Recently recognized as a respiratory virus in the Netherlands in 2001, the human metapneumovirus (hMPV) has been found to cause severe acute respiratory infections all over the world in young children, the elderly, and in immunocompromised people.

**Background**

The virus itself is not new...it has been reported worldwide and has been detected in stored specimens from children and adults collected in 1958, indicating the virus has been circulating in human populations for years. Studies show that virtually all children are infected with hMPV by the age of five. Asymptomatic and subclinical infections are rare since most people usually become ill when they are infected.

Prevalence of hMPV infections vary. Studies report ranges from 2% to 12% as the causative infectious agent for pediatric lower respiratory illnesses with a lesser extent reported in adults. In addition, the virus is responsible for 1 to 3% of all flu-like illnesses.

One study found it to be the second most detected pathogen in children suffering from acute respiratory tract infections, topped only by respiratory syncytial virus (RSV). It is now the agent of an emerging infectious disease (other examples are HIV/AID, Lyme disease, Hepatitis C). They are diseases that have already existed but are rapidly increasing in incidence or geographic range.

**Description of the Virus**

The virus is a paramyxovirus. The Pneumovirinae subfamily is classified into Pneumovirus (which contains RSV) and metapneumovirus genera. It is a single-stranded RNA virus, similar to influenza viruses and RSV. Within that family of viruses, hMPV is genetically most similar to the avian pneumovirus, which is why it was named “metapneumovirus.” Phylogenetic analysis separates the virus into two distinct subgroups A and B.

**Symptoms**

HMPV is predominantly a mild disease in healthy young and elderly adults, characterized by cough, hoarseness, congestion, and rhinorrhea. More than half of patients exhibit sore throat, hoarseness, sputum production, body and muscle aches, with fever being unusual.

In infants and children, symptoms are similar to other viral-associated bronchiolitis, making it indistinguishable from RSV, influenza, and parainfluenza viruses. More than 90% report a cough, 75% rhinorrhea, and more than 50% fever. Symptoms can also include difficulty breathing, abnormally rapid breathing, wheezing, vomiting and diarrhea. Co-infection with another virus can occur, and simultaneous infection with hMPV and RSV can cause severe disease.

**Seasonal Distribution**

Studies indicating the distribution of hMPV found activity in the winter and spring months. Peak activity has been suggested to follow peak activity of RSV and influenza. Year round testing of respiratory specimens for the hMPV is scarce to none; therefore seasonal distribution should be further studied including respiratory specimens collected throughout the calendar year.

Figure 1. The hMPV is a pleomorphic, enveloped virus with an average diameter of 200 nm. The virion contains a single stranded, negative-sense RNA genome that forms a helical nucleocapsid.
Identification Problems
Laboratory testing utilizing viral culture has been less than satisfactory. Isolation of the virus requires inoculation onto cell lines that are not normally utilized in a clinical diagnostic lab. In addition to the inefficiency of the virus to propagate readily in culture, investigators have learned that hMPV also grows slowly compared to other cultivatable human respiratory viruses. Clinical virology laboratories could be discarding routine respiratory cultures before an hMPV-induced cytopathic effect is evident.

HMPV Testing Available at Sanford Laboratories Virology
Because hMPV is now the third most common cause of respiratory infection in the pediatric population (2005-2006), it is not surprising that researchers suggest a rapid, sensitive, specific and cost-effective reproducible methodology be determined as a routine diagnostic tool utilized in the laboratory. This testing would not only be advantageous in reduction of usage of antibiotics and/or corticosteroids after a positive hMPV diagnosis, but it may reduce nosocomial transmission through isolation or other methods used to limit the spread of hMPV.

Sanford Laboratories is pleased to now offer testing for human metapneumovirus. Testing for hMPV is done by direct fluorescent antibody (DFA) staining of respiratory cells present in nasopharyngeal aspirates using virus specific monoclonal antibody. The monoclonals chosen will detect all known subtypes. Sanford Virology Laboratories also determines that no other respiratory viruses will cross react with the monoclonals utilized.

Ordering Information
Test Name: Human Metapneumovirus by DFA
Test Code: 7304
Specimen Requirements: Submit nasopharyngeal (NP) aspirate in a leak-proof container. Refrigerate.
Stability: RMT – 2 hours REFT – 3 days
CPT Code: 87299

Assessing the role of individual pathogens is important for future development of vaccines and specific antiviral therapy. It appears that hMPV is now playing a clinical role in acute viral respiratory tract infections and it is important to properly diagnose the virus. Many laboratories do not include hMPV in their routine virology screens. We are pleased to offer this and other virology services in our region.

**CYCLIC CITRULLINATED PEPTIDE ANTIBODY TEST (CCP)**

Sanford Laboratories is pleased to offer CCP antibody testing in-house. Antibodies to citrullinated proteins are markers for rheumatoid arthritis, (RA), especially for early diagnosis of the disease. In some cases, these antibodies may be detected many years before the onset of the first symptoms. In addition, their presence at disease onset has a high positive predictive value for the development of erosive joint lesions, and the detection of these antibodies can therefore be used in clinical practice to help plan a therapeutic strategy.

Moreover, in view of the high specificity of these antibodies, the test is particularly useful in differential diagnosis between RA and other arthritides that are clinically similar to RA and may be positive for rheumatoid factor (RF), such as hepatitis C, virus (HCV)-associated cryoglobulinemia, undifferentiated polyarthritis, or Sjogren syndrome.

Simultaneous positivity for anti-CCP antibodies and rheumatoid factor increases the probability of rheumatoid arthritis to 90 – 100% (approximately 50% to 90% of patients with RA are RF-positive). The presence of anti-CP antibodies has already been proposed for inclusion among the classification/diagnosis criteria for RA. A positive CCP antibody result indicates a high likelihood of RA, whereas a negative result indicates the opposite.

