

# TURNAROUND TIMES

Department of Pathology and Laboratory Medicine  
January 2006

The University of Kansas Medical Center  
3901 Rainbow Blvd, Kansas City, Kansas 66160

## Welcome to our Newsletter

Lowell Tilzer, MD PhD  
Medical Director, Clinical Laboratories

We are pleased to introduce you to the inaugural issue of the Clinical Lab Newsletter we are calling the Turnaround Times. Every two months, we will be updating you on issues in the K.U. Clinical Laboratory including: Transfusion Medicine, Hematology, Clinical Chemistry, Microbiology, Virology, Immunology and other areas through this intranet site. We are currently resident on the K.U. Formulary Website under the Clinical Laboratories tab. At this site many important items from the lab can be accessed, including archived issues of the Turnaround Times. In addition, tables of normal values, critical values, mandatory Centers for Medicare and Medicaid Services (CMS) lab announcements, organization charts and phone numbers will be available at this website for easy access.

As you can see the format of the Newsletter will be short with information condensed so you don't have to spend inordinate amounts of time keeping up with what is new in the lab. We will include appropriate references for those that want to explore these areas in more depth.

Speaking of what is new in the lab, I would like to introduce our new Administrative Lab Director, Mrs. Shirley Weber. Mrs. Weber started in October, transferring from Organization Improvement. For those who don't know her, she has been at KU Hospital for 4 years, two as Assistant Lab Director, and two years in OI. She has extensive experience in lab management and laboratory information systems. It's nice to have her back in the lab.

Finally, we invite you to send comments and questions to us about items in the Turnaround Times. Please email your thoughts to [ltlilzer@kumc.edu](mailto:ltlilzer@kumc.edu).

## Laboratory Diagnosis of Viral Respiratory Infections

Rebecca Horvat, PhD  
Director, Microbiology

The viral respiratory season starts typically in late October and may run into early April. The laboratory offers several rapid assays that can detect viral respiratory pathogens. The rapid antigen detection assays can identify influenza A and B with a sensitivity of 82% and a specificity of 94% on nasopharyngeal wash specimens. Nasopharyngeal swabs have a decreased sensitivity

(78%) and specificity (92%) and thus are not recommended. A separate assay can detect the respiratory syncytial virus (RSV) with a sensitivity of 89% and a specificity of 98% when performed on nasopharyngeal wash specimens. Nasal swabs are not acceptable for the RSV assay. If these antigen tests are negative a rapid viral culture can be ordered. This culture will detect 7 different respiratory viruses (influenza A and B, parainfluenza 1, 2 and 3, RSV and adenoviruses). The initial results are available after 24 hours of incubation. An internal study has shown that 20% of specimens negative by the antigen assay had a respiratory virus detected in the rapid culture.

The accuracy of both the antigen and viral culture depends primarily on acquiring a good specimen from the patient. Common respiratory viruses live within the host nasopharyngeal cells. Thus a specimen with an adequate number of infected cells should be obtained. The best specimen is a nasopharyngeal wash. This single specimen provides adequate material for both antigen and rapid viral cultures. These tests can be ordered together as needed. Nasal swab specimens are discouraged because of the low number of host cells acquired on a swab and the tendency of the swab material to bind up the viruses.

For surveillance purposes only, our laboratory will attempt to culture influenza A from all antigen positive specimens. These isolates will be submitted to the Kansas State Health Laboratory for typing. This is part of the nation-wide surveillance to allow for the detection of a new influenza strain, such as the H5N1 virus, that could lead to a pandemic. However, surveillance cultures cannot be performed from nasal swabs.

## Fresh Frozen Plasma (FFP) Transfusion and Elevated International Normalized Ratio (INR)

Jigar S Patel MD  
Associate Medical Director, Blood Bank

A meta-analysis from Segal and Dzik, in the September issue of *Transfusion*<sup>1</sup>, attempted to determine if mild elevation of PT or INR increases the risk of bleeding in patients undergoing invasive procedures. A total of 1 randomized trial and 24 observational case series were included in their analysis. Reviewed articles spanned a wide range of procedures and included bronchoscopy (2), central vein cannulation (3), liver biopsy (13) (transjugular

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(5), laparoscopic (2), percutaneous and percutaneous with hemostatic plug (3)), femoral arteriography (3), kidney biopsy (2), thoracenteses (1), paracenteses (1), and a series of mixed procedures (1). Rates of bleeding were similar in the majority of studies. None clearly showed an increased risk of bleeding in patient with abnormal coagulation tests. Many of the studies looked at multiple coagulation defects (prolonged PT, PTT, or thrombocytopenia) but still found no clinically significant increase in bleeding risk. Segal and Dzik concluded that abnormal test results do not predict increased risks of bleeding and further randomized control trials are required to determine what coagulation testing abnormalities predict bleeding.

Current practice in many hospitals is to correct to an absolute INR no matter the circumstances. This approach ignores the lack of sensitivity or specificity of a single abnormal parameter. An INR prolongation without prolonged PTT, thrombocytopenia (less than 50,000 platelets/microliter), or Platelet Function Analyzer (PFA) testing (see current comments by Cunningham) is often of dubious clinical significance. PT and PTT are mostly reflective of factor levels in plasma. This does not take into account the cellular molecules involved in coagulation.<sup>2,3</sup> It is these interactions that are responsible for coagulant activity at the site of an injury. We recommend evaluating the entire clinical situation when INR is elevated and use FFP judiciously to correct isolated prolongations of INR or PTT. Furthermore, the transfusion of two units of FFP will provide adequate levels of coagulant factors ( $\approx 450$  IU of each factor) for hemostasis.

