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April 10, 2008

To: Wisconsin physicians, other clinicians, infection control professionals, local health department directors in Wisconsin

From: Jeffrey P. Davis M.D.
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Subject: **Measles confirmed in Wisconsin residents: important information**

Since April 4, 2008, the public health system has become aware of four cases of measles recently diagnosed in Wisconsin residents (3 Milwaukee County residents and one Waukesha County resident). Following is a brief presentation of the cases plus **very important information** on the following:

- Measles case presentations (Appendix I)
- Measles case definitions (Appendix II)
- Laboratory testing of suspect cases (Appendix III)
- Case reporting (Appendix IV)
- Isolation of suspect cases and quarantine measures for susceptible contacts (Appendix V)
- Immunization recommendations for close contacts and the general public (Appendix VI)

Measles virus is very infectious and the illness it causes is often misdiagnosed, particularly during the current era when the proportion of physicians with experience diagnosing and managing patients of measles is dwindling. Timely and aggressive application of isolation, quarantine (when needed), post exposure vaccination or immune globulin prophylaxis and other important control measures is critical. Please heighten your suspicion of measles and report any suspect cases of measles **immediately upon suspicion** to your local health department. Pictures of individuals with measles can be found at the following website:

<http://www.cdc.gov/vaccines/vpd-vac/measles/photos.htm> Also, please do not assume that someone else will report the suspected case...regardless of whether you are a clinician, a laboratorian or an infection control professional, please report it!! We can handle redundancy. When in doubt please call the local health department (see Appendix IV for phone numbers). Please call your local health department or the Wisconsin Immunization Program at 608-267-9959 if there are questions.

Appendix I

Measles Investigation and Control Guidelines Case presentations

The four cases are presented in chronologic order of illness onset date. Follow-up investigation of all cases is in progress, thus the information following is preliminary.

Case 1: The first case, confirmed by serologic testing, occurred in a 37 year-old male who presented to an emergency department on March 20 with a 5 day history of fever, chills, cough, sore throat, nasal congestion and fatigue and a 4 day history of rash. The rash began near the patient's nose and then spread across his face and down to his chest. Upon examination the rash was described a maculopapular and it appeared on his face, scalp, torso and arms. Also described were pharyngeal injection, a "red rash to his palate" and "white lesions on the buccal mucosa that looked like the start of small ulcers" (These findings were consistent with the enanthem and Koplik spots seen during measles). The patient stated he was up to date on all his vaccinations. A rapid strep test was negative and a monospot was positive. Among the conditions included in the differential diagnosis were mononucleosis, rubella and measles. The patient was advised to see his primary care physician the following day when blood specimens for serologic and other tests would be obtained. When the patient returned for a visit to his personal physician the following day, the patient complained of worsening symptoms, headache and nausea. The maculopapular rash was still present and the patient was admitted to a hospital for management of fever, rash and dehydration plus evaluation of several other findings. He was discharged from the hospital on March 26. Subsequently, results of testing at an out of state laboratory of a serum specimen obtained on March 21 demonstrated an elevation in measles IgM antibodies.

Depending on the date of rash onset (later stated to be March 19), the likely interval that this patient was infectious and transmitting measles virus began some time between March 12 and March 16 and continued through March 23. The patient lives with his wife and daughter. The patient and wife do not have known measles vaccination dates. The patient had no out of state travel. About 1 to 2 weeks prior to illness onset, he had work-related contact with a visitor from China who was ill at the time of the visit.

Case 2: On April 4, 2008, a laboratory confirmed diagnosis of measles was made in a 23 month old girl who had received no prior doses of MMR vaccine. The child had onset of fever on March 26 and onset of rash on March 27. She had associated signs and symptoms that included coryza, cough and conjunctivitis (the 3 C's). She was evaluated in an urgent care clinic on March 28 and was diagnosed as having otitis. Her illness worsened and she was re-evaluated in an urgent care clinic and admitted to a hospital on March 31 for management of dehydration and high fever. Blood for serologic testing, obtained from the patient on April 3 and sent to the Wisconsin State Laboratory of Hygiene, was confirmed as measles specific IgM positive on April 4. The SLH then requested urine and nasopharyngeal swab specimens for PCR and virus culture. PCR testing of the NP specimen was positive for measles virus. An extensive public health measles follow-up investigation conducted by local and state public health agencies was initiated on April 4 immediately following notification of the serologic diagnosis of measles.

