into a diagnostic classification which is comprehensive. They do not cover early and other fatal cases, and nonfatal cases in which tests are partial, delayed, missing or curtailed. Therefore, they are not applicable to more than a proportion of coronary events in the real world. New criteria need to be field tested and related either to the current, or a modified version, of the International Statistical Classification of Diseases and Health Problems (11) before they are adopted, or there will be diagnostic confusion and chaos in hospital and regional morbidity statistics. Comparative figures could reflect the frequency and intensity of troponin measurement, rather than the underlying disease burden.

None of this denies the immense value of the newer biochemical markers such as troponins (12) in increasing the sensitivity and specificity of diagnosis of coronary events; nor the consequent need for older definitions and classifications to be revised for the modern era, and for the purposes specified by the college presidents in their accompanying editorial (1). The WHO MONICA Project criteria were drafted 20 years ago (3) with strong transatlantic collaboration to marry older European qualitative criteria (4), for classifying myocardial infarction and coronary deaths, with American precision. These criteria mapped trends in coronary disease incidence and case fatality across four continents for over a decade, in a third of a million cases (9). It is time they were updated by those with expertise in the field. The names of epidemiologists involved in this recent “consensus” exercise have been used, while they themselves have been kept at arm’s length. Diagnosis means more than these recent “consensus” exercise have been used, while they themselves have been kept at arm’s length. Diagnosis means more than recruitment to clinical trials. We are discussing among ourselves how to carry the need for revised criteria forward from this brave but flawed attempt. We hope to have the help of national and international organizations.

**Hugh Tunstall-Pedoe, FESC**
Cardiovascular Epidemiology Unit
Ninewells Hospital and Medical School
University of Dundee
DD1 9SY Dundee, Scotland
E-mail: h.tunstallpedoe@dundee.ac.uk

PII S0735-1097(01)01154-8

**REFERENCES**


**REPLY**

We would like to thank Dr. Tunstall-Pedoe for his comments. Controversy is the soul of all intellectual activities, and we welcome Dr. Tunstall-Pedoe’s minority opinion concerning the recently published consensus statement on the definition of myocardial infarction. Unfortunately, Dr. Tunstall-Pedoe has seriously misunderstood and misinterpreted both the nature of the European Society of Cardiology/American College of Cardiology (ESC/ACC) conference and the published document.

Dr. Tunstall-Pedoe was invited to participate in the meeting to provide context for our discussions given his many years of involvement with the original and subsequent modified World Health Organization (WHO) definitions of myocardial infarction. The conference was conceived as a joint project of the ESC and the ACC with the hope that it would help to standardize the definition of myocardial infarction in clinical studies, patient care and health care statistics.

**Procedure followed.** The original participants at the first meeting at the European Heart House created a first draft of the document. Because of the large number of individuals involved (50) at this first conference, a smaller number (6) were selected for further work on the manuscript and its eventual report. It was never our expectation that everyone in the medical community nor even everyone at the original conference would be in total agreement with the final report. We sought, therefore, to create a document that would be accepted by most clinicians, investigators and epidemiologists.

A first draft was sent to all participants, including Dr. Tunstall-Pedoe. Anyone who responded to the first draft was sent subsequent drafts. Indeed, anyone who requested the then current draft of the document received it by e-mail. The report went through 13 versions before the document was published. Dr. Tunstall-Pedoe did not respond to the first draft that contained approximately 70% of the material that was eventually published. Three other recognized and widely published epidemiologists received all subsequent drafts of the document and all their suggestions were incorporated into the published report. The final manuscript was read and critiqued by the Scientific and Clinical Initiative Committee of the ESC, the Board of the ESC, selected leaders of the ACC and selected reviewers.

Dr. Tunstall-Pedoe suggests that we should have sought input from interest groups involved with rehabilitation, health promo-
tion (whatever this refers to), employment and insurance. Indeed, such individuals were invited to the conference as well as individuals representing government, industry, and even the WHO. Many of these groups responded and had input into the final document.

Content of the revised definition of myocardial infarction. Dr. Tunstall-Pedoe misinterprets the final document. In the report, the definition of myocardial infarction rests on elevated blood troponin or CK-MB levels in an appropriate clinical setting. Patients who arrive at the hospital 24 or 48 h after the onset of their infarct will still have an elevated troponin level that remains abnormal for 3 to 14 days following the onset of myocardial necrosis. Therefore, such late-arriving patients as described by Dr. Tunstall-Pedoe will meet the new definition of myocardial infarction. Patients with infarction who are first seen many days, weeks or months after their infarction can still meet the diagnosis for “established infarction” as noted in the published ESC/ACC document.

