

## Measles

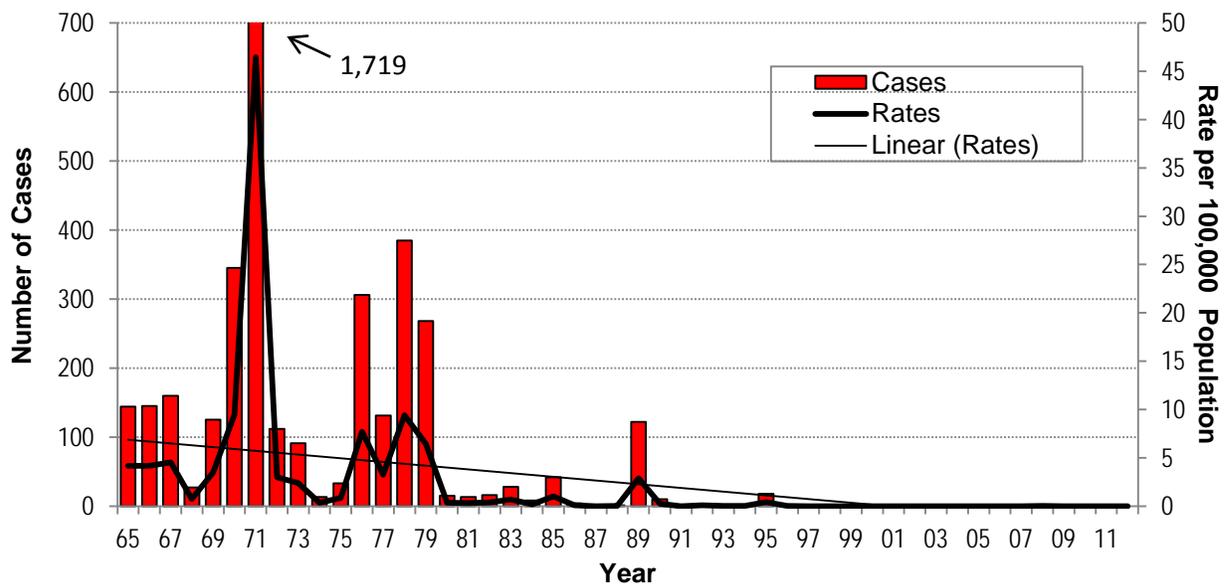
*Measles is a Class A Disease and must be reported to the state within 24 hours by calling the phone number listed on the website.*

Measles (Rubeola) is an acute, highly communicable, respiratory illness caused by the Measles virus. Measles is transmitted by direct contact with infectious droplets or, less commonly, by airborne spread.

In the pre-vaccine era, measles was an epidemic disease; the Centers for Disease Control and Prevention (CDC) estimates that three to four million people in the United States were infected each year, of whom 400 to 500 died, 48,000 were hospitalized and another 1,000 developed chronic disability from measles encephalitis. Most cases occurred in preschool and young school-age children. Practically all children became infected by five years of age. Measles epidemics occurred every two to five years and lasted two to three months during the early spring. In addition to epidemics, a few cases occurred every week throughout the inter-epidemic period.

The first measles vaccine was introduced in 1965; in 1967, immunization was applied on a massive scale. The year 1971 was the last year that the U.S. experienced a large upsurge of measles cases. An improved version of the vaccine replaced the original in 1979. By 1981, Louisiana saw fewer than 20 reported cases each year. In 1989, there was a national measles epidemic and the number of cases in Louisiana rose to 122. Since 1990, intensified immunizations efforts have brought the reported cases down to fewer than ten cases per year, with the exception of a small outbreak of 15 cases in 1995 (Figure 1). As a result of a successful U.S. vaccination program, measles elimination (i.e., interruption of endemic measles transmission) was declared in the United States in 2000.

Figure 1: Measles cases and incidence rates - Louisiana, 1965-2012



The last case of measles in Louisiana was reported in 2008 as an imported case. Although eliminated in the U.S. and the WHO American Region, 20 million cases of measles and 197,000 deaths occur each year worldwide. The 2008 measles case serves as a reminder that measles is still imported into the United States and can result in outbreaks unless population immunity remains high through vaccination.