The case patient lives with her parents and has no siblings. Each parent has a history of having received at least 1 dose of MMR vaccine. The patient did not travel outside of Milwaukee County and had no known contact with individuals who had recently returned from other countries. She had no known contact with anyone having a measles-like illness. She was also seen in the same urgent care clinic on March 17 for treatment of fever, vomiting and diarrhea. During the interval that the patient was likely to be infectious (the probable spread period estimated to be March 22 through April 1) she attended a day care center (DCC) and was also cared for in a child care center in a health club. The other DCC attendees include 11 children under 12 months of age at the time of exposure to the case patient, all of whom had not been vaccinated with MMR vaccine. These children have been placed in home quarantine with active daily surveillance for the earliest signs and symptoms of measles. Because more than 6 days elapsed following exposure of these unvaccinated infants to the case patient, immune globulin was not administered.

Cases 3 and 4: These two additional cases were confirmed by PCR testing of NP swab specimens obtained from two attendees of the DCC that was also attended by case patient 2. These attendees, a 1 year old (DOB 4/5/07) and a 5 month old, had early signs of a respiratory illness reported following initiation of home quarantine and surveillance. Specimens for laboratory (PCR and virus culture) were obtained on April 8 and PCR detection of measles virus infection was made from the NP swab specimens. The 1 year old had onset of rash on April 9.

Extensive investigation of the out patient and in patient health care facilities (isolation precautions, air flow, employee measles related immune status) continues. Because case patients 1 and 2 do not have known sources of infection and cases of measles with spread (subsequent generations) have recently occurred in other regions of the United States, health care professionals throughout Wisconsin are asked to maintain a high index of suspicion for measles in patients presenting with febrile rash illnesses. All suspect cases of measles must be reported to the local health department of jurisdiction upon suspicion. Health care providers should inform the local health department immediately of any suspect cases, without waiting for laboratory confirmation.

Information on measles occurring in California can be found in a Morbidity and Mortality Weekly Report - Early Release, dated February 22, 2008, at:

<http://www.cdc.gov/mmwr/preview/mmwrhtml/mm57e222a1.htm>

Appendix II

Measles Investigation and Control Guidelines Case definitions

The following case definition for measles has been approved by the Council of State and Territorial Epidemiologists (CSTE) and was published in 1997.

Clinical case definition

Measles is an illness characterized by all of the following:

- A generalized maculopapular rash lasting 3 days
- A temperature 101°F (38.3°C)
- Cough, coryza, or conjunctivitis

Laboratory criteria for diagnosis

Laboratory confirmation is made by any one of the following:

- Positive serologic test for measles immunoglobulin M (IgM) antibody
- Significant rise in measles antibody level by any standard serologic assay
- Isolation of measles virus from a clinical specimen

Case classification

Suspected: Febrile illness accompanied by generalized maculopapular rash.

Probable: A case that meets the clinical case definition, has noncontributory or no serologic or virologic testing, and is not epidemiologically linked to a confirmed case.

Confirmed: A case that is laboratory confirmed or that meets the clinical case definition and is epidemiologically linked to a confirmed case. A laboratory confirmed case does not need to meet the clinical case definition.

Reporting

All suspect cases of measles should be reported immediately to the local health department of jurisdiction. Do not wait for laboratory confirmation.

Appendix III

Measles Investigation and Control Guidelines Laboratory Testing

Because measles is an extremely rare disease in the United States, clinical evidence is not sufficient to confirm a case of measles without corroborating laboratory or epidemiologic evidence. Many clinicians have never seen a case of measles, and most patients who present with measles-like illness today do not have measles. Because measles is such a highly contagious disease, with the potential for explosive spread following importation of the virus, it is critical to rapidly identify the measles cases that do occur. It is crucial to the efficient investigation and control of measles to use laboratory diagnosis to confirm actual measles cases. Health care providers and clinical laboratories should inform the local health department immediately of any suspect cases, do not wait for laboratory confirmation.

All specimens should be submitted to the Wisconsin State Laboratory of Hygiene. All diagnostic testing will be performed at no cost to the submitter; transport of specimens can also be arranged via Dunham Express at no cost to the submitter. Specimens should only be submitted from individuals who are symptomatic. Below are the guidelines for laboratory testing.

Specimens should be submitted on all of the following patients:

- **Individuals exposed to measles, presenting with prodromal symptoms of measles with or without rash, AND**
- **Individuals with rash and fever indicative of measles.**

Specimens to be submitted:

- Nasopharyngeal and throat swabs in viral transport media for PCR testing. Both swabs should be combined in one vial of viral transport medium (e.g., M4, M5, etc.). Order test code # 3214 .
- Urine specimen for PCR (in sterile, screw-capped container without additives). Order test code # 3214.
- **If the patient has a rash, collect a serum specimen for measles serology.** Note: A convalescent serum, collected two weeks after onset of rash, should also be submitted. Order test code # 2814.

