GenProbe Group A Strep Direct Test

ChildLab can help with the detection of group A streptococci (GAS) in your patients by using an FDA approved nucleic acid based procedure which can function as an alternative to culture for the definitive detection of GAS in throat swabs. The GenProbe Group A Strep Direct Test identifies the presence of GAS in the specimen by detecting GAS-specific nucleic acids using a probe-hybridization technique; there is no culture and incubation involved. The test is instrument-assisted, takes several hours to complete, and thus is not useful for GAS detection while the patient is in the office or clinic setting. It is best used as a replacement for culture by batch-testing a group of specimens once or twice a day in a central laboratory facility.

The advantages of the GenProbe Group A Strep Direct Test for your practice are:

1. All GAS detections can be completed (reported as positive or negative) within 24 hours from the time of collection.
2. Genprobe is comparable in sensitivity to standard culture for detection of GAS.
3. The GenProbe Group A Strep Direct test is reimbursed by all major health carriers and costs less than a positive throat culture.
4. The GenProbe Group A Strep Direct test will improve GAS diagnosis and turnaround time in your office.

ChildLab recommends this procedure for your practice as a replacement for routine throat culture. This change will not require any procedural changes on the part of your staff. They will continue to collect and submit throat swab specimens as usual.

For questions regarding the GenProbe Group A Strep Direct Test at ChildLab or to obtain dual throat culture swabs, please call ChildLab Client Services at (614)722-5477 or (800)934-6575.
**Monitoring Anticoagulant Therapy**

ChildLab's Special Hematology Laboratory currently offers several assays to monitor anticoagulation therapy. The following chart lists these anticoagulants, their respective tests and recommended therapeutic ranges.

<table>
<thead>
<tr>
<th>Anticoagulant</th>
<th>Laboratory Assay</th>
<th>Test Code</th>
<th>Therapeutic Range</th>
<th>Test Availability</th>
</tr>
</thead>
<tbody>
<tr>
<td>Warfarin (Coumadin®)</td>
<td>PT/INR</td>
<td>PT</td>
<td>Diagnosis dependent (See chart below)*</td>
<td>24 hours/7 days</td>
</tr>
<tr>
<td>Unfractionated Heparin (UFH)</td>
<td>APTT</td>
<td>APTT</td>
<td>64 – 104 seconds</td>
<td>24 hours/7 days</td>
</tr>
<tr>
<td>Unfractionated Heparin (UFH)</td>
<td>Anti-Factor Xa, Unfractionated Heparin</td>
<td>UFXA</td>
<td>0.3 – 0.7 U/mL</td>
<td>Dayshift, Monday – Friday**</td>
</tr>
<tr>
<td>Low Molecular Weight Heparin (LMWH) (Lovenox®)</td>
<td>Anti-Factor Xa, LMWH</td>
<td>AFXA</td>
<td>0.6 – 1.0 U/mL</td>
<td>Dayshift, Monday – Friday**</td>
</tr>
</tbody>
</table>

Notes:
- Low fixed doses of heparin do not necessarily require monitoring.
- Either APTT or Anti-Factor Xa (UFXA) may be used to monitor UFH. APTT is less expensive and available 24/7; the Anti-Factor Xa is preferable under some conditions (e.g. the presence of a concomitant inhibitor).

*INR: Recommended Therapeutic Ranges*

<table>
<thead>
<tr>
<th>Indication</th>
<th>INR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Treatment of Venous Thrombosis</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Treatment of Pulmonary Embolism</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Prevention of Systemic Embolism (tissue heart valves; atrial fibrillation)</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Recurrent Embolism</td>
<td>2.5-3.5</td>
</tr>
<tr>
<td>Mechanical Heart Valves</td>
<td>2.5-3.5</td>
</tr>
</tbody>
</table>

**UFXA and AFXA are available on a STAT basis only after 4:00 p.m. Monday – Friday and on weekends. Pathologist approval is required for “after hours testing.”**

If you have questions regarding monitoring anticoagulation therapy, please contact ChildLab Client Services at (800)934-6575 or (614)722-5477 and ask to be directed to ChildLab’s Special Hematology Laboratory.
**Pediatric Gastrointestinal Dysmotility Pathology**

Chronic constipation is a not infrequent problem in children comprising approximately <10% of consultations in a pediatric practice. In the majority of these children however, there is no distinct evidence of a mechanical obstruction and the pathogenesis is unclear.

Although motility disorders in children may have similar characteristics to those seen in adults, there are frequently important differences in diagnosis and management of each group.

At Nationwide Children’s Hospital Anatomic Pathology Laboratory, the pathologic basis for dysmotility represents an evolving field of study.

The normal motility of the gastrointestinal tract depends on the enteric nervous system (ENS), the muscle layers and the interstitial cells of Cajal (ICC). The ENS is part of the peripheral nervous system (PNS) that operates independently of the central nervous system (CNS) to coordinate the complex behaviors of the gut. It monitors the state of the lumen and wall of the gut and responds appropriately, activating intrinsic reflexes that generate mixing and propulsive peristaltic movements, and change the blood flow and secretions of water and electrolytes. The ENS contains as many neurons as found in the spinal cord and has the same diversity of neurotransmitter expression as the CNS.

