No dawdle in switch to high-sensitivity troponin

Karen Titus

December 2019—At Mayo Clinic, the latest generation of cardiac troponin assay was an overnight success. Literally.

For months, the institution had been preparing to switch to Roche Diagnostics' Elecsys Troponin T Gen 5 Stat assay, says Bradley S. Karon, MD, PhD, chair of the Division of Clinical Core Laboratory Services, Department of Laboratory Medicine and Pathology.

As the time of the rollout neared, an internal medicine colleague who was involved in overseeing the transition asked, "'What will the burn-in period be?'" recalls Dr. Karon, who is also co-director of Mayo's stat labs and point-of-care testing programs. Surely clinicians would be able to continue ordering the Gen 4 assay for a time, right? So how long would that last?

Dr. Karon's dramatic-sounding answer? "Zero hours."

The switch occurred in March 2018. At midnight on the day the new assay was implemented, the Gen 4 order was obsoleted (to use Dr. Karon's word), and the Gen 5 went live. "Anybody who had a panel started got it finished with 4th Gen, and then we just switched whole hog—the whole practice—to 5th Gen," he says.

Dr. Amy Saenger and Dr. Fred Apple at Hennepin County Medical Center, where they and an ED colleague are leading the launch of a high-sensitivity cardiac troponin assay. It will require "education, sometimes a lot of education, and certainly ongoing education," says Dr. Saenger. [Photo: Ackerman + Gruber]

Mayo is no drama queen (a scarce trait in Minnesota generally). Hennepin Healthcare/Hennepin County Medical Center, Minneapolis, is also planning a decisive cardiac troponin assay launch. When Hennepin moves to Abbott's Architect Stat High Sensitivity Troponin-I assay, likely early next year, "It will be

a switch that we flip in one day," says Fred S. Apple, PhD, DABCC, principal investigator, cardiac biomarkers trials laboratory, Hennepin Healthcare Research Institute. "If you start offering the option of either high-sensitivity or contemporary troponin assays, it will be confusing to providers."

There's actually nothing "overnight" about any of this, of course, no matter how matters might look on the surface. For years U.S. labs had looked with envy at Europe's widespread use of high-sensitivity cardiac troponin assays. The exciting news now is that with the relatively recent FDA clearance of four high-sensitivity cardiac troponin assays, "Everything is in play in the U.S. right now," says Dr. Apple, who is also professor, laboratory medicine and pathology, University of Minnesota, and co-director, clinical and forensic toxicology laboratory, Hennepin Healthcare/Hennepin County Medical Center. Siemens Healthineers and Beckman Coulter also offer high-sensitivity troponin I assays, and more are likely on the way. Laboratories have begun offering hs-cTn assays or are at least considering the switch.

As they should be, says Dr. Apple. "Everyone who is using a contemporary assay should, as soon as possible, consider implementing a high-sensitivity troponin assay, whether you're an I or a T user," he says. "The wealth of clinical data for early rule-outs and earlier rule-in of myocardial infarction, within a two- or three-hour window, is a very positive patient care incentive to bring these assays to practice, especially for females."

(Note: Gen 5 was not designated by the FDA as a high-sensitivity assay, though it is considered to be a hs-cTn in Europe. It is, however, more sensitive compared with the Gen 4 cTnT assay, "so it's in between," says Dr. Karon. This has not created problems for his clinical colleagues, he says. "It doesn't seem to bother them. I think they've gotten the fact that this is an FDA labeling issue," and that the Gen 5 is being used in clinical protocols that are based on hs-cTn assays.)

The assays also provide welcome risk stratification, which hadn't been possible with previous assays, Dr. Apple says. High-sensitivity cardiac troponins provide a reference interval, similar to that offered by high-sensitivity C-reactive protein, he says, "where we're actually able to look at a continuum of risk in patients to determine separately for males and females what their relative risk is, both for all-cause mortality as well as major adverse cardiac events over, say, a 180-day period."