The patient who dies shortly after arriving in the coronary care unit represents a problem for diagnosis of myocardial infarction. This is true today and will remain true in the future. As pointed out by the pathology group in the published ESC/ACC document, infarction cannot be recognized pathologically until at least 6 h has passed since the onset of ischemia/infarction. Thus, there is currently a window of “blindness” for the diagnosis of infarction that lasts for approximately 6 h after the onset of myocardial necrosis. Abnormal CK-MB levels may be seen as early as 3 to 4 h after the onset of necrosis and abnormal blood myoglobin levels may be observed even earlier. Perhaps, subsequent revised editions of the ESC/ACC report will contain suggestions about diagnosis of infarction in the early few hours after the onset of myocardial necrosis. Further data will be needed before any such suggestion can be made. In addition, patients with unequivocal ECG evidence (pathologic Q-waves) for infarction but no serological assays can still be labeled as having had an infarct based on the criteria for “established infarction.”

Even though the enzyme assays are not standardized in the original WHO and derived MONICA criteria, Dr. Tunstall-Pedoe vigorously defends the MONICA definition for the diagnosis of myocardial infarction (1). This is understandable, but may be ill-advised given the recent report of Porela et al. (2) that failed to document prognostic significance associated with this method for diagnosing infarction. Indeed, Dr. Tunstall-Pedoe states that the MONICA investigators have been seriously considering revising their own definition of myocardial infarction. This is commendable given the recently published data cited above.

We welcome Dr. Tunstall-Pedoe’s suggestion that the new definition be “field tested,” and indeed, a number of investigators are already proceeding with such studies. As noted already, the data of Porela et al. (2) support the concept of myocardial infarction defined by means of abnormal blood levels of myocardial enzyme, CK-MB. These same investigators failed to find similar supportive data for the MONICA definition of infarction. We anxiously await the results of further “field testing.”

The unfortunate fact is that the “new” definition of myocardial infarction was already being widely used before our meeting in Nice, France, took place. Indeed, many hospitals and many clinicians around the world already define myocardial infarction based on an abnormal blood troponin value. It was this fact, and the resulting confusion created between hospitals and physicians who used the new sensitive and specific cardiac markers versus those who did not, that led us to organize the ESC/ACC consensus conference. Thus, the “confusion and chaos” referred to by Dr. Tunstall-Pedoe were already present when we began sending out invitations to the meeting at the European Heart House.

In conclusion, we believe that the process as well as the product that led to the ESC/ACC new definition for myocardial infarction were both fair, reasonable and represented the opinion of most of the participants at the ESC/ACC conference as well as a variety of experts who subsequently examined the manuscript and made useful comments. We look forward to further work in this area that will undoubtedly result in revisions to the currently recommended definition for myocardial infarction.

Benefit of Aspirin Plus Angiotensin-Converting Enzyme Inhibitor

The conclusions of your recent editorial commentary (1) on a meta-analysis (2) of the trials of angiotensin-converting enzyme (ACE) inhibitors in acute myocardial infarction (MI) go far beyond the randomized evidence and could well be mistaken. As treatments for acute MI, aspirin substantially improves survival (3) and ACE inhibitors moderately improve survival (2,4). The trials of aspirin were done at a time when ACE inhibitors were not routinely used in acute MI, and demonstrated the substantial effectiveness of aspirin. The trials of ACE inhibitors were done more recently, at a time when aspirin was already widely used in acute MI, and the meta-analysis of their results showed that the addition of ACE inhibitors produced a small but significant additional benefit: that is, that aspirin + ACE inhibitors produce slightly better survival than aspirin alone (2). It was concluded that aspirin is of value in the treatment of acute MI, and that the combination of aspirin + ACE inhibitors is slightly but significantly better than aspirin alone. A similar conclusion was suggested by meta-analyses of the trials of long-term aspirin therapy (3) and of the trials of long-term ACE inhibitor therapy (5); aspirin is of value, but the combination of aspirin + ACE inhibitors is somewhat better than aspirin alone.

In the trials of ACE inhibitors both during and after MI, there was no significant interaction between the presence of aspirin and the efficacy of ACE inhibitors (2,5), and it was a bizarre non-

References