D40 Use of Clinical Laboratory Assays in a Forensic Setting: A Review

Nannepaga Y. Zachariah, PhD and Nizam Peerwani, MD, Tarrant County Medical Examiner's Office, 200 Feliks Gwozdz Place, Fort Worth, TX 76104; Michael J. Nicar, PhD, Diagnostic Systems Laboratories, Inc., 445 Medical Center Boulevard, Webster, TX 77598*

After attending this presentation, attendees will be better aware of laboratory methods typically used in clinical differential diagnosis that can be applied to forensic setting. A literature review will be provided at the poster.

This presentation will impact the forensic community and/or humanity by making forensic scientists more aware of laboratory options to assist in determination of cause of death. The methods discussed are typically used for differential diagnosis in the living. They may be applied to forensic investigations providing additional information to forensic investigations.

Quantitative determinations of biochemical components, such as electrolytes, glucose or serum proteins, have been used in postmortem blood specimens to aid in determination of cause of death. In a variety of forensic studies, determination of esoteric biochemical markers has been useful in establishing postmortem diagnosis of the underlying cause of death. These are the tests typically used in an emergency room setting or tests used for differential clinical diagnosis. Following is a review of some of these tests.

Procalcitonin (PCT) is a propeptide of calcitonin, with a half-life of 25 hours, and is deprived of hormonal activity. In the living, PCT has been shown to have a good correlation in the differential diagnosis of bacterial and non-bacterial inflammation. Moreover, PCT has been able to differentiate between sepsis and systemic inflammatory response syndrome of non-infectious origin. For example, in postmortem specimens, PCT levels with severe sepsis have been shown to be as high as 90 ng/ml. Non-sepsis specimens had PCT levels less than 1ng/ml. And measurement of PCT seems reliable until 140 hrs postmortem. Because of its stability and the ease of measurement by immunoluminometric assay, PCT may be a more specific postmortem marker for sepsis than Creactive protein (CRP). Rather, CRP is more related to systemic inflammation in general, and has recently shown application as a predictor of cardiovascular disease risk. Interleukin-6 was also found to be elevated in postmortem specimens of sepsis, and can be assayed by convenient manual immunoassays. Diagnosis of sepsis is a problem that continues to challenge forensic pathologists.

Troponin is clinically routine cardiac marker. The troponin complex consists of three myofibrillary proteins (TnC, TnI, TnT) and after myocardial injury TnI and TnT are extensively released into the blood. Automated immunochemical methods, as well as point-of-care tests, are used to measure these proteins in blood. In the living, TnI is non-detectable and has proven to be a sensitive marker for diagnosis and management of myocardial infarction. TnI measurement in postmortem specimens can provide evidence of death due to myocardial infarction (MI) and estimation of postmortem interval. Immuno-histochemical expression of TnI and TnT of postmortem cardiac tissue and their gradual decline would assist in making a firm diagnosis of MI. A rapid assay method (Roche CardiacT) designed for use in an emergency room setting, has been used to measure TnT in postmortem blood. In a study of 20 cases with final autopsy report of death due to MI, 85% were positive; and out of the 30 control cases studied only 30% were false positive. While these methods may provide quick supplemental information they are no substitutes for autopsy since they can not rule out other underlying reasons for the cause of death.

Glycosylated hemoglobin (HbA1C) is used as a marker for glycemic control in patients with diabetes. HbA1C reflects the average blood glucose level over a period of six weeks. Studies indicate that postmortem HbA1C can be an accurate marker to predict diabetes mellitus and therapeutic compliance. HbA1C specimens are reliable if stored at 4 degrees C, and temperatures from 27-35 degrees C for 7 days caused only an increase of 4-7% above original values. Levels of HgA1C greater than 8.5% in postmortem specimens indicate chronic hyperglycemia. Chromatographic methods are commonly used for HbA1C determinations. High levels of fructosamine in vitreous humor were also found to be indicative of diabetes. Insulin/C-peptide ratio may be used to make a forensic diagnosis of exogenous insulin administration especially in suspected homicide cases. Because endogenous insulin is cleared slower than C-peptide, physiological insulin/C-pepide ratio is less than one. Exogenous insulin/C-peptide ratio will result in greater than one. Commercially available RIAs are available for all of these assays.

Prostate Specific Antigen (PSA) is used clinically to detect and manage prostate disease, and is found in large quantities in seminal fluid. Several sensitive PSA immunoassays have been developed and are commercially available. Newer membrane assays are relatively easy to perform and offer similar sensitivity as immunoassays. It was reported that seminal fluid from vaginal swabs collected from sexual assault cases, even stored at room temperature for three months, could be extracted and PSA detected by membrane assays. Saliva specimens were used as negative controls. Thus, the membrane assays could be used for forensic identification of seminal fluid.

These are but a few examples of tests that could be helpful to the forensic scientist; tests that are

usually thought of as clinical tests. Commercially available assays are available and offer more options in the armamentarium for determining forensic cause of death and other investigations.

Procalcitonin, Troponin, Glycosylated Hemoglobin

 ** Presenting Author*