## References

1. Segal JB, Dzik WH; Transfusion Medicine/Hemostasis Clinical Trials Network. Paucity of studies to support that abnormal coagulation test results predict bleeding in the setting of invasive procedures: an evidence-based review. *Transfusion*. 2005 Sep; 45(9):1413-25.
2. Monroe DM, Hoffman M, Roberts HR. Platelets and thrombin generation. *Arterioscler Thromb Vasc Biol*. 2002 Sep 1; 22(9):1381-9.
3. Hoffman M, Monroe DM, Roberts HR. Cellular interactions in hemostasis. *Haemostasis*. 1996; 26 Suppl 1:12-6.

## The PFA Test: An Automated Bleeding Time that Aids in the Evaluation of von Willebrand Disease and Other Bleeding Disorders

Mark T. Cunningham, MD  
Medical Director, Hematology Laboratory

## Introduction

The manual bleeding time, first introduced in 1901, has traditionally been used to detect defects in primary hemostasis (platelet-vessel wall interactions). Several studies show that the manual bleeding time performs poorly as a screening test for specific platelet function disorders such as von Willebrand disease, platelet storage pool disease, and drug-induced platelet dysfunction. It is also a poor predictor of bleeding following surgery or invasive procedures, particularly in the absence of a bleeding history or recent ingestion of anti-platelet drugs.<sup>1</sup>

The PFA (Platelet Function Analyzer) is an automated test that was developed to mimic the manual bleeding time. PFA testing performs better than the manual bleeding time with regard to diagnostic sensitivity and reproducibility<sup>2</sup>, and will eventually replace the manual bleeding time at the University of Kansas Medical Center.

## Principle of Method

The PFA test uses a special instrument that simulates an in-vivo vascular injury and is designed to detect platelet dysfunction. Citrate anticoagulated whole blood flows through a small aperture in an artificial membrane that mimics a cut vessel. Two different artificial membranes are used; one is coated with collagen (COL) and epinephrine (EPI) and the other with COL and adenosine diphosphate (ADP). These coating agents induce platelet adhesion and aggregation at the aperture. The time it takes the platelet/red cell thrombus to occlude the aperture is measured as the "closure time".

## Causes of an Abnormal Test

A variety of inherited and acquired platelet function disorders cause a prolonged closure time for both the COL/EPI and COL/ADP membranes. Examples include von Willebrand disease (VWD), Glanzmann thrombasthenia, Bernard Soulier syndrome, and uremia. Aspirin causes a prolonged closure time for the COL/EPI membrane, but not the COL/ADP membrane. Of note, clopidogrel (Plavix) does not cause an abnormal PFA test.

The diagnostic sensitivity of the PFA test for a variety of platelet disorders is shown in the table below.<sup>3,4</sup> The data on VWD are from a well designed study that measured von Willebrand factor (VWF) levels and PFA results in parallel, controlling for the wide day-to-day variability in vWF levels that can occur.<sup>3</sup>

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Platelet Dysfunction	N	PFA Sensitivity
von Willebrand Disease		
Type 1	36	100%
Type 2A	10	100%
Type 2N	2	100%
Type 3	4	100%
Acquired	5	100%
Pseudo	3	100%
Storage pool disease	7	43%
Primary secretion defect	9	44%
Glanzmann Thrombasthenia	2	100%

The data from the table shows that the PFA test is most valuable as a screening test for most types of VWD (except type 2N) and Glanzmann thrombasthenia. The sensitivity of the PFA test for other platelet disorders such as inherited storage pool disease and primary secretion defects is too low to be useful for screening. Therefore it is recommended that platelet aggregation studies also be ordered for a thorough evaluation of platelet dysfunction.

Treatment of patients with VWD and other platelet function disorders (storage pool disease, primary secretion defects) with desmopressin (DDAVP) also causes full correction of a prolonged baseline closure time. Therefore the PFA test is useful in determining the efficacy of DDAVP treatment.

Platelet counts less than 150 K/uL and hematocrits less than 35% also cause prolonged closure times. This occurs because the rate of formation of the platelet/red cell thrombus is dependent on the platelet count and hematocrit.

## Ordering Information

Ordering Code on SMSNet: PFA

Specimen type: Two 3 mL light blue top (citrate) tubes plus one 3 mL purple top (EDTA) tube

Specimen Stability: Specimens should be delivered to lab immediately. Keep specimen at room temperature

Availability: 7 days per week, 24 hours per day

Turn Around Time: Routine 2 - 4 hours. Also available STAT

Reference Ranges: COL/EPI = 80-192 seconds

COL/ADP = 60-112 seconds

Result Reporting: CBC results and pathologist interpretation will be provided with numerical results for COL/EPI and COL/ADP membranes.

## Test Indications:

Screening for von Willebrand disease (type 1, 2A, 2B, 3)

Monitoring efficacy of DDAVP treatment

Screening for aspirin effect

## Test Limitations:

Will not detect coagulation factor defects

Will not detect clopidogrel (Plavix) effect

Poor sensitivity for certain platelet function defects

Test Interference: Prolonged results may occur if platelet count is less than 150 K/uL or hematocrit is less than 35%.

## References

1. Peterson P, et al. The preoperative bleeding time test lacks clinical benefit: College of American Pathologists' and American Society of Clinical Pathologists' position article. Arch Surg 133: 134-139, 1998.
2. Franchini M. The platelet function analyzer (PFA-100): an update on its clinical use. Clin Lab 51: 367-372, 2005.
3. Fressinaud E, et al. Screening for von Willebrand disease with a new analyzer using high shear stress: a study of 60 cases. Blood 91: 1325-1331, 1999.
4. Cattaneo M, et al. Evaluation of platelet function with the PFA-100 system in patients with congenital defects of platelet secretion. Thromb Res 96: 213-217, 1999.