The switch was a logical choice at Mayo, says Dr. Karon. For years, the institution has had active research programs in cardiovascular medicine and troponin testing. So once 5th Gen became approved in the United States, "there was a desire to implement that into our practice."

Desire alone sustains only poets, however. Ardor needs action.

At both Mayo and Hennepin, the work has been taken up by those outside as well as inside the laboratory. As Dr. Apple puts it, "The more the merrier. You don't want to have anyone feel like they weren't consulted."

Mayo formed an implementation group, which was led by a hospitalist and included two cardiologists, Dr. Karon, and the practice chair of emergency medicine. Beyond that core group, "We pulled in representatives from the outpatient practice, surgery, anesthesia—pretty much every area of practice," Dr. Karon says.

The group began its work in fall 2017. The laboratory's first step was collecting 1,500 samples, from slightly more than 800 patients, and measuring both 4th Gen and 5th Gen troponin T. "That allowed us to present to the implementation group the implications of moving to the 5th Gen T," Dr. Karon says. "We had discussions on what our reference intervals would be, and those were all up to the implementation group to decide."

Ultimately they went with fairly low intervals—10 ng/L for females and 15 ng/L for males—based on the European guideline, and forgoing the package insert.

They adopted a zero-, two-, and six-hour panel to replace the previous panel of zero-, three-, and six-hour measurements. The implementation group "was constantly asking questions" about the number of patients

available for comparison; since there were no previous two-hour samples, “as we designed the protocols we assumed the two-hour value would behave more or less like the three-hour value from our sample set,” Dr. Karon says.

A one-hour measurement was even more appealing, says Mayo’s Allan S. Jaffe, MD, but ultimately the group decided against it. The precision of the new assay and the tight, very small differences that needed to be detected made it “very likely, if not absolutely clear, that we would misclassify some patients” in the course of shaving an hour off the protocol. “So we went with a two-hour protocol to avoid that specifically,” says Dr. Jaffe, professor of cardiology, professor of laboratory medicine and pathology, and former chair of the clinical core lab services division of the Department of Laboratory Medicine and Pathology. An expert on the use of cTn, he has been responsible for the troponin component of the universal definition of myocardial infarction.

Among the key questions that arose, Dr. Karon says, “was how many patients in the ED will have an elevated value compared to the current state.” The lab had an answer, based on those 1,500 samples: About 30 percent of patients in the ED had elevated 4th Gen T, and slightly more than 60 percent had an elevated 5th Gen T, he says.

“It actually didn’t concern the ED as much as it has in most other institutions,” says Dr. Karon. That’s because for a decade the lab had already been relying on a troponin panel that included calculated delta values between time points reported directly into the EMR, as well as information from Dr. Jaffe and recommendations from national and International Federation of Clinical Chemistry and Laboratory Medicine guidelines about best practices for fifth-generation implementation.

Under the new protocol, most patients in the ED get a zero- and two-hour value; 80 to 90 percent do not need a six-hour measurement. “So the ED can make decisions faster,” Dr. Karon says. “It makes them very happy.”

At Mayo Rochester, adopting the new protocol has been a seamless transition, he says. “I think six, eight months in we got it to work quite well. We don’t hear many issues or complaints or confusion.” This is due in part to the fact that “we’re operating in the world of panels, where you need to look at the individual absolute panels and the deltas between time points. And the lab, in the EMR, provides an interpretation of the delta as changing or not changing.” A full decade before the switch to 5th Gen, clinicians had been using panel testing with the 4th Gen—the approach was a familiar one, in other words. Adoption has hit a few potholes at Mayo’s other sites, which have less experience using panels, he says.

Values are reported as whole numbers in ng/L, while previous assays used ng/mL. Mayo’s clinicians adapted with relative ease, Dr. Karon says. “We have very good internal education, so prior to implementation Dr. Jaffe and others in cardiology presented at many, many practice groups.” Mayo also uses a real-time point-of-care information system internally, called Ask a Mayo Expert, which included information developed by cardiology and emergency medicine. That, too, helped smooth the path.

