Defining a disease is a process whereby physicians and clinical scientists are able to place a label on a specific pathologic entity. If this label is used carefully, it will characterize that disease process to facilitate future interactions between the patient and the healthcare system. Labeling a patient with a specific diagnosis has important implications for that person with respect to his or her relationship to the rest of society. For example, when a patient is labeled as having suffered a myocardial infarction, that individual’s ability to hold or perform certain jobs (e.g., airline pilot) is altered. He or she may also become eligible to participate in a variety of clinical experiments aimed at improving either the diagnosis or the treatment of patients with myocardial infarction. Unfortunately, clinicians and clinical investigators often define the same disease differently. Furthermore, different clinicians may use different definitions of myocardial infarction. For example, characteristics used to define myocardial infarction in one city or country may be interpreted differently by physicians in another city or country, thereby rendering comparisons between cities or countries difficult if not impossible. In a similar fashion, the definition of myocardial infarction in one international study may differ from that used in another clinical trial. This makes it very difficult to compare the results of different pharmacologic, interventional, and epidemiologic studies of patients with putative myocardial infarction.

Attempts in the past to arrive at a standardized definition of myocardial infarction have failed, often because of evolving diagnostic technologies and complexity or ambiguity in the suggested definition. In an attempt to alleviate some of the confusion and arrive at an internationally acceptable definition of myocardial infarction, the American College of Cardiology and the European Society of Cardiology recently completed a consensus process in 2000 that sought to define myocardial infarction in a universally acceptable manner. The consensus process produced a document that was simultaneously published in the European Heart Journal and the Journal of the American College of Cardiology (1, 2) and reprinted in Clinical Chemistry. In that report, myocardial infarction was defined from several different perspectives, including clinical, pathologic, electrocardiographic, biochemical, and epidemiologic aspects.

The document stressed the importance of connecting the definition of myocardial infarction with several qualifying prognostic factors surrounding the index infarct in question. Such qualifications referred to the size of the infarct; the amount of surviving, functional left ventricular myocardium; the circumstances under which the infarct occurred, e.g., during percutaneous transluminal coronary angioplasty/stent placement or spontaneously; and the timing of the episode of myocardial necrosis in question in relation to the time of observation, i.e., whether the infarct was new or old. Each of these factors involved important prognostic implications. It was concluded that it would usually be insufficient for the clinician merely to ascertain the volume of myocardium undergoing necrosis during the period of observation.

The newly revised definition of myocardial infarction required specific clinical and/or electrocardiographic findings to be coupled with increased blood concentrations of myocardial troponin (released into the circulation after myocardial cell death). Troponin (I or T) is the favored biomarker for myocardial necrosis because it is both highly sensitive and specific (1–3). Furthermore, the document confirmed that a normal electrocardiogram (ECG) does not rule out myocardial infarction because the new, sensitive biomarkers detect very small amounts of myocardial necrosis in a range where ECG abnormalities may not develop.

The new definition had several implications for the epidemiology and social consequences of myocardial infarction. Thus, the use of new, sensitive biomarkers of myocardial necrosis led to an increase (as much as 20%–30%) in the incidence and prevalence of myocardial infarction, potentially creating consternation for students of epidemiology. Indeed, it will undoubtedly be difficult to compare current and future public health statistics dealing with troponin-defined myocardial infarction with data from earlier eras. Therefore, it is essential that many clinical centers continue to measure both the new biomarkers and traditional enzymes and continue to apply older definitions of myocardial infarction to ascertain the magnitude of change engendered by use of the new biomarkers. In the social sphere, public health statistics, insurance calculations, disability applications, airline pilot licenses, and many other areas will be affected by the changing demographics of myocardial infarction entailed in the new definition.

In the consensus document of 2000, myocardial infarction would be diagnosed if an appropriately timed blood sample contained a troponin concentration that exceeded that at the 99th percentile of a reference population or contained a troponin concentration that exceeded the concentration at which the assay achieved a 10% CV if that concentration was higher than the concentration at the 99th percentile. The consensus document specified that the interval between successive troponin samples should be 6 h.

In this issue of Clinical Chemistry, MacRae et al. (4) determined that an interval as short as 3 h between troponin samples yielded the same accuracy in defining an acute myocardial infarction as the 6-h samples used previously. However, this conclusion applied only when the reference sample was taken at least 6 h after the onset of symptoms of myocardial infarction (4). Sample intervals <3 h yielded less accurate information. Given these findings, it should now be possible for clinicians to confirm the diagnosis of myocardial infarction earlier than had been considered possible in the past.
tant caveat from the data of MacRae et al. is that the time from symptom onset to collection of blood for troponin measurements must be 6 h for the sample to be valid for accurate diagnosis of acute myocardial infarction. A weakness in this approach is the subjectivity of patient recollection concerning the onset of symptoms.

The results of the data presented by MacRae et al. (4) will be of considerable interest to clinicians seeking urgent or emergent revascularization of ischemic myocardium. The results of their trial could enable clinicians to identify an acute myocardial infarction earlier than had been thought to be the case in the past (4). Clinical scientists will also be interested in this report. In the future, experimental interventions might be initiated earlier because myocardial infarction can now be identified at an earlier point than was the case before the publication of MacRae et al. Looking back over the last 10–15 years, there has been a remarkable increase in the accuracy, efficiency, and speed in the diagnosis of acute myocardial infarction. clinicians and clinical scientists can look forward to further refinements in the field of biomarker identification of myocardial necrosis.

References

Joseph S. Alpert
University of Arizona Health Science Center
1501 North Campbell Avenue
Tucson, AZ 85724-5035
E-mail jalpert@email.arizona.edu

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