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### Reference

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### Published rather than Proposed Definitions for Invasive Fungal Infection Must Be Applied to Allow Standardization in Clinical Trials

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SIR—In 1997, the European Organization for Research and Treatment of Cancer Invasive Fungal Infections Cooperative Group and the National Institute of Allergy and Infectious Diseases Mycoses Study Group (EORTC/MSG) created a task force to examine the definitions for invasive fungal infection (IFI) used in the medical literature [1, 2]. This task force identified considerable inconsistency in defining IFI in patients with cancer and in recipients of haematopoietic stem cell transplants (SCTs) and highlighted a need for standard definitions for use in clinical and epidemiological research [1].

The EORTC/MSG task force prepared draft guidelines for standard definitions of IFI that were subsequently revised and published in 2002 [3]. These standard definitions classify IFI as proven, probable, or possible on the basis of the level of certainty of diagnosis. The classification depends on 3 elements: host factors, clinical features, and microbiological results.

It is of note that draft definitions are still available on internet Web sites [4] and vary from the final published definitions [3]. Draft definitions included the microbiological criterion “pulmonary abnor-

malty and negative bacterial cultures of any possible bacteria from any specimen relating to the lower respiratory tract including blood, sputum, broncho-alveolar lavage (BAL)” [4]. However, this was omitted from the final published consensus definitions [3].

In 3 Scottish centers, from December 2000 through December 2001, adult haemato-oncology patients receiving intensive chemotherapy or SCT had clinical, radiological, and microbiological data prospectively recorded from hospital admission until neutrophil recovery or, for allogeneic SCT recipients, until day 100 after receipt of transplant (or beyond, if graft-versus-host disease developed). Evidence of IFI was retrospectively determined using both the draft and published EORTC/MSG definitions. Data were obtained from 136 patients (204 treatment episodes). According to the EORTC/MSG draft definitions [4], 21 episodes had evidence of IFI; there were 2 proven cases, 8 probable cases, and 11 possible cases. According to the published EORTC/MSG definitions [3], the same 21 episodes had evidence of IFI; however, these were now classified as 2 proven cases, 6 probable cases, and 13 possible cases. The removal of the microbiological criterion resulted in 2 probable episodes of IFI being reclassified as possible episodes of IFI.

The draft guidelines allowed any patient with a host factor (such as prolonged neutropenia) and 2 minor clinical features (such as lower respiratory tract [LRT] symptoms and any pulmonary infiltrate) to be classified as having probable IFI if cultures of blood, sputum, or BAL fluid samples were negative for bacterial infection. Because fever is often the first clinical sign to manifest itself, many patients are already receiving broad-spectrum antibiotic therapy before LRT symptoms and radiological features develop; therefore, bacteriological culture results are frequently negative. In our opinion, the removal of this microbiological criterion is appropriate.

EORTC/MSG definitions were designed

to standardize the diagnosis of IFI in clinical and epidemiological research; however, draft guidelines are still available on Web sites, and although in our study this did not impact on the total number of cases of IFI, it affected the proportions defined as proven, probable, and possible cases of IFI. To ensure that the consensus guidelines achieve their aim of standardizing definitions of IFI for use in clinical and epidemiological research, clinical investigators and those responsible for internet Web sites must ensure that they are using the published 2002 definitions.

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