High-sensitivity cardiac troponin, like a fringe religious sect, seems to both excite the imagination and arouse fear. On his listening tour, Dr. Jaffe did hear plenty of the-world-is-going-to-end angst. “Of course that didn’t happen,” he laughs.

Clinicians asked about running both tests side by side, but Dr. Karon and colleagues were adamant. As the aforementioned pilot study made clear, the logistics of running both tests and reporting results is not trivial, Dr. Jaffe says.

It also confirmed that the correlation between the Gen 4 and Gen 5 is not precise. “A less than .01 on a Gen 4 could be less than six on a 5th Gen. It could also be a 20, it could be a 30. The tests don’t correlate well at values [5th Gen] below 100 ng/L,” says Dr. Karon. “My concern on a burn-in is one patient would have less than .01 with a less than six, and this next patient would have less than .01 with a 25, and somebody’s going to call the lab and say, ‘Which one is right?’ Well, they’re both right. They don’t correlate well at those levels.”

It’s also becoming evident that using the same cutoff for women and men is not an ideal match. The decision to

use sex-specific cutoffs follows recommendations by the IFCC Committee on Clinical Applications of Cardiac Biomarkers and the AACC Academy, says Amy K. Saenger, PhD, DABCC, and is endorsed in clinical guidelines, primarily the "Fourth universal definition of myocardial infarction (2018)" (Thygesen K, et al. *J Am Coll Cardiol.* 2018;72[18]:2231–2264). Her support for sex-specific cutoffs is unwavering. "It is clear that males and females have different cutoffs, with females having a lower 99th percentile," says Dr. Saenger, medical director of the clinical laboratories, Hennepin County Medical Center, and associate professor, Department of Laboratory Medicine and Pathology, University of Minnesota.

'I think six, eight months in we got it to work quite well. We don't hear many issues or complaints or confusion.' — **Bradley Karon, MD, PhD**

"You're probably missing some elevations in women if you're not using them," Dr. Karon says.
Dr. Apple agrees that incentive to use sex-specific cutoffs is strong. "There are data to show that women will benefit much more strongly than men because we will be picking up a greater percentage of women who would have been missed for smaller MIs."

"My thought on this," he continues, is "it's no different than CK-MB," the assay of choice two test generations ago. "We had statistically different male versus female cutoffs, and we implemented and used those in practice."

Not to put too fine a point on it, he adds, this is the norm of working in laboratory medicine. "What do we do?" he asks. "We do the appropriate validation to look for reference ranges that are statistically different. I think it's a disservice to any patient population not to use those."

The lower 99th percentile for women makes sense from a pathophysiological standpoint, says Dr. Saenger, given that the amount of myocardium differs between the sexes. Nevertheless, she says, "Reporting sex-specific cutoffs is more controversial on the clinical side," with many cardiologists thinking they're unnecessary or that a randomized controlled trial is needed to prove their usefulness. Echoing Dr. Apple, she says, "We do not do that for any other assay. If there are studies that show there are sex-specific differences, like in the case of creatinine, we validate or verify this with our assay and report the reference intervals in that manner. High-sensitivity troponin assays should be no different."

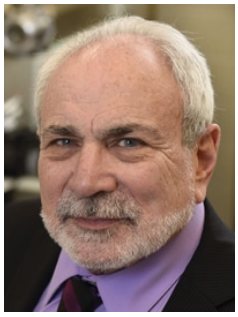
Dr. Jaffe notes the variety of opinions in the field, and then points out that much of it depends on the assay—some have a large difference between the 99th percentile values in women and men. "My concern has always been, and still is, that many of the studies done in Europe did not include an adequate cohort of women to know if sex-specific cutoffs are or are not important." Remember, he says, the majority of European studies included only patients whose symptoms were typical, which restricted the involvement of women, who often present atypically. "So they decided they didn't need to use it. I think in retrospect that it's very likely that if they had had a broader

screen, and been more open to the idea" of the sexes presenting differently, "they may well have come to a different conclusion." Moreover, with many of the population studies done in Europe, patients were not as sick as those typically seen in U.S. EDs.

