The simple lab test is sometimes more complex than we think, if we think about it at all

We are all exposed to initiatives from multiple stakeholders telling us to order fewer tests. Many of these efforts to control costs and improve efficiency and quality of care are directed at populations of patients and are broad concepts: provide screening only to those most likely to benefit (eg, don't screen for prostate cancer in men with a lifespan < 10 years); avoid procedures that provided limited benefit in controlled trials (eg, limit routine arthroscopic treatment of knee osteoarthritis); and avoid reflexive practices unlikely to improve patient outcomes (eg, eliminate routine preoperative testing before elective procedures in otherwise healthy patients).

Whether system-based changes will be implemented and have an impact remains to be determined. But I sense that with all the attention being focused on population management and healthcare practices, including an emphasis on documenting and coding our encounters with patients, whether substantive or simply digital housekeeping, we are increasingly distracted from the patient in front of us and are spending less time reviewing the principles underlying the diagnoses we make and the tests we order—just as we are taking less time to perform relevant physical examinations.[1] The latter may mostly relate to time pressures. The former, I believe, is a product of both time pressures and a false sense of confidence in our knowledge of seemingly commonplace laboratory tests.

As I lecture, work with trainees, and reflect on my own patients, I realize that we are slowly but progressively minimizing the importance of a working knowledge of the basic foundations of clinical practice—perhaps because facts can always be looked up. I am not referring to knowledge of arcane biochemical pathways, eponymous references, or the latest recommended treatment of inclusion body myositis. I am thinking instead of the value of regularly refreshing our knowledge of laboratory tests and diagnoses we frequently encounter.

Having access to multiple clinical databases literally in our pockets is likely bolstering a false sense of confidence in our knowledge. The National Library of Medicine may be only a tap on a smart phone away, but accessing it regularly is a different thing. Attending conferences and reading educational journals help to keep our broad-based knowledge of internal medicine refreshed, but time pressures may significantly limit our ability to regularly pursue these activities.

On page 37 of this issue of the *Journal,* Drs. Moghadam-Kia et al discuss their approach to asymptomatic elevations in creatine kinase (CK). Although no longer included in the most commonly used lab panels, CK measurement is often ordered in patients taking statins, even if they have no relevant muscle-related symptoms. Thus, evaluating a patient with an asymptomatic elevated CK level is not rare. The authors delve into the clinically relevant test characteristics, and their important caveats about interpreting elevated CK levels are germane not only to the asymptomatic pa-

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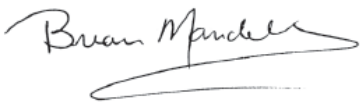
tient, but also to the patient being evaluated for myalgia or weakness. This latter situation is one I frequently face in both the hospital and the outpatient clinic. I am often asked to consult on patients who have incompletely defined symptoms and elevated CK.

As discussed in the article, the laboratory definition of "normal" must first be considered. Laboratory test results must always be interpreted in the clinical context. An isolated elevation in parathyroid hormone cannot be interpreted without knowing the patient's vitamin D level. Nor can "normal" low-density lipoprotein or serum urate levels be interpreted properly without knowing if the patient is accumulating excess cholesterol or urate deposits. As we order and interpret test results, we must consider the biology of the substance being measured as well as the test characteristics; too often, we react to abnormal laboratory results with an incomplete understanding of these aspects.

Moghadam-Kia et al do not dwell on the organ involvement causing CK elevations, but specificity is another very important aspect when clinically interpreting the results of a CK test. Many patients with muscle damage or inflammation have elevations in serum aspartate aminotransferase and alanine aminotransferase levels (the ratio of elevation depends on the time course of the muscle damage and on the relative clearance rate of the two enzymes). Without knowing that the CK is elevated, one might assume that an aminotransferase elevation reflects hepatitis. I have seen several patients with elevated aminotransferases and complaints of weakness and fatigue who were subjected to liver biopsy before it was recognized that the source of the enzyme elevation ("liver function test changes") was muscle (or hemolysis). Frequently unrecognized is that aldolase, which has a cell distribution similar to that of lactate dehydrogenase, does not have the relative specificity of localization to muscle that CK has. CK is quite useful in distinguishing myocyte from hepatocyte damage.

This paper presents a wonderful reminder of the value of updating and reviewing what we know about tests that we order, even if we feel comfortable when ordering them. Before initiating a cascade of additional tests and consultations to explore the cause of an abnormal test result, a little time spent reviewing its basic characteristics and biology may pay dividends.

As 2015 comes to a close, we at the *Journal* share with you our sincere wishes for personal satisfaction and a globally more peaceful 2016.



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1. **Verghese A, Charlton B, Kassirer JP, Ramsey M, Ioannidis JP**. Inadequacies of physical examination as a cause of medical errors and adverse events: a collection of vignettes. Am J Med 2015; 128:1322–1324.