

A Personalized Paradox

My previous columns have considered the tensions between those who believe genomics will revolutionize medicine and those who feel that genomic medicine is only a pipe dream. Confined in the bubble of the NIH, I at times wonder whether genomics is having much of an affect outside of rare genetic conditions and “early adopter” institutions. Clearly, in cutting edge health care systems genomics and “Personalized Medicine” are changing care – for example a major academic teaching hospital has announced plans to offer tumor genomic profiling to all cancer patients to better tailor care. Nice for those that can afford the estimated \$2000 cost and land at such a hospital - but at rank and file community hospitals, for bread and butter primary care diagnosis – is there really much intersection?

Last week a relative of mine was admitted to a rural community hospital for atypical chest pain. Prior to the admission the patient had no known risk factors for hypercoaguability save age, but was found to have lower extremity thrombus and bilateral pulmonary emboli (PE). The chest CT that picked up the PE also identified a 2 cm cystic pancreatic mass thought to represent an intraductal papillary mucinous neoplasm. Over the course of the next several days the patient’s care intersected with genomic medicine on three distinct occasions, each illustrating the reach of genomic insights: pharmacogenetic testing; predictive genetic testing; and prognostic genetic testing. First he was started on warfarin as long term preventive therapy for recurrent PE. Currently FDA mandated labeling of warfarin suggests health care providers consider pharmacogenetic testing to guide dosing. Simultaneous to the patient’s admission Medicare issued a provisional statement recommending that warfarin pharmacogenetic testing be covered in the setting of research trials designed to look at health outcomes (<https://www.cms.hhs.gov/mcd/viewdraftdecisionmemo.asp?from2=viewdraftdecisionmemo.asp&id=224&>). This recommendation provides an indication that Medicare believes that such testing holds promise for improving health outcomes. The patient wasn’t tested, but it was a consideration. Second, his primary care hospital team ordered testing for a source of his apparent hypercoaguability, including a test for the Factor V Leiden (FVL) gene mutation. The results from FVL testing bear on predicting future disease risk (deep vein thrombosis and PE) for the patient and his family. Finally, the patient was informed by his gastroenterologist that the next step in working up the pancreatic mass includes endoscopy and fine needle aspiration of the cyst. The patient was informed that the aspirate will be subjected to a series of tests, one of which is a state of the art molecular diagnostic assay for k-ras mutations. Such testing has been shown to aid in differentiating benign versus malignant tumors, a key to downstream tumor management (resection versus observation). Little more than a decade ago these genomic tests would have been considered exotic – if available at all- outside of a major tertiary care setting.

Readers may wonder a bit at the word ‘paradox’ appearing in the title of this piece. At the same time the patient’s providers were delivering cutting edge care, our health care system provided a clear example of how a broken system works against itself. The patient spent three extra days in the hospital because he was told his insurance would not

cover injectable low molecular weight heparin as an outpatient. This directly cost the health care system a substantial sum simply because the pocket paying for an acute stay isn't connected to the pocket that pays for outpatient therapy with heparin. Indirectly, the prolonged admission diminished hospital system capacity, and exposed the patient needlessly to three additional days of possible hospital-induced iatrogenic harm. Such inefficiencies must be addressed – otherwise the resources to implement and study technological advances will continue to be a rate-limiting step to the application of genomics in health care.

My relative's admission for a PE to a rural community hospital illustrates how, with little fanfare, genomics and personalized medicine are suffusing into the practice of medicine. Likely none of the individual care-givers even realized that they had delivered "Personalized Medicine" as it has come to be known in the genomic era; rather they provided the "personalized medicine" good clinicians have always strived to deliver. Those in primary care that have raised the question "Where's the beef?" regarding genomics in medicine should take notice of this case. The "beef" is arriving daily, in small, often unexpected steps, and not necessarily in great leaps. Genomic medicine is no longer a dream. It is time for all levels of medical education to provide the grounding in genomics that physicians will need to practice in the coming decades.

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