Dr. Saenger agrees: "Data now indicates that MI is underdiagnosed in females not because their symptoms are more vague or they present later in life, but largely due to the fact that we were using the wrong cutoff." Labs couldn't distinguish analytical differences in 99th percentiles before the advent of hs-cTn, she says. When sex-specific cutoffs are used, MI rates for males and females are nearly the same, though she too notes that it depends on the assay.

Much of the literature is based on European experience, but the data globally are overwhelming for rule-outs, Dr. Apple says. That, plus multiple guidelines, should persuade labs to adopt the newer high-sensitivity assays. "It's a huge patient safety positive impact when you bring this assay up," he says. "You bring it up, and you eventually have enough of your own data. You analyze your own data to see how it's doing."

Hennepin is fortunate in the data department, says Dr. Saenger, noting that the majority of the U.S. data for Abbott's hs-cTnI assay is based on the Hennepin UTROPIA study cohort. On both the lab and clinical side, "We have seen some of the nuances and can predict how implementing this test will impact our positivity rates." She is confident that the upcoming move from contemporary cTnI using an overall 99th percentile to hs-cTn using sex-specific percentiles "will not result in a major increase in the number of patients with an 'abnormal/flagged' value."



'There are many more type two MIs now. Using sex-specific cutoffs, we're finding more modest, or small, MIs, particularly in women.' — Allan Jaffe, MD

European traditions, while fine for Europe, can benefit from a bit of tweaking on American shores (a point not lost on colonial Americans). Dr. Jaffe noted some of the differences in a paper he co-wrote on implementing the Gen 5 assay (Sandoval Y, Jaffe *AS. Am J Med.* 2017;130[12]:1358–1365). Several European studies, for example, advocated using an absolute baseline cutoff value of 52 ng/L (for hs-cTnT) as a positive one-hour rule-in for acute myocardial injury. "It's not that it doesn't work in an ideal circumstance," says Dr. Jaffe. But the United States is not an ideal controlled study population, and the European experience "didn't take into account that in the United States we draw troponins on a much larger number of patients."

In Europe, studies were oriented to patients with chest pain—and those who present with typical chest pain at that. "And the older you are, the less typical you become," says Dr. Jaffe. "As an obligatory rule-in, 52 ng/L would sweep half of critically ill patients into the hospital," he says, as well as older individuals with comorbidities.

That hasn't happened at Mayo, though Dr. Jaffe heard his fair share of doomsday scenarios from worried

colleagues before the implementation. There's been no great uptick in patients admitted or additional procedures, he reports. The majority of patients—more than 80 percent—are triaged within a couple of hours, he says, and 10 to 20 percent require later samples.

Some gaps have occurred. "We used an absolute delta of 10. And as you start getting values that are higher and higher and higher," Dr. Jaffe says, "that's just too low. So we would argue for changing that, and simply say that when the value is over 100, start using a percentage criteria of, say, 20 percent."

A second gap—"We alerted people, but obviously we didn't educate adequately," Dr. Jaffe says—concerned patients who present late after the onset of their MIs. "We guessed 12 hours, but that may not always be the ideal number," Dr. Jaffe says. "They're on the downslope of the time-concentration curve for troponin, which is much slower than the upslope." As result, it's easy to miss a delta.

In fact, he continues, "I have a whole collection of such cases," where the MI was missed and elevated troponin values were instead attributed to ischemic heart disease.