Transport of specimens to the State Laboratory of Hygiene:

- **Specimens should be packaged according to regulatory requirements. The cost of specimen transport can be billed to the State Laboratory of Hygiene if arrangements are made with Dunham Express, billing to Account # 7263.**

Serologic Testing

Generally, in a susceptible person exposed to measles virus, the IgM response starts around the time of rash onset and is transient, persisting 1–2 months. The IgG response starts more slowly, at about 7 days after rash onset, but typically persists for a lifetime after infection. The IgG also remains positive after successful vaccination. The diagnosis of acute measles infection can be made by detecting IgM antibody to measles in a single serum specimen or by detecting a rise in

the titer of IgG antibody in two serum specimens drawn roughly two weeks apart. Uninfected persons are IgM negative and will either be IgG negative or IgG positive depending upon their previous infection or vaccination histories. Tests for measles antibodies are often positive on the day of rash onset. However, in the first 72 hours after rash onset, up to 30% of tests for IgM may give false negative results. Tests that are negative in the first 72 hours after rash onset should be repeated. IgM is detectable for at least 28 days after rash onset and frequently longer.

PCR

Detection of measles virus by reverse transcription polymerase chain reaction (RT-PCR) in clinical specimens confirms the diagnosis of measles. However, a negative RT-PCR does not rule out measles because test sensitivity is affected by the timing of specimen collection and the quality and handling of the clinical specimens. If measles virus is detected by RT-PCR, the viral genotype can be used to distinguish between measles disease (caused by a wild-type measles virus), and measles vaccination. Genotyping will be done by the CDC. Specimens for PCR should be collected at the same time as the acute serum specimen.

Appendix IV

Measles Investigation and Control Guidelines Case Reporting

Measles is a Category I disease under the Wisconsin Statute Chapter 252.05 and Administrative Rule Chapter HFS 145 which requires the reporting of communicable diseases. Category I diseases are to be reported **immediately** by telephone or fax to the patient's local health officer upon identification of a case or suspected case. A listing of local health departments can be found at: <http://dhfs.wisconsin.gov/localhealth/>. In addition to the immediate report, within 24 hours complete and mail an Acute and Communicable Diseases Case Report (DPH 4151). Patients should be informed that the local health department will be in contact with the family to initiate case investigation and control measures.

The newly revised DPH 4151 "Acute & Communicable Disease Case Report Form" can now be downloaded from the Division of Public Health forms page in two formats:

Microsoft Word fillable form: <http://dhfs.wisconsin.gov/forms/DPH/dph04151.doc>
PDF fillable form: <http://dhfs.wisconsin.gov/forms/DPH/dph04151.pdf>

Appendix V

Measles Investigation and Control Guidelines Guidelines for isolation and quarantine during the measles outbreak

Use of Quarantine:

Except for the early stages of an outbreak, imposing quarantine measures for outbreak control is usually both difficult and disruptive to schools and other organizations. Under special circumstances (i.e., in the early stages of an outbreak), restriction of an event or other quarantine measures might be warranted. However, such action is not recommended as a routine measure for control of most outbreaks. The primary strategy for control of measles outbreaks is achieving a high level of immunity through immunization.

Exposed and susceptible individuals:

- Only exposed and susceptible individuals who cannot readily document measles immunity should be vaccinated or excluded from the setting (school, hospital, etc.).
- Only doses of vaccine with written documentation of the date of receipt should be accepted as valid. Verbal reports of vaccination without written documentation shall not be accepted.
- Local health departments must coordinate quarantine orders with exposed individuals who live in one jurisdiction but attend daycare, school or work in another.
- Previously unvaccinated exposed persons must be quarantined until 21 days after exposure to the last case of measles, unless the vaccine was given within 72 hours of the first exposure or IG was given within 6 days of the first exposure.
- Persons receiving their first dose before or within 72 hours of exposure may be readmitted immediately to the school or child care facility.

Surveillance of exposed individuals and household contacts:

- Individuals who have been exposed and are susceptible should be monitored on a daily basis for signs and symptoms of measles disease. This is highly recommended to identify additional cases should they develop.
 - Coordination between health department jurisdiction will be needed to ensure active daily surveillance
 - Physicians and local health care providers should inform parents and patients that the local health department will be following up with them during this quarantine period.
- Household contacts of exposed individuals need to have their immunization status verified and be immunized if vaccine is not contraindicated.
- Individuals who have been exposed but are not susceptible should be counseled regarding the signs and symptoms of measles.

