Masquerading as Liver Disease: Why Practice Guidelines Matter
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A 62yo man presented to Hepatitis clinic after being referred by his primary physician for evaluation of persistently elevated transaminases, first noted on screening liver function tests (LFTs) 5 years ago. The patient reported that about 5 years ago he retired and established care with a new provider who noted AST/ALT that were 2x the upper limit of normal. He was healthy appearing, without significant medical history, and the decision was made to observe him and follow up his labs at a later date. After 4 years of persistent elevation, a work-up was undertaken. The patient had always denied significant alcohol consumption, current medications consisted of testosterone injections, ibuprofen, and occasional colchicine, and viral hepatitis serologies were negative. The patient had a normal BMI and reported exercising daily. Ultrasonography was negative for evidence of fatty infiltration and an abdominal computed tomography scan was similarly unrevealing. The patient was then tested and found to be negative for alpha-1 anti-trypsin deficiency, autoimmune hepatitis, primary biliary cirrhosis, the HFE gene for hereditary hemochromatosis, and Wilson's disease. He was then referred to hepatology with a question of need for biopsy. On history and physical, the patient confirmed what was already documented, but further history revealed that he had been cycling 50miles/day largely without fail since retiring, though had recently cut back to 25miles/day after a recent gout flare. Serum creatinine kinase testing was undertaken which returned high at 950 units/L. The diagnosis of skeletal muscle releasing AST/ALT secondary to excessive exercise was made. The patient scaled back his exercise regimen and had rapid resolution of his transaminitis. Liver biopsy was deferred.

This case illustrates how testing can be self perpetuating, cascading towards an invasive procedure without anyone stopping to consider the value of the next test or the patient’s preferences. LFTs were ordered for screening (which has little evidence without symptoms or risk factors) and were abnormal, which led to further testing in a completely asymptomatic patient. These “pre-invasive” tests led towards invasive liver biopsy, which has the following attendant risks: 25% experience significant pain, 6-14% experience transient bacteremia, 0.32% experience bleeding complications, 0.09% develop bile peritonitis, 0.063% develop hemothorax, and 0.0078% develop pneumothorax.

When faced with uncertainty regarding a diagnosis, clinicians need to consider disease probability to guide the next steps, rather than ordering a battery of tests covering a range of possibilities both common and uncommon. In this case for example: Wilson’s disease was tested for, which has a prevalence of 1/30,000 live births and presents before 40 years old in the vast majority of cases; testing for Alpha-1 antitrypsin deficiency was performed with a prevalence of 1/5000 though extremely uncommon without pulmonary symptoms; hemochromatosis was tested for, but while the gene is common (1/200 causasions) the disease penetrance is extremely low, and an iron panel would be the best first test; autoimmune hepatitis only has a prevalence of 11-25/100,000 and affects females to male at a 3.6:1 ratio; and primary biliary cirrhosis has a prevalence of 2.7/100,000 with 95% of cases occurring in females.

Fortunately for this patient, serious harm was avoided, but only just. Reflexive testing without reflection sent him down a path towards invasive biopsy, which could have been avoided with careful history taking. And while true harm may have been prevented, the patient was still exposed to unnecessary radiation, for which the body of literature regarding harm is growing, as well as anxiety about his health, which should not be forgotten.