PHARMACY UPDATE — Joshua Bird, Pharm.D Student & Deepti Vyas, Pharm D

The Future of Warfarin Dosing: What is in the Pipeline?

Pharmacogenetic testing has been researched to find genetic variability among individuals who require warfarin therapy and to possibly reduce the occurrence of adverse events; indeed, the FDA recently approved a labeling change for Coumadin and issued a statement that "lower initiation doses should be considered for patients with certain genetic variations in the CYP2C9 and VKORC1 enzymes." The latter enzymes are the primary agents in the metabolism of warfarin; researches have found 37 different alleles for the CYP2C9 gene with CYP2C9*1 representing the wild (normal metabolizer) type.

Patients who are homozygous for a variant allele generally require less warfarin. The most common variants are CYP2C9*2 and CYP2C9*3, with the latter producing the slowest metabolism of warfarin. The variant alleles have been found to be most common in European-American and African-American populations. While studies demonstrate that pharmacogenetic testing helps to guide dosing and improve safety, it remains to be seen whether such testing proves to be cost effective.

Reference: Limdi, NA & DL Veenstra, *Warfarin Pharmacogenomics*, Pharmacotherapy, 2008, 28(9), 1084-97

CASE REPORT — Robert Folzenlogen MD

A 76 year old male was transferred to MU for management of pneumonia and rhabdomyolysis. He gave a history of cough, green sputum, fever, chills and malaise for the past several weeks; these symptoms did not improve after a 14 day course of Augmentin. He developed increasing weakness, anorexia and an inability to stand up and was taken to his local ER for evaluation. His chronic mild dyspnea had begun to increase and he gave a vague history of weight loss; he denied hemoptysis. Evaluation in the ER revealed WBC 32.3 with 88 segs, Hgb 10.4, BUN 35, Cr 2.6 and CK 1706. A CT of the head was negative but a CXR showed a RUL infiltrate. He was transferred to MU for further evaluation and management.

The patient reported a history of pulmonary fibrosis (diagnosed in 1989), chronic kidney disease secondary to ANCA+ vasculitis (since 2003), peripheral neuropathy and myelodysplastic syndrome. Medications included Prednisone 5mg qd and Cytoxan every 14 weeks. He lives and works on a farm where he raises pigs and grows corn, beans and wheat. Pets include a dog and three cats. He quit tobacco use 20 years ago and stopped using alcohol several years ago; he denied any past use of illicit drugs. He was in the Navy during the Korean war. Though he was a hunter, he has not done so for 6 years and has not travelled over the past six months; he denied recent tick bites. He also denied a past +PPD, history of TB or exposure to TB.

Initial exam revealed a weak, lethargic, elderly male who was otherwise in no acute distress. T was 38.2 and BP was 132/92. No rash or jaundice was noted. HEENT was unremarkable except for poor dentition. Neck revealed no adenopathy or JVD. Chest was reported to be clear and cardiovascular exam was normal; there was no peripheral edema. Abdominal exam was normal with no organomegaly or tenderness.