Finally, Dr. Jaffe says, physicians need to be sensitized to the fact that "there are many more type two MIs now. Using sex-specific cutoffs, we're finding more modest, or small, MIs, particularly in women." Some, though not all, fit into the category of myocardial infarction with nonobstructed coronary arteries, a constellation of microvascular dysfunction, some of which can be due to unseen plaque ruptures. "This is an increasing commonality that we need to be careful about."

The major lab-related issue at Mayo, says Dr. Karon, involves analytical outliers. "We have made somewhat of a hobby out of studying them," he says. Data so far show the frequency of analytical outliers is higher with the 5th Gen than with the 4th Gen.

"The issue is you're making decisions on much smaller changes in troponin concentration," he says. That could give rise to analytical outliers due to fibrin strands or activated platelets, for example, or centrifugation conditions or instrument-to-instrument/platform-to-platform differences. (Mayo has a benchtop immunoassay analyzer in the stat lab and large, automated equipment in the core lab.) "You need to worry about those more, because now we're saying a change, or at least an indeterminate delta, is 4 to 9 ng/L. So if a change is over 3 ng/L over two hours, we're saying potentially that it's significant. It's called indeterminate in our practice."

Yet he fully recognizes that this represents a very tiny change in concentration. "We're asking this assay to do more when we're using it for a panel and trending over time," Dr. Karon says. "So the two issues we've found to be more significant, and we spend more time on, is detecting our analytical outliers and looking at how our different instruments and platforms agree with each other."

Dr. Jaffe calls these fliers. "We had a little more than three percent nonrepeatables, which is high. These assays are highly sensitive. And consequently, little things can cause bigger signals than we're used to seeing."

Dr. Apple, who is familiar with Mayo's data on outliers, says instrument/platform differences can be vexing. A three-hospital system may have three different instruments, which can present different results. And yet clinicians can't be expected to know why. "It's tough to educate clinicians," Dr. Apple says, "because they don't give a rip if it's instrument A, B, or C. They just want a reliable number."

Preanalytical issues like hemolysis and biotin may present challenges when reporting results, Dr. Saenger says. If the hemolysis threshold is fairly low and/or subject to visual interpretation, then hs-cTn results might be reported as falsely low or falsely high. "This would obviously affect interpretation of a single hs-cTn result," she says, "but also could affect interpretation of serial results." Some commercially available troponin assays are sensitive to biotin interference at fairly low biotin concentrations, Dr. Karon says, "though there is not great evidence about how often patients are presenting with biotin levels that would pose a significant risk to interpretation of troponin values." As with hemolysis, he adds, biotin effects will change over time, potentially confounding interpretation of troponin panels.

The IFCC committee on clinical applications of cardiac biomarkers routinely updates several tables on its website (http://j.mp/2qKSK25) with analytical information related to all hs-cTn, contemporary, and POC troponin assays, Dr. Saenger says; one of these tables lists analytical specificity information for each troponin assay related to interference from hemolysis and biotin.

The various hs-cTn assays also have their own differences. Dr. Apple is principal investigator of the CONTRAST study, a comparison of the Roche T and Abbott I hs-cTn assays involving about 2,000 participants. "There are considerable differences between positives and negatives between the two assays," he says. "There's a subgroup of maybe 10, 15 percent of patients who don't match up at all." It's unclear why.

But one thing is clear already, he says: Switching from one assay to another "will have to be looked at very carefully if that's what you decide to do, as troponin assays are not standardized."

He's also finalizing another clinical study, called Scorecard, which involves 1,000 emergency department patients from three cohort sites—Scotland, Mayo, and Hennepin—and is looking at measurement of only baseline samples and 30-day outcomes. "We're just starting to analyze the data to see what percent of patients would be able to be safely discharged based on each assay," Dr. Apple says.

"As more people start studying troponin, we're going to see a lot more good data coming out that will solidify within 12 months in the U.S.," he predicts. "That literature will become more robust with evidence-based information."