The enteric neurons interact with the ICC providing pacemaker cell activity to the gut wall and mediating neurotransmission between the ENS and the smooth muscle layers.

It is suggested that some motility disorders originate from developmental defects while others are due to neurodegeneration. The pathologic basis for dysmotility represents an evolving field of study and the Anatomic Pathology Laboratory is keeping at the fore of this important field, actively supporting Center for Advanced Research In Neuromuscular Gastrointestinal Disorders (CARING) at Nationwide Children’s Hospital.

The best defined etiology of dysmotility is aganglionosis (Hirschsprung’s disease) and, in keeping with recent literature, we offer both acetylcholinesterase (AChE) and nicotinamide adenine dinucleotide phosphate diaphorase (NADPH) enzyme histochemistry. This diagnosis can often be established by suction rectal biopsies.

Other etiologies of dysmotility require full-thickness intestinal biopsies for evaluation. There is very limited literature describing the histopathologic basis for non-Hirschsprung’s intestinal motility disorders. For these cases, we have developed a systematic protocol to evaluate the neural, smooth muscle, connective tissue and inflammatory-mediated components. In addition to currently having an extensive immunohistochemical menu to study the GI tract, we are also continually investigating newer markers in an attempt to better ascertain the pathogenesis of these disorders on a case-by-case basis.
We also have access to a considerable bank of age matched control tissues for comparison with the dysmotility pathology.

**Hirschsprung's Disease (HD)**

There is considerable debate as to the best way to diagnose this disorder. HD is characterized by an absence of ganglion cells, increased AChE activity in the lamina propria and muscularis mucosa, thick nerve fibers in the submucosa, and a lack of NADPH activity in nerve fibers in the muscularis mucosa and very weak activity in nerve trunks.

However, as enzyme histochemistry requires frozen tissue and some histo-technological expertise, there is a demand for an antibody marker for immunohistochemical studies on routine formalin-fixed paraffin processed tissue. Many claims have been made to the use of various antibodies as a new and reliable diagnostic method, e.g. Ret oncoprotein, bcl-2, bone matrix proteins, S-100, NGFR, NSE, cathepsin and microtubule-associated proteins. We are actively investigating the suitability of these and other markers.

**Apoptosis in the ENS**

There is some speculation that changes in the intracellular mechanisms involved in enteric neuronal survival may play a role in GI dysmotility. Decreased expression of bcl-2 has been demonstrated in the enteric neurons in patients with severe chronic intestinal pseudo-obstruction (CIPO), along with the presence of swollen or shrunken neurons in the myenteric plexus.

In addition, patients with slow-transit constipation, and in HD, show an increase in apoptotic bodies and decrease in bcl-2 expression.

**Enteric Glial Cells**

The ENS comprises both neurons and glial cells. The enteric glial cells play a role in sustaining the functional integrity of the neurons. It is plausible that they play a role in pathological processes involving a neuroinflammation or neurodegeneration. The numbers of glial cells in the gut have been shown to increase in response to various cytokines. Studies in slow-transit constipation may support the supposition that glial cell damage may lead to enhanced neuronal apoptosis and neurodegeneration in the intestine.

**Interstitial Cells of Cajal**

ICC mesenchymal cells are found throughout the GI tract. They are the pacemaker cells responsible for initiating slow wave activity in the muscle layers, and their precursors can develop as either myenteric or muscular ICCs. They are recognized by the immunohistochemical demonstration of the receptor tyrosine kinase Kit (C-kit; CD117). Many GI motility disorders show a change in number and/or structure of ICCs.

cont. on page 5
Smooth Muscle

In cases of gastrointestinal dysmotility, pathology almost exclusively studies the ENS and ICCs. Abnormalities of the enteric musculature itself have only rarely been considered. Myopathies may affect the intestine in a segmental, multifocal, or diffuse manner.

In most studies the histological evaluation of the intestinal musculature is limited to conventional staining techniques. We have employed several markers, e.g smooth muscle myosin heavy chain and smoothelin, in the study of the smooth muscle contractile apparatus and have displayed striking abnormalities unnoticed by both routine staining and alpha-smooth muscle actin, suggesting a defect in the smooth muscle cells involved in the pathogenesis of gastrointestinal motility disorders.

To allow us to expand our studies of GI dysmotility, we have adapted a unique approach in handling colon resection specimens that allows us to evaluate the myenteric plexus longitudinally along the length of the resection, and at the same time allows us to prepare tissue for frozen sections analysis and well as routine paraffin sectioning.

Handling of Colon for Dysmotility Studies

[Diagram showing handling of colon for dysmotility studies]
**INFORMATION TO KNOW**

♥ **Change in Viral/Chlamydial Culture Transport Tube**

Beginning February 2010, ChildLab will be changing the specimen transport container currently supplied for viral testing (culture, PCR or antigen detection by direct fluorescent antibody staining) and chlamydial cultures from the current small, glass, black-cap vial to a larger, conical, plastic blue-cap tube.

