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## Measles Outbreak Update

Measles, caused by rubeola virus, is among the most contagious of infectious diseases. Measles is spread by contact with an infected person or their respiratory secretions. The virus can remain active and contagious for up to 2 hours in the air and on surfaces. Measles is most contagious when respiratory symptoms are at peak, however, the contagious period probably extends to several days before & after onset of the rash. Incubation period is 10 to 14 days.

Symptoms of measles include a prodrome of high fever, cough, coryza, conjunctivitis and Koplik's spots, followed by an erythematous rash. Koplik's spots on the buccal mucosa are considered pathognomonic of measles and may precede onset of rash by several days. Patients who are immunocompromised or pregnant are at highest risk for complications which can include pneumonia, encephalitis, and death. The CDC suggests the diagnosis of measles should be considered in any patient with fever  $\geq 101^{\circ}\text{F}$  ( $38.3^{\circ}\text{C}$ ) and rash that lasts 3 days or more, along with compatible respiratory symptoms.

On June 22, 2011 the CDC released a health advisory regarding an increased number of reported measles cases in the United States. During the first six months of the year, 156 cases were confirmed, which is the highest number since 1996. Currently, several European countries, as well as Africa and Asia report measles as endemic or an outbreak. The U.S. cases to date have involved residents with an international travel history, unvaccinated visitors, and associated contacts.

Testing for suspected measles infection should include rubeola/measles IgM & IgG serology. Positive IgG results with negative IgM results indicate immunity to infection. Positive IgM results with or without positive measles IgG indicates recent infection. Negative IgM and IgG results usually indicate non-immunity and absence of current infection however, specimens drawn early

in the acute phase of infection may also yield negative results. In suspected cases with negative serology, testing should be repeated in 7-10 days. The specimen requirement for measles/rubeola IgG and IgM is one red top or serum gel tube of blood. Testing is performed at Mayo Medical Laboratories.

Suspected measles patients should be isolated & reported immediately to local and/or state public health departments. Additional information, including vaccine recommendations can be found at <http://www.cdc.gov/measles/index.html>.

## Ehrlichiosis Season is Here

Ehrlichia species are small, obligate intracellular bacteria, similar to rickettsia. Organisms are transmitted to humans through tick bites, most commonly *Amblyomma americanum* (Lone Star tick) or *Ixodes*, which is also associated with Lyme disease. *Ehrlichia chaffeensis* is the causative agent of human monocytic ehrlichiosis (HME), while *Anaplasma phagocytophilum* is responsible for human granulocytic ehrlichiosis (HGE). Incubation period between tick bite and disease is generally 7 to 10 days.

HGE frequently presents with fever, myalgia, and malaise, with abdominal pain, nausea, vomiting, diarrhea and arthralgia in less than half of patients, and rash in less than 10%. Especially during the first week of illness, thrombocytopenia, leukopenia, and elevation of hepatic transaminases are common. CSF pleocytosis and meningo-encephalitis are rare in HGE. Overall mortality rate is 0.5-1%.

HME infections are caused by *E. chaffeensis*. The most frequent presenting symptoms are fever, malaise, and headache however, secondary symptoms of anorexia, nausea, vomiting, diarrhea, and abdominal pain are more frequent than in HGE. The illness closely resembles Rocky Mountain spotted fever, except that rash is present in only 36% of cases. Serious complications include hypotension, respiratory failure, meningo-encephalitis, acute renal failure, & coagulopathy.

Laboratory findings include leukopenia, thrombocytopenia, and elevated hepatic transaminases. CSF often shows elevated protein and pleocytosis, usually lymphocytes. The mortality rate of HME is 2-7%.

Recommended testing for acute HME/HGE includes PCR and serology. HME/HGE serology includes IgG and IgM antibody for both organisms. Diagnostic titers usually appear by the third week after symptom onset. Cross-reactivity between HME & HGE antibodies is common. Since both IgM and IgG antibodies may be negative in early infection, PCR for HME/HGE is recommended for suspected acute disease. Specimen requirement is one red top tube for serology and one lavender top tube, refrigerated, for PCR. Ticks should not be submitted for identification or testing. Likewise, the examination of peripheral blood smears for ehrlichia morulae is very low yield ( $\leq 20\%$ ) and is unreliable as a diagnostic test.

### **ADAMTS13: To Do or Not to Do?**

In 1982, Moake discovered that patients with relapsing acquired or congenital TTP had unusually large multimers of von Willebrand Factor (VWF) circulating in their plasma. He proposed that TTP patients lacked a VWF protease that normally cleaved ultra-large VWF to prevent it from causing intravascular platelet aggregation and thrombosis. In 1996, VWF-cleaving protease was identified in human plasma and the following year VWF-cleaving protease was shown to be missing from the plasma of patients with congenital TTP. Soon after, adults with acquired idiopathic TTP were reported to have severe VWF-cleaving protease deficiency caused by IgG autoantibodies that inhibit the enzyme. VWF-cleaving protease was named ADAMTS13 because it is the 13<sup>th</sup> member of the "A Disintegrin-like And Metalloprotease with Thrombospondin repeats" family of metalloproteases.

Approximately 66 to 75% of patients with idiopathic TTP have severe ADAMTS13 deficiency (activity < 5%). Severe deficiency identifies a subset of patients with idiopathic TTP who suffer from VWF-dependent microvascular thrombosis. Etiology remains unknown for patients with idiopathic TTP who do not have severe ADAMTS13 deficiency.

Severe congenital ADAMTS13 deficiency (Upshaw-Schulman syndrome) is an autosomal recessive

condition which may present in children or adults as episodes of TTP. More than 70 mutations within the ADAMTS13 gene have been reported in families with congenital TTP.

Patients with TTP secondary to bone marrow transplantation, HIV, pregnancy or malignancy almost never have severe ADAMTS13 deficiency. In addition, ADAMTS13 deficiency rarely if ever occurs in hemolytic uremic syndrome caused by Shiga toxin-producing *Escherichia coli*.

For idiopathic TTP, the value of distinguishing patients with and without ADAMTS13 deficiency remains uncertain. Patients with and without severe ADAMTS13 deficiency have had similar response rates and short-term survival (80%-90%). All patients with idiopathic TTP should be treated with plasma exchange until they achieve a remission, regardless of ADAMTS13 level. Therefore, rapid testing for ADAMTS13 is unnecessary.

ADAMTS13 testing is not particularly useful for patients with secondary TTP because this subset can be identified without it. Patients with secondary TTP do not respond to plasma exchange.

ADAMTS13 levels do have some prognostic utility. Approximately 30% of patients with severe deficiency relapse compared to 9% of patients without severe deficiency.

Assays for autoantibodies to ADAMTS13 provide additional prognostic information. The presence of detectable antibody at diagnosis correlates with a higher risk of relapsing disease. High-titer antibodies also have been associated with a delayed response to plasma exchange, refractory disease, and early death.

Laboratory monitoring after treatment with plasma exchange might identify patients with ADAMTS13 deficiency and a high risk of imminent relapse. Relapses occur in 60% of patients with persistent severe ADAMTS13 deficiency compared with only 19% of patients without deficiency.

Test should be ordered as ADAMTS13 Evaluation, which includes both activity and inhibitor levels. Specimen requirement is two citrated (blue top) tubes of blood.