In the meantime, Drs. Apple and Jaffe helped write an article that serves as a starting point for labs making the switch to hs-cTn (Wu AHB, et al. *Clin Chem.* 2018;64[4]:645–655). In addition, Dr. Apple urges labs to do their due diligence when deciding on an upper reference limit (URL), since they vary based on population. He sounds a cautionary note: A URL based on a data set from a package insert may or may not take into account exclusions due to, say, surrogate biomarkers, such as increased hemoglobin A1C, elevated natriuretic peptides, or statin use, which would eliminate silent pathophysiologies and lower sex-specific URLs.

Looking back over Mayo's experience, Dr. Karon suggests that time is the laboratory's best friend. "Work toward implementation well ahead of when you say you're going to bring this up," he says. "Analytical validation took a lot longer than even I expected it would." The protocols were developed over the fall of 2017, and the implementation group kicked into high gear in January/February 2018.

It also took time to get the IT right and to train the lab staff. The clinician orders a zero- and two-hour value, and the LIS calculates whether a six-hour sample (ordered reflexively) is needed. That six-hour order appears from nowhere, or so it seemed to lab staff. "It's probably one of the more complicated, and maybe the most complicated, sort of reflex lab protocol to support," says Dr. Karon. "So it does take some efforts from our phlebotomists, our laboratories to work together to do this right. It's fairly well automated now, but it can be challenging to support. There's always weird exceptions that happen—you know, how did somebody get a six-hour sample collected before their two-hour?"

"The biggest impediment we had was trying to get our IT systems to accommodate something new," Dr. Jaffe agrees.

IT issues and clinical buy-in are also influencing the pace of the rollout at Hennepin, Dr. Apple says. "It takes time to change order sets in LIS/Epic, and it takes time to meet with all the different clinical divisions to discuss how practice patterns may change based on a new assay." The assay is hardly new in Hennepin's lab. But, he says, "As much as we know about hs-cTnI, we need to gain the confidence of all the providers—clinicians, nursing, et cetera—of what the new world of a new troponin assay will entail."

Hennepin has started working on the rollout. A three-person team that includes Dr. Apple, Dr. Saenger, and Stephen Smith, MD, an emergency medicine colleague, is leading the launch. Educational discussions are being scheduled, similar to the Mayo pathway. It will require "education, sometimes a lot of education, and certainly

ongoing education," says Dr. Saenger.

"We're going to essentially put together a teaching deck based on our own experiences and the literature," Dr. Apple says. The group will meet with emergency medicine physicians, cardiologists, surgeons, and hospitalists and talk about how the assay will be implemented. Even with all the experience, it's not a matter of flipping the switch the lab's finger has been hovering over for six years. (To be fair, even Riccardo Muti occasionally glances at his Verdi score.)

The primary teaching, says Dr. Apple, is "not to be fearful that there's going to be a lot more positives."

If everything goes according to plan, Hennepin will likely roll out the new assay in the first quarter of 2020, using a zero-/two-hour algorithm, "with an additional six-hour draw for patients you're not sure about," Dr. Apple says.

A zero-/one-hour protocol was tempting, but—like Roger Maris' home run record—its use carries an asterisk. The algorithms for early presenters are particularly problematic, Dr. Apple says. "So we don't want to miss an early presenter with a potential worse sensitivity, or negative predictive value. And to be honest, it's going to be easier to draw a blood sample and not miss the time window at zero-/two-hours."

Once hs-cTnI is in place, Dr. Apple says, "We hope to be able to discharge, conservatively, 20 percent of patients based on their zero-hour and zero-/two-hour measurements—a substantial financial savings to the hospital."

Nevertheless, physicians are nervous, he acknowledges. "I think one fear factor with clinicians is they have [the] misconception that they're going to have a hundred more consults a day because of additional increases in troponin," he says. He downplays the scope while acknowledging there will indeed be at least some increase in positive findings, especially in females. Even if it's not an indication of an MI, the elevation would be important as a marker of myocardial injury with an underlying need for risk assessment. "It's a flag that's being waved," he says. Perhaps an outpatient cardiology consult is in order—a patient with a primary neurological problem, for example, and an elevated troponin is at increased risk for an adverse event. Sorting through this is going to be a learning curve for providers but significantly better for patient care, he says.