### The Case of Measles That Was Not, or Delusional Measles

The CDC Morbidity & Mortality Report of April 20, 2012, Vol61 #15;253-257 was an update on the measles situation in the U.S. “In 2000, the United States achieved measles elimination (defined as interruption of year-round endemic measles transmission). However, importations of measles into the United States continue to occur, posing risks for measles outbreaks and sustained measles transmission. During 2011, a total of 222 measles cases (incidence rate: 0.7 per one million population), and 17 measles outbreaks (defined as three or more cases linked in time or place) were reported to the CDC, compared with a median of 60 (range: 37 to 140) cases and four (range: 2 to 10) outbreaks reported annually during 2001 to 2010”.

According to the Measles 2010 case definition available in the Council of State and Territorial Epidemiologists position statement 09-ID-48, available at [http://www.cdc.gov/osels/ph\\_surveillance/nndss/casedef/measles\\_2010.htm](http://www.cdc.gov/osels/ph_surveillance/nndss/casedef/measles_2010.htm) ...

“**Confirmed measles cases** in the United States are reported by state and local health departments to the CDC using a standard case definition. A measles case is considered confirmed if it is laboratory-confirmed, or meets the clinical case definition (an illness characterized by a generalized rash lasting  $\geq$  three days, a temperature of  $\geq 101^\circ\text{F}$  [ $\geq 38.3^\circ\text{C}$ ], and cough, coryza, or conjunctivitis), and is linked epidemiologically to a confirmed case”.

Laboratory confirmation of measles is made by either one of the following:

- Detection in serum of measles-specific immunoglobulin M (IgM)
- Significant rise in measles immunoglobulin G (IgG) level
- Isolation of measles virus
- Detection of measles virus by nucleic acid amplification from a clinical specimen”.

Note:

- IgM may take four days after rash onset to appear and last for 28 days. After immunization, 2% are positive at one week, 75% are positive at one month, 10% are still positive after two months.

- IgG rarely occurs before seven days after onset.

Cases are considered **importations** if exposure to measles virus occurred outside the United States seven to 21 days before rash onset and rash occurred within 21 days of entry into the United States, with no known exposure to measles in the United States during that time.

**Patient A's Onset:** On 3/6/12, Patient A vomited during the day and developed a rash that evening. The next day a rash appeared on the face and spread to chest and legs over the next few hours. No diagnosis was made at that time. Later, Patient A had fever (100.7°F) with conjunctivitis starting the next few days. On 3/10/12, A's parents returned for medical care.

**A Is Diagnosed With Measles:** Upon returning after four days, A's parents were told that A had measles; blood was drawn for measles testing and sent to a private lab. The parents were advised to keep A out of day care for four days. The physician who had seen measles was certain that the rash is measles.

**Was It Really Measles?** Apparently the issue was not raised in spite of the lack of risk factors and the fuzzy clinical picture: Patient A had had two MMR vaccines at age one, the first one in January 2010 and the second one in July the same year. Now, eight months later, he is suspected of measles. A and his family had no history of travel outside the U.S. and had no visitors from abroad. There was no history of any relatives, friends or anyone with a rash.

**But the Lab Is Positive:** On 3/14/12 the lab results showed highly positive anti-measles anti-IgG and highly positive measles anti-IgM antibodies. At that time, the case was reported to the health department.

**All Evidence Points Away From a Real Measles Case:**

Although not completely typical of measles (lack of prodrome lasting for a few days before the onset of the rash, moderate fever, onset of rash, fever and conjunctivitis at the same time) it is conceivable that the rash could have been considered 'suspect'. One wonders, if the rash was so typical why was measles only suspected some four days into the rash? On 3/6/12 the child's parents were told to keep their child away from day care but no recommendation was made to warn the day care center, no report was made to public health. It is only one week after onset and after receiving lab test results that the medical center reported the case.

After vaccination it is no surprise to observe positive serologic results. Serology is not very useful under these circumstances.

Epidemiologically, it would be extraordinary to have a child with two MMRs having measles in an area with no measles, no history of travel, no contacts with visitors from abroad, no contacts with anyone with measles suspect rashes.

**But the Story Goes On ...** Leaving no stone unturned, Public Health followed up with the day care, warning the center director and the parents, making sure all children had proper immunizations, excluding those who were not immunized, establishing a surveillance for the staff and contacts at the medical clinics. All in all, Public Health contacted 95 parents who had had children in the same waiting room as Patient A, 36 contacts through the day care, eight at the health care facilities and 10 family contacts. None of these have reported any rash or any measles-like symptoms.

