



January 2005

## **Gibson Named Director of Pathology Services**

Dr. Fred Plapp and Anne Byrd are very pleased to announce that Kristy Gibson, MT(ASCP), MBA has accepted the position of Director, Pathology Services. She succeeds Anne Byrd who was recently promoted to Vice President of Saint Luke's Hospital.

Kristy is a graduate of our Clinical Laboratory Science (CLS) program. She has capably served in various management roles including Immunology/Immunoassay Section Manager, Anatomic Pathology Manager and Laboratory Operations Manager over the past 20 years. Kristy will be responsible for all testing and support sections of the Laboratory as well as the CLS and Phlebotomy educational programs and our outreach services, Saint Luke's Regional Laboratories.

## **Does a Shortened APTT have any Clinical Significance?**

In the realm of coagulation testing, much attention has been paid to the investigation and clinical significance of a prolonged APTT. Little if any attention has been given to the significance of a shortened APTT. There is evidence that increased levels of several coagulation factors (factors VIII, IX, XI, II, and fibrinogen) are independent risk factors for venous thromboembolism (VTE). These factors participate in the coagulation cascade in the intrinsic pathway (factors VIII, IX and XI) and common pathway (factor II and fibrinogen). A shortening of the APTT should reflect increased levels of these factors. Based on this hypothesis, a recent study (*Blood*, 2004;104: 3631-34) investigated the association between a shortened APTT and the risk of venous thromboembolism (VTE).

A case control study was carried out to compare the APTT values in 605 patients referred for thrombophilia testing after an episode of

documented VTE and 1290 healthy controls. The APTT was performed at least 3 months (range 3-79 months) following the thrombotic event, and patients were excluded if they were on anticoagulant drugs, or if they had other conditions potentially affecting the APTT (e.g. lupus anticoagulant, pregnancy). Thrombophilia testing was also performed including factor V Leiden, prothrombin gene mutation, antithrombin, protein C and protein S. The APTT values in patients and controls were expressed as a ratio of the test APTT to a reference (pooled normal plasma) APTT.

The median value for the test/reference APTT ratio was 0.97 in patients and 1.00 in controls – a small difference that was nonetheless statistically significant. The odds ratio for VTE was 2.4-fold increased in patients with an APTT ratio less than 0.87. In Saint Luke's Regional Laboratories this value would correspond to an APTT of less than 25 sec (our APTT normal range is 22-32 sec). The relative risk of VTE increased as the APTT ratio decreased – the odds ratio for VTE was 4.6 for an APTT ratio of equal to or less than 0.8 (corresponding APTT 23 sec). When patients with the shortest APTT's were compared with those with the longest APTT's, the relative risk of VTE was increased 5-fold. These odds ratios have been adjusted for age, sex, and the presence of inherited thrombophilic disorders. Factor VIII assays were performed on a subgroup of the samples. When the results were adjusted for factor VIII levels, the increased relative risk of VTE remained significant, indicating that high levels of factor VIII were not the only determinants of the shortened APTT's.

In summary, this study suggests that a shortened APTT may be associated with an increased risk of VTE, independent of inherited thrombophilic defects. A direct causal effect of the hypercoagulability reflected by the shortened APTT cannot be established. If the results of this study are confirmed and extended by others using a variety of different reagents, the APTT may prove

to be a simple, cheap and useful screening test for high coagulation factor levels in the investigation of thrombophilia.

### **Gamma Glutamyltransferase**

Gamma glutamyltransferase (GTT) is a membrane-bound peptidase that hydrolyzes peptides to amino acids and smaller peptides. It is found in proximal renal tubule, liver, pancreas and intestine. GGT activity in serum comes primarily from liver. The circulating half-life is 7 to 10 days. However, the half-life increases to 28 days in alcohol-associated liver injury, suggesting impaired clearance.

Several factors affect GGT, other than liver injury.

- GGT activity can fluctuate between 10 and 15% from day to day.
- GGT activity decreases immediately after eating.
- GGT activity is 25 to 50% higher in obese individuals.
- GGT activity is 10% higher in individuals smoking 1 pack per day & doubles with heavier smoking.
- GGT activity is approximately 2 fold higher in healthy African Americans.
- GGT activity decreases 25% during early pregnancy.

GGT is most useful in determining the cause of elevated alkaline phosphatase and as a marker of chronic alcohol consumption. GGT is a useful adjunct to determine the origin of elevated alkaline phosphatase activity, because it is elevated by liver disease, but not bone disease.

| <b>GGT</b> | <b>ALP</b> | <b>Diagnosis</b> |
|------------|------------|------------------|
| Normal     | Elevated   | Bone disease     |
| Elevated   | Elevated   | Liver disease    |

GGT is not very useful in the differential diagnosis of liver disease. The highest GGT levels are seen in cholestatic liver disease; levels are typically more than 5 to 12 times the upper limit of normal and rise in parallel with alkaline phosphatase. GGT typically rises during the first week of viral hepatitis, peaks at 5 times the upper limit of normal during the second or third week, and remains elevated up to six weeks. GGT levels are also elevated in hepatoma, liver metastases, chronic active hepatitis, alcoholic hepatitis, extrahepatic obstruction, intrahepatic

cholestasis, and inactive cirrhosis. GGT levels do not correlate with the severity of liver disease. GGT is particularly sensitive to alcohol consumption and may be elevated even when other liver function tests remain normal. However, liver biopsies in patients with solitary GGT elevations seldom show irreversible hepatic injury. Social drinking does not elevate GGT, but chronic alcohol consumption induces the synthesis of GGT more than alkaline phosphatase. A GGT: ALP ratio of >5:1 favors a diagnosis of alcoholic liver disease.

Pancreatitis also causes moderate elevations in GGT activity. Patients with diabetes, hyperthyroidism, rheumatoid arthritis, and obstructive pulmonary disease often have an increased GGT, but the reason for this elevation is unknown.

Many drugs increase GGT levels up to 2 times the upper limit of normal. Examples include:

- Acetaminophen
- Carbamazepine
- Cimetidine
- Coumadin
- Furosemide
- Heparin
- Isotretinoin
- Methotrexate
- Phenobarbital
- Testosterone
- Tricyclic antidepressants
- Valproic acid

Phenytoin may cause levels to increase 5 fold. Oral contraceptives can decrease GGT concentration.

Reference range is 15 to 80 IU/L. Specimen requirement is one red top tube of blood.

### **Change in Transferrin Receptor Assay**

Starting Jan 1 2005, Saint Luke's Regional Laboratories switched to a new automated method for the serum transferrin receptor assay. The new assay has a different reference range and units – the new reference range is 0.80-2.00 mg/L. Transferrin receptor assay is available Sunday through Friday, 6am to 10pm. One 5mL red-top tube of blood is required.