Fears about a soaring number of abnormals, especially for cardiac troponin T, has led many institutions to implement a cutoff above the 99th percentile, Dr. Saenger reports. While many clinicians think these are false-positives, she says, the hs-cTn assays actually are detecting subtle but relevant changes. "It just takes some time for them to feel comfortable interpreting these changes and determining appropriate treatment." That being said, however, it can be difficult to identify a relevant serial change for troponin, given that each assay is different and serial changes can vary due to timing of collection protocols, early versus late patient presentation to the ED, and comorbidities, Dr. Saenger notes.

Has Dr. Apple faced pushback, even despite his years of advocacy at Hennepin? "Let's say I have 10 cardiologists in a room," he says. "There's always going to be one or two who fight it." Indeed, there are still cardiologists carrying the Lost Cause banner for CK-MB, he says. In the case of hs-cTn, however, he expects reluctance to fade in a matter of weeks once it's implemented. "It's awesome," he reiterates. There may be more questions about what to do with results, but he doesn't expect people to push back against having those results. "I think clinicians will grow to like it," he predicts. "And there will be less worry once it's in place six months to a year."

The ED is excited, Dr. Apple says. So are cardiologists who understand the field of troponin. The ones who haven't paid attention, he says, who dismiss the need for biomarkers and cling to the older version, are less thrilled.

It sounds as if he barely cares. "I embrace it," Dr. Apple says. "It's the next step in better patient care."

Dr. Apple takes it one step further, in fact. "I'm hoping manufacturers will stop producing those old assays," he says. Alluding to an old *Seinfeld* episode, he compares conventional and hs-cTn assays to cinnamon and chocolate babkas, respectively. "There are people out there who love cinnamon," he acknowledges. But compared with the chocolate versions, "It is an inferior babka."

Karen Titus is CAP TODAY contributing editor and co-managing editor.

High-sensitivity cardiac troponin in the outpatient setting

November 2019—At least for now, Mayo Clinic does not offer the panel in the outpatient setting. While there is evidence that anything above the upper reference limit, or even a rising level within the URL, on an outpatient implies greater risk, “there’s not a lot of information on what you do about it,” says Dr. Karon.

Might there be a role for individual test orders? The data to support such use is strong, Dr. Jaffe says, and single orders will likely grow. Nevertheless, next steps are unclear. “Some clinicians are reluctant to go there, because they say, ‘I don’t know what to do.’ Others say, ‘If a person has an elevated troponin, I ought to know about it.’” Perhaps that information can be useful if the patient goes to the ED, goes the thinking, or can be integrated into the patient history/physical exam to help prevent disease.

As for himself, “I use it very commonly in patients with atrial fibrillation,” Dr. Jaffe says. “I think eventually we’ll be using this a lot in the outpatient setting.”

Dr. Saenger points to cardio-oncology data on the use of high-sensitivity cardiac troponins to evaluate cardiotoxicity from chemotherapeutic agents. She also foresees a time in the (much more standardized, much more harmonized) future when hs-cTn could be used over long periods of time to monitor health, similar to glucose/HbA1c, creatinine/eGFR, or lipid testing, for example.

One of the biggest discussions going on today, says Dr. Apple, is in noncardiac surgery: Should baseline and post-op troponins be measured? “There’s a great wealth of data showing that patients are at risk—even without an MI—when they have post-op elevations,” he says. The big question, of course, is medicine’s evergreen query: What do you then do with these patients? “Because not every pathophysiology has a treatment mode.” There is, Dr. Apple says cheerfully, “only one way we’re going to learn—we kind of live it.”*—Karen Titus*