Monoclonal B-cell Lymphocytosis

Multiparametric flow cytometry allows the detection of very small clones of monoclonal B-cells in peripheral blood from normal individuals. The significance and long term implications of these is uncertain, and the term monoclonal B-cell lymphocytosis (MBL), as defined below, is recommended to distinguish these cases from patients with B-cell chronic lymphocytic leukemia (B-CLL). One of the earliest population based studies of MBL was performed at Saint Luke’s Hospital in collaboration with Community Blood Center. (Br J Haematol 2007;139:832-836) This and other population studies showed the prevalence of MBL to be 0.14% - 5.1%. The diagnostic criteria for MBL and B-CLL were recently updated by the International Workshop on Chronic Lymphocytic Leukemia. (Blood 2008;111:5446-5456)

According to the recommendations from this workshop, the diagnostic criteria for MBL include the presence of a monoclonal B-cell population with:

- B-cells in blood <5,000/µL
- Absence of lymphadenopathy and hepatosplenomegaly (by physical examination and CT scans)
- Absence of cytopenias due to marrow involvement by the monoclonal proliferation

The immunophenotype of the clonal B-cells of MBL is most often identical to that seen in B-CLL, with expression of B-cell markers CD19, CD20, and CD23, co-expression of CD5, and dim intensity of surface light chain expression. Other immunophenotypes are rare, including some cases that lack CD5 expression. (Br J Haematol 2007;139:701-708)

The relationship between MBL and B-CLL was investigated in a recent study from the United Kingdom. (N Engl J Med 2008;359:575-583) In this study, MBL with B-CLL immunophenotype was detected in 5.1% of 1520 individuals without lymphocytosis. Symptomatic B-CLL requiring treatment developed at the rate of 1.1% per year in a subset of these patients that were followed for a median of 6.7 y. In this respect, MBL is similar to monoclonal gammopathy of undetermined significance (MGUS), with a very low rate of progression to symptomatic disease.

Patients diagnosed with MBL based on flow cytometric evaluation of blood should be worked up to exclude B-CLL or other B-cell lymphoproliferative disorders, and then offered periodic follow up to watch for progression.

Revised Protocol for Diagnostic Evaluation of von Willebrand Disease

Von Willebrand disease (vWD) is a common inherited bleeding disorder caused by a quantitative or qualitative deficiency of the coagulation protein von Willebrand factor (vWF). There are three types of inherited vWD, based on the type of abnormality in vWF – partial quantitative deficiency (type 1), complete quantitative deficiency (type 3), and qualitative deficiency (type 2). A rare acquired type of vWD is also described, usually seen in adults with no prior or family history of a bleeding disorder.

Initial testing for the diagnosis of vWD includes quantitative and qualitative evaluation of vWF and measurement of factor VIII, which is closely associated with vWF. Measurement of vWF antigen (vWF:Ag) provides quantitative assessment of vWF. Qualitative assessment of vWF is traditionally based on the ristocetin cofactor assay (vWF:RCo). However, this is a very time and labor intensive manual assay. A new automated immunoassay using latex particles coated with an antibody against the platelet binding site of vWF has recently become available and serves as an excellent screening test for qualitative assessment of vWF. The sensitivity of this assay in detecting vWD is similar to that of the vWF:RCo assay (98.6-100%), as shown by two studies with a combined total of 188 specimens from normal and vWD...

Saint Luke’s Regional Laboratory will begin using the new vWF activity assay (vWF:Activity) for initial screening for vWD in January 2009. In conjunction with the vWF:Ag assay, a ratio of vWF activity to vWF antigen will be provided. If vWF activity is decreased or the ratio is less than 0.7, the ristocetin cofactor assay will be performed as a reflex test, for further evaluation and classification of the type of vWD.

### Changes in Cord Blood Testing

Previously, the laboratory at Saint Luke’s Hospital performed a blood type and direct antiglobulin test (DAT) on cord blood from all infants born to mothers who were either Rh negative or Group O, as well as on all infants who were admitted to the neonatal intensive care unit.


Nationwide, many laboratories have stopped performing DAT on babies that are born to Group O mothers because:

- ABO incompatibility seldom causes clinically significant hemolytic disease of the newborn
- Cord blood testing often produces falsely positive DAT results
- Strength of a positive DAT does not correlate with severity of jaundice that a baby might or might not develop

Accordingly, the laboratories in the Saint Luke’s Health System will change their cord blood testing policy on January 5, 2009. They will discontinue routine blood typing and DAT testing on cord blood from babies born to Group O women and discontinue the DAT on cord blood from babies admitted to the neonatal intensive care unit. Cord blood samples will be stored for 7 days so that a physician can order additional testing whenever there is clinical evidence of hyperbilirubinemia and or anemia. However, it should be noted that DAT testing on stored cord blood samples is unreliable and a fresh blood sample from the infant is recommended for optimal results.

### Introduction of a Sensitive Thyroglobulin Assay

Thyroglobulin (Tg) is a large glycoprotein that is synthesized in thyroid follicles and serves as the precursor of thyroid hormone. Measurement of serum Tg is primarily used to detect recurrence of follicular-cell derived thyroid cancer.

Serum concentrations of Tg are highly specific for thyroid tissue in the body, but are not specific for malignancy. The value of Tg measurement for thyroid cancer follow-up is diminished in patients with more than a remnant of postsurgical thyroid tissue. Consequently, many physicians recommend postsurgical radiiodine (RAI) remnant ablation to enhance the ability of Tg to detect recurrence.

The success of RAI ablation has been traditionally assessed by diagnostic RAI scanning or by postablation stimulated Tg measurements, either after thyroid hormone withdrawal or, more commonly in recent years, after recombinant TSH (rhTSH) administration. However, neither of these approaches is ideal because thyroid withdrawal is unpleasant and rhTSH is costly.

The introduction of a sensitive Tg assay, with a lower limit of detection of 0.1 ng/mL, may make both of these approaches obsolete. Recent data from the Mayo Clinic suggests that a 4 to 8 week postablation unstimulated serum Tg concentration less than 0.1 ng/mL indicates complete remnant ablation. They also demonstrated that unstimulated serum Tg levels <0.1 ng/mL during follow-up exclude thyroid cancer recurrence, except in patients with Tg antibodies and in very rare individuals with highly dedifferentiated tumors (J Clin Endocrinol Metab 2007;92:82-87).

The laboratory at Saint Luke’s Hospital will begin offering sensitive Tg on December 22, 2008. The reference ranges for Tg and anti-Tg will change at that time.

<table>
<thead>
<tr>
<th></th>
<th>Old range</th>
<th>New range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tg</td>
<td>1.6 - 55 ng/mL</td>
<td>0 – 35 ng/mL</td>
</tr>
<tr>
<td>Anti-Tg</td>
<td>0 - 40 IU/mL</td>
<td>0 – 2.3 IU/mL</td>
</tr>
</tbody>
</table>