Control of outbreaks in medical settings:

Persons who work in health-care facilities (including volunteers, trainees, nurses, physicians, technicians, receptionists, and other clerical and support staff) are at increased risk of exposure to measles, and all persons who work in such facilities in any capacity should be immune to measles to prevent any potential outbreak.

- Immunity to measles (through vaccination) means a minimum of 2 doses of MMR vaccine for all persons born in or after 1957 who work in health care facilities.
- If one or more cases occurs within or in the areas served by a hospital, clinic, or other medical or nursing facility:
 - All personnel born in or after 1957 (including volunteers, trainees, nurses, physicians, technicians, receptionists, and other clerical and support staff) should receive a dose of MMR vaccine, unless they have documentation of measles immunity (Table 1).
 - Serologic screening of health-care workers during an outbreak to determine measles immunity is not generally recommended, because arresting measles transmission requires the rapid vaccination of susceptible health-care workers, which can be impeded by the need to screen, wait for results, and then contact and vaccinate the susceptible persons.
 - ✓ Susceptible health-care workers exposed to measles should receive a dose of MMR vaccine.
 - ✓ Susceptible health-care workers exposed to measles should be removed from all patient contact and excluded from the facility from the fifth day after their first exposure to the 21st day after the last exposure, even if they receive MMR vaccine or post-exposure IG.
 - ✓ Personnel who become ill with fever or rash should be removed from all patient contact and excluded immediately from the facility until 4 days after the onset of their rash.

Isolation of suspect individuals coming to a clinic, hospital or ED:

If at all possible, parents should call ahead to make sure arrangements can be made to handle a person suspected of having measles and needing to be seen by a health care professional. Coordination of effort is needed to ensure that individuals who may have measles do not expose susceptible patients in a clinic setting.

Airborne transmission precautions prevent transmission of infectious materials when suspended in the air. The preferred placement for patients suspected of having measles and who require airborne precautions is in an airborne infection isolation room (AIIR). An AIIR is a single-patient room that is equipped with special air handling and ventilation capacity that meets the Am. Institute of Architects/Facility Guidelines Institute (AIA/FGI) standards (i.e. monitored negative pressure relative to the surrounding area, with a minimum of 6 air exchanges per hour, air exhausted directly to the outside or re-circulated through HEPA filtration before being returned).

In settings where Airborne Precautions cannot be implemented due to limited engineering resources, masking the patient, placing the patient in a private room with the door closed, and providing health care workers who are susceptible to measles N95 or higher level respirators or masks if respirators are not available. These precautions are necessary to reduce the likelihood of airborne transmission until the patient is either transferred to a facility with an AIIR or returned to the home environment.

All exam rooms used by the suspect measles case must be thoroughly disinfected before they are used for other patients.

It is recommended that only health care workers who are immune to measles have contact with cases or suspect cases of measles.

Isolation of hospitalized patient:

In addition to standard precautions, airborne transmission precautions are indicated for 4 days after the onset of rash in otherwise healthy patients and for the duration of the illness for immunocompromised patients.

Definitions

Isolation - represents separation of symptomatic individuals for a period at least equal to the period of communicability.

Quarantine - restriction of activities for well persons who have been exposed to a case of communicable disease during its period of communicability to prevent transmission during the incubation period.

Table 1

Acceptable Evidence of Immunity for Health Care Workers					
Disease or Vaccine	Documented vaccination *	Number of doses	Laboratory evidence of immunity	Diagnosis or verification of disease by a health care provider	Birth before a specified date
MMR	Yes	2			
Rubella	Yes	1	Yes [†]	No [§]	No [¶]
Measles	Yes	2	Yes [†]	No [‡]	See footnote ^{**}
Mumps	Yes	2	Yes [†]	No [‡]	See footnote ^{††}
Varicella	Yes	2	Yes ^{§§}	Yes	No ^{***}

* A documented vaccination is one that has been written in a conventional or electronic record and includes the name of the vaccine and the month, day, and year it was administered.

† Serologic screening for measles, rubella, or mumps immunity generally is neither necessary nor recommended if a persons has other acceptable evidence of immunity to the disease.¹

§ HFS 124.07(4) does not recognize history of disease as evidence of immunity to rubella.

¶ HFS 124.07(4) does not recognize birth before any date as evidence of immunity to rubella.

‡ Per Wisconsin Council on Immunization Practices (WCIP) recommendation.

