BACKGROUND:
von Willebrand disease (VWD) is the most common inherited bleeding disorder characterized by either quantitative or qualitative defects of von Willebrand factor (VWF). VWF subunits assemble into a series of multimers. Higher molecular weight (MW) multimers are more effective in initiating hemostasis at sites of vascular injury. When multimers are released into the circulation, ADAMTS13 cleaves them into somewhat smaller MW sizes.

Patients with VWD have either quantitative or qualitative defects in VWF, which may be inherited or acquired. Accurate diagnosis of the “type” of VWD is essential to provide effective treatment of bleeding symptoms. The multimer distribution is normal in types 1, 2M, and 2N VWD. These types of VWD are diagnosed based on quantitative VWF assays such as ristocetin cofactor, antigen, and binding studies.

Loss of the higher MW multimers (high and sometimes also intermediate MW) is seen in type 2A, type 2B, and platelet-type VWD. When an abnormal multimer pattern is found, further testing is required to distinguish between these three types. Loss of the very highest MW multimers can be acquired secondary to cardiac defects [such as Ventricular Septal Defect (VSD), an abnormal valve, or use of ventricular assist device (VAD)], pulmonary hypertension, Disseminated Intravascular Coagulation (DIC), Hemolytic Uremic Syndrome (HUS), and acute Thrombotic Thrombocytopenic Purpura (TTP); it can also be caused by sample processing artifacts or filtering of the plasma sample. Higher than normal MW multimers may be seen post-DDAVP, in newborns, in patients with recurrent TTP during remission, and with an acute phase response.

Quantitative multimer analysis provides an objective measure of VWF structure to better characterize subtle changes observed in the subtypes of VWD and may help to determine the nature of any additional clinical laboratory testing to reach a clear-cut diagnosis.
REASONS FOR REFERRAL:
• Confirmation of normal multimer distribution in patients with suspected type 1 VWD
• Evaluation of patients with abnormal VWF:RCo/VWF:Ag ratio
• Distinction of type 2A, 2B, or platelet-type VWD from other VWD types
• Evaluation of bleeding symptoms in a patient with a VAD in place

METHOD:
Multimer analysis is performed by LiDS-agarose (0.65%) electrophoresis. This technique is considered “low resolution” because the VWF triplet structure is not seen. Electrophoresis separates VWF into multimer bands based on molecular weight (MW). Multimers are detected after transfer to nitrocellulose using monoclonal antibodies with chemiluminescent detection and densitometry analysis. The percentage of low MW (LMW) multimers defined as bands 1 – 5, mid-MW (MMW) multimers (bands 6 – 10) and high MW (HMW) multimers (bands >10) is calculated and compared to the normal plasma control.

LIMITATIONS:
von Willebrand disease type cannot be determined based upon the assay of multimer structure alone. Additional testing including (but not limited to) VWF antigen, VWF Ristocetin Cofactor Activity, and FVIII activity are required for classification of variant VWD.

SPECIMEN REQUIREMENTS:
0.5 mL citrated plasma aliquot, frozen in a plastic tube.

SHIPPING REQUIREMENTS:
Place the frozen specimen and the requisition into plastic bags, seal and place in an insulated container. Surround with at least 5 pounds of dry ice. Seal the insulated container, place into a sturdy cardboard box, and tape securely. Ship the package in compliance with your overnight carrier guidelines. Label with the following address:

Client Services/Hemostasis Reference Laboratory
BloodCenter of Wisconsin
638 N. 18th St.
Milwaukee, WI 53233
800-245-3117, ext. 6250

TURNAROUND TIME: 7 - 10 days

CPT CODES: 85247

REFERENCES: