Because of the requirement for at least two sets of positive blood cultures, the sensitivity of the microbiology definition potentially could be limited if the practice of obtaining only one set of blood cultures was common among patients with bloodstream infections. Of the five patients with bloodstream infections by the NNIS criteria classified as contaminants using the microbiology definition, however, only one did not have at least one additional set of blood cultures drawn within 5 days of the positive isolate, suggesting that the practice of obtaining only a single set of blood cultures among these patients is uncommon and does not substantially affect the performance of the microbiology definition among adult patients.

Variation in application of NNIS criteria may have accounted for some of the discrepancies between our microbiology method and our gold standard review. The importance of inter-observer and intra-observer variability in applying NNIS criteria has begun to be assessed only recently. A CDC study found that specially trained reviewers frequently disagreed with hospitals' original classifications, noting both apparent false positives and false negatives.[9] Subsequent adjudication attributed substantial numbers of the discrepancies to each phase of the review. The methods used in that study differed sufficiently from ours to preclude direct comparison; however, we also noted variation between initial reviews performed by hospital-based practitioners and the reviews performed by a second blinded reviewer (observed agreement rate of 86% and kappa statistic of 0.56 among 65 isolates from adults). We believe these discrepancies are the result of variability in documentation and interpretation of the clinical information described above.

A larger percentage of discrepant results was noted among common skin-contaminant isolates involving single positive blood cultures obtained from pediatric patients with clinical evidence of infection and an intravascular device. Among instances involving a single positive blood culture and presence of an intravascular device, pediatric patients were more likely than adult patients to have "appropriate" antibiotics initiated and therefore to be classified as having bloodstream infections by the NNIS definition. It is unclear from this observation whether the underlying pathophysiology of children is different, or, as we believe more likely, the standard of practice among pediatricians is different. Based on these results, the microbiology definition does not appear to be useful for evaluation of pediatric bloodstream infections.

The use of a definition dependent on microbiology data alone provides resource-efficient surveillance information that is less susceptible to variability in classification than traditional definitions. Reliance on relatively objective criteria should allow for more meaningful comparison of bacteremia rates over time and between hospitals.

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Genetic Code of *Mycobacterium tuberculosis*

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The genetic code of *Mycobacterium tuberculosis,* as reported by an international team of scientists in the June 11 issue of *Nature,* has more than 4,000 genes with 4,411,529 base pairs. This makes the *M tuberculosis* genome the second-largest bacterial genome ever identified, behind that of *Escherichia coli.* The research team, composed of scientists from the United Kingdom, France, Denmark, and the United States, sequenced the genome of the H37Rv strain of the tuberculosis bacterium, a commonly studied variety that is not highly infectious.

Among the new discoveries they revealed about the centuries-old bacterium is that its genome contains a large number of repeating sequences of base pairs that apparently code for proteins that make up the outer coat of *M tuberculosis.* The result seems to be a regularly changing protein coat that makes the bacterium capable of dodging attacks by the immune system.

Experts hope that with the genome sequenced, the pace of new drug and vaccine development will accelerate.

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