<sup>5</sup> When the umbrella of herd immunity is compromised, such populations are highly vulnerable.

Unlike many infectious diseases, measles is a public health problem with a clear scientific solution. Measles vaccination is highly effective and safe. Each complication or death related to measles is a preventable tragedy that could have been avoided through vaccination. The recent upsurge in U.S. measles cases, including the worrisome number seen thus far in 2019, represents an alarming step backward. If this trend is not reversed, measles may rebound in full force in both the United States and other

countries and regions where it had been eliminated. Promoting measles vaccination is a societal responsibility, with the ultimate goal of global elimination and eradication — relegating measles to the history books.

Disclosure forms provided by the authors are available at NEJM.org.

From the Department of Infectious Diseases, Penn State University College of Medicine, Milton S. Hershey Medical Center, Hershey, PA (C.I.P.); and the Office of the Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, MD (H.D.M., A.S.F.).

This article was published on April 17, 2019, at NEJM.org.

1. Rota PA, Moss WJ, Takeda M, de Swart RL, Thompson KM, Goodson JL. Measles. *Nat Rev Dis Primers* 2016;2:16049.
2. Moss WJ. Measles. *Lancet* 2017;390:2490-502.
3. Dabbagh A, Laws RL, Steulet C, et al. Progress toward regional measles elimination — worldwide, 2000–2017. *MMWR Morb Mortal Wkly Rep* 2018;67:1323-9.
4. Thornton J. Measles cases in Europe tripled from 2017 to 2018. *BMJ* 2019;364:l-634.
5. Ge YL, Zhai XW, Zhu YF, et al. Measles outbreak in pediatric hematology and oncology patients in Shanghai, 2015. *Chin Med J (Engl)* 2017;130:1320-6.

DOI: 10.1056/NEJMp1905099

Copyright © 2019 Massachusetts Medical Society.

 An audio interview with Dr. Fauci is available at NEJM.org

## Is CBO Forecasting Good Enough for Government Work?

Sherry Glied, Ph.D., and Thomas H. Lee, M.D.

The observation that it's difficult to make predictions, "especially about the future," has been made by baseball players (Yogi Berra) and physicists (Niels Bohr), but the economists at the Congressional Budget Office (CBO) don't have a choice. The CBO was created in 1974 as a non-partisan agency in the legislative branch of the U.S. government

and tasked with providing budget and economic information to Congress. It doesn't make recommendations, but has the role of forecasting the effects of legislative proposals.

The questions are complex, the stakes are high, and the work can be thankless. In 2017, the CBO modeled the effects of Senate Republicans' proposed legis-

lation to repeal the Affordable Care Act and projected that it would leave 22 million additional Americans without health insurance over the next decade. The White House responded with a statement saying, "The CBO has consistently proven it cannot accurately predict how healthcare legislation will impact insurance coverage. This history of inaccu-