Measles Outbreak

Measles is caused by the rubeola virus, which is a single-stranded, enveloped RNA virus that is a member of the genus Morbillivirus in the Paramyxoviridae family. Humans are the only natural hosts of measles virus. Measles virus normally grows in the cells that line the back of the throat and lungs. Measles is a disease that kills an estimated 90,000 people worldwide each year and is still common in some European countries, Africa, Asia, and the Pacific. Measles was declared eliminated in the U.S. in 2000 due to high 2-dose measles vaccine coverage, but there has been a resurgence of infections periodically since 2008.

Thirty-four cases of measles from 11 states (including Missouri & Kansas) have been reported to the Centers for Disease Control and Prevention (CDC) between Jan. 1 and March 30, 2018. There were 117 cases from 15 states reported for 2017. Most cases in the United States involve patients who are unvaccinated and are exposed to infections acquired in another country.

Measles is a highly contagious disease and is transmitted by contact with an infected person through coughing and sneezing. Patients are considered to be contagious from 4 days before until 4 days after the rash appears. After an infected person leaves a location, the virus remains contagious for up to 2 hours in the air and on surfaces.

Measles symptoms usually appear 7-14 days after infection beginning with a prodrome of high fever, cough, coryza, and conjunctivitis, followed by Koplik’s spots 2 to 3 days later. An erythematous, maculopapular, confluent rash that begins on the face and spreads in a cephalocaudal direction appears about 4 days after the initial symptoms. Sometimes immunocompromised patients do not develop the rash. Koplik’s spots on the buccal mucosa are considered pathognomonic of measles and may precede onset of rash by several days.

Approximately one in 10 children with measles also develops an ear infection, 1 in 20 pneumonia, 1 in 1000 encephalitis, and 2 in 1000 die. People at high risk for severe illness and complications from measles include infants and children aged <5 years, adults aged >20 years, pregnant women and people who are immunocompromised.

According to a recent health advisory issued by the Missouri Department of Health and Senior Services, measles cases have been confirmed recently in the Kansas City metro area in both states. Suspected measles patients should be isolated & reported immediately to local and/or state public health departments, prior to any laboratory testing. In Missouri, specimens may be submitted for IgM serology and PCR testing after consultation with the State Public Health Laboratory at 573/751-6113. In Kansas, suspected cases should be reported immediately to KDHE at 1-877-427-7317, and testing will be facilitated based on consultation. Additional information, including vaccine recommendations can be found at http://www.cdc.gov/measles/index.html.

Specimen Rejection

Clinical laboratory test results are a very important parameter in screening, diagnosis, monitoring and management of diseases. 70-80% of clinical decisions in hospitals are based on laboratory test results. “With great power comes great responsibility”, the laboratory professionals handle these specimens like a sacred task.

The laboratory can reject specimens for any reasons:
- Hemolysis/lipemia
- Clots present in an anticoagulated specimen
- Nonfasting specimens when test requires fasting
- Improper blood collection tube
- Short draws, wrong volume
- Improper transport conditions
- Contaminated specimen/leaking container
• Discrepancies between requisition and specimen label
• Unlabeled or mislabeled specimen

Many of these reasons appear to be related to the analytic or technical aspects of the testing. Which is true, but is not the only reason why laboratory rejects these specimens. A compromised specimen has potential of causing patient harm given the important role laboratory parameters play during the management of patients.

Medical errors are the third leading cause of death in the United States. If laboratory would not reject specimens and report out results from compromised specimens, the magnitude of this potentially fatal problem will be even bigger.

In addition, appropriate laboratory test utilization is also important to prevent patient harm. Inappropriately ordered test can lead to a false positive result, which can lead to additional unnecessary tests, procedures or treatments that may cause patient harm.

At Saint Luke’s Health System, the laboratory leadership works closely with healthcare providers, managers and executives to ensure high standards of patient safety.

Testing for Protein C Deficiency

Protein C is an important negative feedback loop in coagulation pathway. After activation by thrombin (an activated procoagulant), activated protein C in combination of protein S, degrades upstream procoagulant factors (Va and VIIIa) limiting rate of subsequent thrombosis. Deficiency of protein C is one of the risk factors for venous thromboembolism including deep vein thrombosis (VTE) and pulmonary embolism.

Hereditary protein C deficiency is estimated to occur in approximately 0.14-0.5% of general population and confers approximately 7-fold increased risk of VTE.

Hereditary protein C deficiency can be quantitative (type I) or qualitative (type II). Acquired protein C deficiency is more common and occurs secondary to liver dysfunction, consumption (disseminated intravascular coagulation, surgery, and trauma), warfarin or L-asparaginase therapy, and vitamin K deficiency.

Laboratory testing of protein C can differentiate quantitative type I (similar decrease in quantity and function) and qualitative type II (decrease in function with normal antigen levels). The available methods for quantitation rely on binding of antibody reagent to protein C present in the blood and includes enzyme-linked immunosorbent assay (ELISA). The functional assays for protein C are either clot-based or chromogenic (spectrophotometric). The clot-based assays mostly use modified activated partial thromboplastin time (aPTT) or Russell viper venom (RVV) method. Briefly, the method measures the time to clot formation after treatment with protein C activator which is inversely related to the function. Chromogenic assays directly detects the enzymatic activity of protein C by measuring cleavage of a specific chromogenic substrate, which upon degradation generates color.

Pre-analytical factors affecting protein C activity include history of anticoagulation therapy such as warfarin and direct thrombin inhibitors (DTI) (eg argatroban). Warfarin falsely reduces the activity, on both clot-based and chromogenic assays. In contrast, DTIs falsely increase protein C activity, especially in clot-based assays. Other factors such as elevated factor VIII can falsely reduce and lupus anticoagulants can falsely increase the protein C activity results obtained specifically by aPTT-based clotting assays.

A protein C activity assay is preferable screening test for patients suspected of hereditary protein C deficiency, to help in detection of type II deficiencies. At Saint Luke’s Hospital, both protein C antigen and activity assays (chromogenic) are performed, Monday-Friday. Specimen required is 2 mL blue-top.

<table>
<thead>
<tr>
<th></th>
<th>Heparin Tolerance</th>
<th>FVIII Elevation</th>
<th>Lupus Anticoagulant</th>
<th>DTI</th>
<th>FV Leiden</th>
<th>Detects Type II Deficiency</th>
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<tbody>
<tr>
<td>aPTT Clot-Based</td>
<td>up to 1 or 2 U/mL</td>
<td>False Low</td>
<td>False High</td>
<td>False High</td>
<td>False Low</td>
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<tr>
<td>RVV Clot-Based</td>
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<td>Maybe False Low</td>
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<tr>
<td>Chromogenic</td>
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<td>No Effect</td>
<td>No Effect</td>
<td>No Effect</td>
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<tr>
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<td>No Effect</td>
<td>No Effect</td>
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<td>No Effect</td>
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</tr>
</tbody>
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