In this process Public Health uncovered **more rashes**:

- Patient N with a rash on arms and legs starting on 3/14/12, history of MMR in 2008.
- Patient C with a rash started on 3/6/12 with fever, rash on his face and sore throat attributed to strep throat, spreading the next day to his entire body. In the course of the next nine days, C went to two more health care facilities where the initial diagnosis of scarlet fever rash morphed into urticarial rash to end up “probably a viral rash”.

To avoid increasing the same original confusion, **nasopharyngeal swabs** were collected on any suspect of measles as well as blood for serologic testing. All were negative. For Patient A the naso-pharyngeal was collected very late after onset. All sera were positive for IgG (not surprising since all had been well immunized with MMR), and negative for IgM at the CDC laboratories.

It comes as no surprise that **a clinical diagnosis of measles has a very poor predictive value**. In 2004, Katz reviewed four studies on the clinical diagnosis of measles – 1981 & 1994, (Evaluation of the Measles Clinical Case Definition. Katz et al. J Infect Dis. (2004) 189 (Supplement 1): S153-S159). The clinical case definition was: generalized maculopapular rash, fever ( $\geq 38.3^{\circ}\text{C}$ , if measured), and either a cough, coryza, or conjunctivitis. Serological confirmation was used as the confirmatory test. The predictive value of clinical diagnosis of measles decreased from 74% to 1% as the incidence of measles decreased from 171 per 100,000 per year in the population, to less than 1.3 per 100,000. The low positive predictive value of the clinical case definition in settings of low incidence demonstrates that serological confirmation is essential to ensure an accurate diagnosis of measles when measles is rare.

Nowadays with the elimination of measles, even the predictive value of a positive serologic test is also very poor. **False positive IgM results are not uncommon**:

- In the State of Alaska Public Health Bulletin No. 26 (11/16/1994) the State Laboratory employed a widely used commercial test kit approved by the U.S. Food and Drug Administration for measles IgM testing. Of the 16 IgM positive cases, only eight (50%) of the cases were confirmed at the CDC Laboratories which used a methodology developed in-house.

- A number of different viruses, including measles and rubella viruses, parvovirus B19, enterovirus and adenovirus, can give clinical presentations similar to measles and therefore laboratory confirmation is essential. In addition, it has been shown that reactivation of IgM responses to multiple viruses (including measles and rubella viruses and parvovirus B19) can occur in response to infection by one of the viruses. (Tipples G et al 2003. Assessment of Immunoglobulin M Enzyme Immunoassays for Diagnosis of Measles. Clin. Microbiol. vol. 41 # 10 4790-4792).

<b>False Positive IgM Results for Measles May Be Due To...</b>	<b>Suspect a False Positive Measles IgM Test When...</b>
<ul style="list-style-type: none"> <li>• Presence of rheumatoid factor</li> <li>• Another rash illness: parvovirus 19, enterovirus and more</li> </ul>	<ul style="list-style-type: none"> <li>• Subject adequately immunized</li> <li>• No source or spread of cases</li> <li>• Case does not meet clinical case definition</li> <li>• IgG result is positive within seven days of rash onset</li> </ul>

**Positive rubeola test results lead to extensive and expensive epidemiologic investigations and public health control measures. Better laboratory tests are needed to reduce the number of unnecessary investigations.**

**Measles virus is present in urine, nasopharyngeal aspirates, heparinized blood, or throat swabs.** Specimens for PCR or virus culture should be obtained from every person with a clinically suspected case of measles and should be shipped to the state public health laboratory or the CDC, at the direction of the state health department. Clinical specimens for viral identification should be collected at the same time as samples taken for serologic testing. Because the virus is more likely to be isolated when the specimens are collected within three days of rash onset, collection of specimens for virus isolation should not be delayed until serologic confirmation is obtained. Clinical specimens should be obtained within seven days, and not more than 10 days, after rash onset. A detailed protocol for collection of specimens for viral isolation is available on the CDC website.

### **1-Throat swab**

Vigorously swab tonsillar areas and posterior nasopharynx with a viral culturette. Use tongue blade to depress tongue to prevent contamination of swab with saliva. Place swab into a Viral Transport Medium (VTM).

### **2-Urine specimen**

Collect 10 to 40 ml of urine in a **sterile** 50 ml centrifuge tube or a urine specimen container. First-morning voided specimens are ideal, but any urine collection is adequate. Have patient void directly into container, collecting from the first part of the urine stream if possible.

### **3-Nasal or nasopharyngeal swab**

Use sterile swabs to swab the nasal passage or the nasopharynx with either a viral culture swab or culturette. Do not use special (e.g., anaerobic) media. Place swab into VTM.