- The transport medium in the tube will remain the same (M4 medium), but the volume of M4 in the new tube is 3 mL, not 2 mL as in the current vial.
- This change is being made to facilitate the process of transferring a swab specimen to the transport medium after specimen collection, particularly when using “notched” nylon flocked swabs for posterior nasopharyngeal specimen collection.
- The larger tube will allow the plastic swab shafts to be easily snapped in the tube, allowing the swab tip to fall into the transport medium and insuring that the screw cap on the tube can be tightened securely without interference by the swab shaft, thus reducing the likelihood of specimen leakage.
- The new transport tubes need to be stored refrigerated just like the older vials.

Please contact ChildLab Client Services at (614)722-5477 or (800)934-6575 if you have any questions regarding the new Viral/Chlamydial Culture Transport media tube.

![Old Viral/Chlamydial Culture Transport Tube](image1.png) ![New Viral/Chlamydial Culture Transport Tube](image2.png)

♥ **ChildLab Website PDF Links**

ChildLab.com has been upgraded to a new platform. Due to this upgrade, Internet Explorer 6.0 will no longer open Adobe pdf files by simply clicking on the link to the document. All users that have Internet Explorer 6.0 will have to save Adobe pdf documents to their desktop in order to view them. This includes the frequently referenced *Weekly Respiratory Pathogen Report*.

We have been told that Internet Explorer 6.0 will be phased out this summer, and the problem will be resolved. We encourage you to upgrade to Internet Explorer 7.0 or 8.0 to immediately alleviate this problem. If you cannot upgrade your browser, you may access the pdf documents on our site by following the directions below.

**Directions to open pdf files on ChildLab.com:**

1. **Right click on the link you want to open** (ie. *Weekly Respiratory Pathogen Report*).
2. **Select Save Target As**
3. **Select area where you want to save the file** (ie. desktop)
4. **Open desktop and select saved pdf.**
5. **Open pdf.**

If you have questions regarding accessing pdf documents or the Weekly Respiratory Pathogen Report on ChildLab.com, please call ChildLab Client Services at (614)722-5477 or (800)934-6575.
Test Changes

♥ Free T4 Assay

The manufacturer of ChildLab’s current FT4 assay kit has reformulated the assay to improve performance. We handle a reformulated assay just like a new assay and study the performance of the new assay in parallel with the old assay before implementation. Our study of nearly 300 specimens has confirmed what the manufacturer of the assay has stated: the new assay gives FT4 results that are up to 20% lower than the current assay through the entire reportable range of the assay (0.3 to 6 ng/dL). The consequences of such a change are that a small percent of patients (approximately 3% of total tested) would have their FT4 results reclassified from high to normal or from normal to low with the new assay. These are patients whose FT4 results fall very near the age-adjusted reference range limits.

Unfortunately, the manufacturer has depleted its supply of old assay kits and we have had to begin testing with the new assay effective Friday, January 15, 2010. At this point, we are maintaining our current FT4 age-adjusted reference ranges. We will be tracking the percent of high and low FT4 results going forward and comparing to such results from the past three months as well as to TSH results. We will certainly share any new information with you.

If you feel that the FT4 results on a patient do not fit the clinical picture, please contact ChildLab Client Services at (800)934-6575 or (614)722-5477 and ask to speak to someone in the Specialty Chemistry Laboratory or Dr. Marcon.

We thank you for your understanding and patience during this adjustment.

Helpful Reminders

♥ Cold Weather Reminder

Now that winter has arrived, it is important that samples placed in a lockbox out of doors prior to transport to ChildLab be maintained at the appropriate temperature. If refrigerated samples are stored in the lockbox, then a room temperature, non frozen cold pack should be placed in the lockbox to maintain the samples at the refrigerated temperature. The cold pack should not be frozen, since you do not want refrigerated whole blood samples to freeze.

Many laboratory tests performed at ChildLab require adequate refrigeration of specimens. By following this lockbox practice, you will help insure the integrity of the samples and ultimately obtain reliable laboratory results.

♥ New Year Resolution

As we begin a new year, ChildLab would like to take the opportunity to remind everyone to always check the expiration dates of your collection containers prior to collecting samples. It is good practice to check your collection supplies on a monthly basis to avoid sample rejections, time taken to recollect the specimen, and delay of treatment.

NOTE: Not sure how to dispose of your O&P and Cary-Blair (stool culture) medias that ChildLab provides? Send them back with the courier to ChildLab’s Central Processing with a note stating ‘Expired Media - Please Dispose’ and we will be happy to dispose of them for you.

For questions regarding media disposal, please call ChildLab Client Services at (614)722-5477 or (800)934-6575.
How can ChildLab help your practice?

- Pediatric pathologist consults on lab results!
- Wide acceptance of insurance plans!
- Excellent 24/7 customer service!
- Services to enhance the laboratory process in your practice!
- Interface systems compatible with your EMR!

If you would like to be a client or learn more information about ChildLab, contact ChildLab Client Services at (800)934-6575 or visit our website at www.ChildLab.com.

Would you like to receive ChildLab Links Newsletter electronically? Please email us at ChildLab@childLab.com and let us know!