**Health care facilities should consider recommending a dose of MMR vaccine for unvaccinated workers born before 1957 who are at risk for occupational exposure to measles and who do not have a history of measles disease or laboratory evidence of measles immunity.¹

††Because birth before 1957 is only presumptive evidence of immunity, health-care facilities should consider recommending 1 dose of live mumps virus vaccine for unvaccinated workers born before 1957 who do not have a history of physician-diagnosed mumps or laboratory evidence of mumps immunity.²

§§Commercial assays can be used to assess disease-induced immunity to varicella but they lack sensitivity to always detect vaccine-induced immunity (i.e., they might yield false-negative results).³

***Birth in the United States before 1980 is not considered evidence of immunity to varicella for health care personnel. Certainty regarding immunity of health care personnel is desirable because of the possibility of nosocomial transmission to high risk patients.³

¹Centers for Disease Control and Prevention. Measles, Mumps, and Rubella – Vaccine Use and Strategies for Elimination of Measles, Rubella and Congenital Rubella Syndrome and Control of Mumps: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 1998;47(No. RR8):11-12.

²Centers for Disease Control and Prevention. Updated Recommendations of the Advisory Committee on Immunization Practices (ACIP) for the Control and Elimination of Mumps. MMWR 2006; 55(22):629-630.

³Centers for Disease Control and Prevention. Prevention of Varicella: Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2007;56(No. RR04):16-17.

Appendix IV

Measles Investigation and Control Guidelines Immunization Recommendations

Preschool age children: Administer the first dose of MMR vaccine to children at 12 to 15 months of age followed by a second dose required at school entrance around age 4 or 5 years. However, in an outbreak situation such as a family or day care exposure, it is permissible to administer the 2nd dose of MMR a minimum of 4 weeks after the first dose. At this time we are not recommending MMR vaccine be administered to children less than 12 months of age.

School age children, adolescents and adults: Two doses of MMR vaccine are recommended for children in kindergarten through 12th grade. Students in colleges and universities and international travelers who were born during or after 1957 need two doses of MMR vaccine and those born before 1957 are assumed to be immune (Table 2). Health care workers who were born during or after 1957 need two doses of MMR vaccine and those born before 1957 need one dose. For the general public, persons born before 1957 can be presumed to be immune. For persons born in or after 1957 one dose a measles containing vaccine is recommended. Exposed day care and school personnel born in or after 1957 need two doses of MMR vaccine.

Note: Per the American Academy of Pediatrics Red Book “Minor respiratory, gastrointestinal or other illness with or without fever do not contraindicate use of live virus vaccines, such as MMR”. Vaccine including MMR should not be deferred in the case of fever or mild-to-moderate illness.

Post exposure prophylaxis

Susceptible individuals with a known or highly probable exposure, depending on timing and age, can be treated with MMR vaccine or IG to prevent or modify measles. In cases where both are acceptable, MMR is preferred.

- **MMR Vaccine** (for persons 12 months of age or older): Exposure to measles is not a contraindication to vaccination. MMR or measles vaccine, if administered within 72 hours of initial measles exposure, may provide some protection. If exposure to measles, rubella, or mumps does not cause infection, post exposure vaccination with MMR should induce protection against subsequent infection. If the exposure results in infection, no evidence indicates that administration of MMR vaccine during the presymptomatic or prodromal stage of illness increases the risk for vaccine-associated adverse events.
- **Immune Globulin:** IG is indicated for susceptible household contacts of measles patients, particularly those for whom the risk for complications is increased and who cannot receive MMR vaccine (i.e., infants aged 12 months or less, pregnant women, or immunocompromised persons). If administered within 6 days of exposure, IG can prevent or modify measles in a nonimmune person. However, any immunity conferred is temporary unless modified or typical measles occurs. The usual recommended dose of IG is 0.25 mL/kg (0.11 mL/lb) of body weight (maximum dose = 15 mL). However, the recommended dose of IG for immunocompromised persons is 0.5 mL/kg of body weight (maximum dose = 15 mL). For persons receiving IG therapy, i.e. ongoing therapy for

other conditions, administration of at least 100 mg/kg within 3 weeks before measles exposure should be sufficient to prevent measles infection.

TABLE 2

Acceptable presumptive evidence of immunity to measles for other than health care workers

	Routine	International travelers institutions	Students at post-high school educational
Measles	(1) documentation of adequate vaccination: - preschool-aged children and adults not at high risk: 1 dose - school-aged children (grades K-12): 2 doses, or (2) laboratory evidence of immunity, or (3) born before 1957, or (4) documentation of physician-diagnosed measles	(1) documented administration of 2 doses of live measles virus vaccine, or (2) laboratory evidence of immunity, or (3) born before 1957, or (4) documentation of physician-diagnosed measles	(1) documented administration of 2 doses of live measles virus vaccine, or (2) laboratory evidence of immunity, or (3) born before 1957, or (4) documentation of physician-diagnosed measles