Ordering Information
Test Name: CCP Antibodies, IgG by ELiA
Test Code: 8418
Specimen Requirements: 1.0 mL frozen serum (min 0.5 mL). THIS TEST REQUIRES ITS OWN FROZEN ALIQUOT. Lithium heparin, citrated, and EDTA plasma also acceptable.
Stability: Frozen only
CPT Code: 86200
Reference Range: < 7.0 U/mL

To facilitate your phone call, please provide your 6-digit Sanford Laboratories’ account number to our Client Support Representative.

Thank you for your assistance.
Information from Guidelines for the Diagnosis and Management of Asthma (The National Asthma Education and Prevention Program, or NAEPP) reports that allergies are considered one of the most important factors in the development, persistence, and potential severity of asthma. It has also stated that allergy testing is necessary to educate patients about allergen avoidance and symptom control.

The Guidelines

The Guidelines were first published in 1991 and revised in 1997 and 2002. This latest update (August 2007) highlights the importance of keeping asthma under control through four critical components of asthma care: 1) assessment and monitoring, 2) patient education, 3) control of environmental factors contributing to asthma severity, and 4) pharmacologic therapy.

One of the key differences in the 2007 National Institutes of Health (NIH) asthma guidelines is that “evidence strengthens recommendations that reducing exposure to inhalant indoor allergens can improve asthma control.” The first and most important step in controlling allergen-induced asthma is to advise patients to reduce exposure to relevant indoor and outdoor allergens to which the patient is sensitive.

Background

Approximately 22 million Americans have asthma and more than six million of these are children, making it one of the most common chronic diseases of childhood. The nearly 500,000 asthma-related hospitalizations annually are a significant economic burden on our healthcare system. Allergies are involved in approximately 60% of adult asthmatics and 90% of pediatric asthmatics.

Clearly, knowledge gained from allergy testing allows asthma patients to make necessary adjustments to their environment to decrease their risk for asthma attacks and subsequently hospitalization.

Testing

Many asthmatics or parents of children who suffer from symptoms are not aware that a simple blood test can be conducted to identify what is triggering an asthma attack. Allergy testing using a specific IgE blood test is a safe and accurate method to identify triggers early to help effectively manage patients.

ImmunoCAP was the first allergy test to be cleared by the FDA as a truly quantitative test for identifying allergens; additionally, allergy blood testing is recognized by NIH for the management of patients with asthma. Specific IgE is produced as a result of sensitization to an allergen and increases with exposure to that substance. Sanford Laboratories uses the ImmunoCAP technology to measure IgE antibodies to specific allergens in a small sample of blood.

ImmunoCAP Specific IgE Respiratory Profile is superior to RAST with a 95% positive predictive value and sensitivity equivalent to skin testing. For allergic asthma, it will identify the allergic triggers. If the results are negative, the clinician can then focus on non-allergic triggers. ImmunoCAP test results guide asthma management including avoidance, medication selection, and appropriate referral.

Medical Treatment

Medications may be needed to control asthma symptoms. Initiation of long-term control therapy is recommended for children 0–4 years of age who had four or more episodes of wheezing in the past year that lasted more than 1 day and affected sleep.

<table>
<thead>
<tr>
<th>Asthma Classification</th>
<th>Symptom Frequency</th>
<th>Medications Required to Maintain Long-term Control</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Step 4 Severe persistent</strong></td>
<td>Daytime: continual Nighttime: frequent</td>
<td>High-dosage inhaled corticosteroid and long-acting beta2 agonist</td>
</tr>
<tr>
<td><strong>Step 3 Moderate persistent</strong></td>
<td>Daytime: daily Nighttime: more than 1 night per week</td>
<td>Children 5 years and younger: low-dosage inhaled corticosteroid and long-acting beta2 agonist or medium-dosage inhaled corticosteroid</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Adults and children older than 5 years: low- to medium-dosage inhaled corticosteroid and long-acting inhaled beta2 agonist</td>
</tr>
<tr>
<td><strong>Step 2 Mild persistent</strong></td>
<td>Daytime: more than 2 days per week, but less than 1 time per day Nighttime: more than 2 nights per month</td>
<td>Low-dose inhaled corticosteroid (delivered by nebulizer or metered-dose inhaler with holding chamber, with or without a face mask, or by dry powder inhaler in children 5 years or younger)</td>
</tr>
<tr>
<td><strong>Step 1 Mild intermittent</strong></td>
<td>Daytime: 2 days per week or less Nighttime: 2 nights per month or less</td>
<td>No daily medication needed</td>
</tr>
</tbody>
</table>

Continued from page 3.

Summary/Conclusion
For patients who have persistent asthma, the clinician should evaluate the potential role of allergens, particularly indoor inhalant allergens (Evidence A):
• Use the patient’s medical history to identify allergen exposures that may worsen the patient’s asthma.
• Use skin testing or in-vitro testing to reliably determine sensitivity to perennial indoor inhalant allergens to which the patient is exposed.
• Assess the significance of positive tests in the context of the patient’s medical history.

For selected patients who have asthma at any level of severity, detection of specific IgE sensitivity to seasonal or perennial allergens may be indicated as a basis for education about the role of allergens for avoidance and for immunotherapy. Determination of sensitivity to a perennial indoor allergen is usually not possible with a patient’s medical history alone.

In-vitro allergy testing by ImmunoCAP is a reliable method to determine the presence of specific IgE allergens. Sanford Laboratories offers a comprehensive menu of individual specific IgE allergens along with geographically and age-dependent profiles to assist health care providers in managing patients with asthma, as well as treating other allergic responses.