Measles 50 Years After Use of Measles Vaccine

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KEYWORDS

• Measles elimination • Vaccine preventable • Vaccination • Exemptions • Mortality • Rash • Fever

KEY POINTS

- Measles can be severe; globally, measles causes an estimated 400 deaths each day.
- Measles still occurs in the United States following virus importations, primarily among intentionally unvaccinated children and young adults; clinicians should keep measles in their differential diagnosis of febrile rash illness and encourage on-time, complete vaccinations.
- Measles can and should be eradicated, and all 6 World Health Organization (WHO) regions have set a goal for measles elimination by or before 2020; continued global funding and support are key strategies to achieve these goals.
- Until measles is eliminated globally, public health agencies will need to remain vigilant and on the frontline to maintain measles outbreak preparedness and rapid response capacity to contain outbreaks when they occur.

INTRODUCTION

Before the availability of measles vaccine in 1963, measles was a common childhood disease that caused an estimated 135 million cases of measles and more than 6 million measles-related deaths globally each year, including an estimated 4 million cases and 450 deaths in the United States.[1–3] Although measles was eliminated from the United States in 2000, measles still occurs following measles virus importations from other countries, most commonly by unvaccinated US residents who become infected while traveling abroad. These importations can result in measles outbreaks if the measles-infected

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person comes in contact with susceptible persons, particularly in communities with low vaccination coverage. In recent years, the annual number of reported measles cases in the United States has increased and larger outbreaks have occurred, predominantly among persons who are unvaccinated by choice.[4] Today, many physicians are less familiar with the clinical presentation of measles and do not always keep measles in mind for the differential diagnosis of febrile rash illness. This article reviews experience with a half century of use of measles vaccine in the United States and globally, including the historical perspective of the virus, events leading to vaccine development, vaccine safety, effectiveness and impact, clinical manifestations, and the current challenges and future considerations for measles eradication.

MEASLES HISTORICAL ASPECTS AND VIROLOGY

Measles virus emerged more than 1000 years ago when our human ancestors domesticated cattle.[5,6] Close contact with domesticated cattle over a prolonged period likely allowed the animal virus rinderpest to mutate enough to make the transition from cows to humans as host. Humans are the only natural host for sustaining measles virus transmission. Clinical measles was first described and differentiated from smallpox in the tenth century by the Persian physician Rhazes. After emerging as an Old World virus, measles became endemic in humans; after importations into the Western Hemisphere from trans-Atlantic human migration, measles caused massive devastation, disease, and death among entirely measles-susceptible populations in the New World.[7] Measles was first described in the United States in Boston in 1657 and became endemic, causing periodic severe epidemics resulting in substantial illness and death.[5,6]

Measles virus was first isolated from a measles-infected boy (Edmonston-B strain) in the United States by Thomas C. Peebles while he was working in the Children's Hospital Boston laboratory of John F. Enders in 1954 (**Fig. 1**).[8] The virus is a negative-strand RNA virus that belongs to the genus *Morbillivirus* of the family Paramyxoviridae. Measles virus is monotypic with only one serotype. The full genomes of vaccine and wild-type strains have been sequenced.[9] The WHO Global Measles and Rubella Laboratory Network established a set of reference sequences for these genotypes and periodically updates measles virus nomenclature; WHO recognizes 24 measles virus genotypes, organized into 8 clades of measles (A–H).[10]

MEASLES PATHOGENESIS

The pathogenesis of measles is not fully understood; however, the development of new molecular techniques has recently advanced pathogenesis studies. The initial measles virus infection occurs via cell entry of measles virus into the respiratory tract, although the cell receptors and specific target cells are not well defined. From the respiratory tract, the virus enters the lymphatic system where virus amplification occurs, leading to acute viremia. In the blood, monocytes and lymphocytes become infected and carry the virus to organs throughout the body.[11,12] Measles virus enters and replicates in the lymphoid tissues and organs, including the skin, lungs, gastrointestinal tract, liver, and kidneys.[13] Measles virus infection of white blood cells leads to a decline in CD4 lymphocytes and causes transient immunosuppression starting before the rash and lasting up to at least 1 month; however, the duration and specific mechanisms leading to immune system dysregulation are unknown. Measles infection induces robust humoral and cellular immune responses, resulting in lifelong immunity.

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