May 2004

2004 West Nile Virus Season Begins

The first human West Nile Virus (WNV) case of 2004 has been reported in a 79 year old Ohio resident. The patient was hospitalized in April with WNV encephalitis. Avian, animal and mosquito infections also have been reported in Alabama, California, Florida, Georgia, Louisiana, New York, Pennsylvania, and Texas as of May 5.

There were 9858 total human WNV infections reported to the CDC in 2003, with the majority of cases occurring in Colorado, Nebraska and South Dakota. Most (6829) cases were classified as West Nile fever without evidence of neuroinvasion. Encephalitis or meningitis accounted for 2863 cases with 262 deaths.

Although most WNV infections are asymptomatic, an estimated 20% develop West Nile fever, which is a mild illness that may be accompanied by malaise, anorexia, rash, lymphadenopathy, myalgia, headache, nausea, vomiting or eye pain. Less than 1% of infections result in severe neurologic disease. The most significant risk factor for neurologic disease is advanced age.

The diagnostic test of choice for WNV and other arboviral infections is serologic analysis of serum or CSF for IgM and IgG antibodies, available through Saint Luke’s Regional Laboratories. The specimen requirement is one red top tube of blood or 1.0 mL CSF.

Primary Amyloidosis

Amyloidosis refers to the deposition of amyloid protein in organs and tissues. Primary amyloidosis is a plasma cell neoplasm that secretes an abnormal immunoglobulin. Amyloid protein is produced by the abnormal cleavage of immunoglobulin light chains and their aggregation into insoluble beta pleated sheets. Amyloid is deposited in various organs and tissues including tongue, intestines, skeletal and smooth muscles, nerves, skin, ligaments, heart, liver, spleen and kidneys. Most symptoms of amyloidosis are nonspecific. Weight loss is the most common, combined with weakness and fatigue. Dyspnea, edema and paresthesias are also common symptoms. Clinical presentations include:

- Nephrotic syndrome
- Infiltrative cardiomyopathy without ischemic history
- Hepatosplenomegaly with no filling defects visible by imaging
- Nondiabetic peripheral neuropathy
- Macroglossia
- Facial purpura

Amyloid occurs most frequently in individuals between the ages of 60 and 67 years. Only 1% of amyloidosis patients are under age 40. The male to female ratio is 2:1. Approximately 6% of patients with multiple myeloma develop amyloidosis.

No blood tests, radiographs or scans can diagnose amyloidosis. Biopsy is the gold standard for diagnosis. Any affected organ or tissue can be biopsied. Because amyloid proteins are carried throughout the bloodstream, any biopsy that includes blood vessels can be used to demonstrate the presence of amyloid. Rectal mucosa biopsies are noninvasive, easy to perform and have a low incidence of complications, but are not favored by many patients. Fat tissue is a common site of amyloid deposition. Aspiration of subcutaneous abdominal fat is a simple procedure with a low incidence of complications and high patient acceptance. It detects 70 to 80% of patients with amyloidosis. Congo red stain is diagnostic of amyloid fibrils, but must be performed by laboratories with extensive experience with this technique.

Bone marrow biopsy can also be used to detect amyloid deposition as well as clonal plasma cells. Sixty percent of patients with amyloidosis will have <10% plasma cells in the bone marrow and 20% of patients will have >20% plasma cells. Bone marrow biopsy combined with abdominal fat aspirate will detect 90% of patients with amyloidosis.
Serum protein electrophoresis will detect a monoclonal protein in approximately two thirds of patients with amyloidosis. Immunofixation is more sensitive and will detect a monoclonal protein in approximately 90% of patients.

<table>
<thead>
<tr>
<th>Monoclonal Protein</th>
<th>Percentage of Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serum &amp; urine</td>
<td>58%</td>
</tr>
<tr>
<td>Urine only</td>
<td>20%</td>
</tr>
<tr>
<td>None detected</td>
<td>15%</td>
</tr>
<tr>
<td>Serum only</td>
<td>7%</td>
</tr>
</tbody>
</table>

**Hypoglycemia**

Hypoglycemia is defined by the presence of Whipple’s triad: plasma glucose concentration less than 50 mg/dL, symptoms of nervousness, anxiety and sweating, and relief of symptoms with administration of glucose. It occurs infrequently in hospitalized patients. The most common causes of hypoglycemia in inpatients are diabetes mellitus, renal failure, liver disease, infection, pregnancy, metastatic cancer, and burns.

Hypoglycemia is also rare in outpatients. The best way to diagnose this condition is to instruct the patient to eat a meal similar to the one that produces symptoms and then have their blood drawn for a plasma glucose level when they become symptomatic. If plasma glucose is not <50 mg/dL, then the person does not have hypoglycemia.

If a person has an abnormal screening test, they should be further evaluated with a 72 hour fast unless an obvious cause is indicated in the medical history, physical exam or laboratory tests. The 72 hour fast attempts to document Whipple’s triad under controlled conditions. This test is difficult to perform correctly. Criteria for discontinuing the fast are strict: blood glucose level must be lower than 45 mg/dL and the patient must be symptomatic. All nonessential medications must be discontinued and only water, black decaffeinated coffee, and diet sugar-free sodas can be consumed.

The 72 hour fast is a sensitive test for insulinoma. Most patients with insulinoma become hypoglycemic within 48 hours. Patients who are abusing oral antihyperglycemic agents (OAA) will not become hypoglycemic during the test.

The majority of otherwise healthy hypoglycemic individuals will be found to have insulin mediated hypoglycemia, either due to inappropriate insulin production, insulin injection, or ingestion of OAA. At the time of true hypoglycemia, they should be tested for insulin, C-peptide, proinsulin and OAA. Insulin mediated hypoglycemia is recognized if insulin is detectable (>3 mU/mL with chemiluminescent methods) at the time of hypoglycemia. Interpretation of test results is shown in the table below.

<table>
<thead>
<tr>
<th>Disorder</th>
<th>Insulin</th>
<th>C-pep</th>
<th>Pro</th>
<th>OAA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Insulinoma</td>
<td>↑</td>
<td>↑</td>
<td>↑</td>
<td>➖</td>
</tr>
<tr>
<td>Insulin injection</td>
<td>↑</td>
<td>➖</td>
<td>➖</td>
<td>➖</td>
</tr>
<tr>
<td>OAA</td>
<td>➖</td>
<td>➖</td>
<td>➖</td>
<td>➖</td>
</tr>
<tr>
<td>Non-insulin mediated</td>
<td>➖</td>
<td>➖</td>
<td>➖</td>
<td>➖</td>
</tr>
</tbody>
</table>

The normal response to hypoglycemia is suppression of insulin secretion. Insulin is synthesized in the pancreas as proinsulin and this protein is cleaved to form insulin and C peptide. Both are secreted into the circulation simultaneously.

- If endogenous insulin is being hypersecreted, both insulin and C peptide will be inappropriately high in the presence of a low blood glucose level.
- If exogenous insulin is being administered in quantities sufficient to cause hypoglycemia, islet cell secretion of endogenous insulin and C peptide will be suppressed.
- OAA ingestion gives the same biochemical picture as an insulinoma, causing endogenous hyperinsulinemia by releasing insulin from the pancreas. An OAA screen should be performed to rule out this etiology.

Cases of factitious hypoglycemia have several common clinical characteristics:

1. The patient is usually female
2. The patient or their spouse is a health professional
3. The patient has a close relative with diabetes treated with OAA
4. The patient has an unusual affect or psychiatric history
5. The patient has an abrupt onset of severe symptoms without previous milder symptoms
6. The 72 hour fasting test does not produce hypoglycemia