these three points. First, in the EPaNIC trial, early parenteral nutrition failed to improve the outcome in the preplanned subgroup of 863 patients with a very high nutritional risk.³ Second, the assumption that more severely ill patients would benefit from early enhanced feeding was proven wrong; when subgroups were defined according to severity of illness on admission, it was clear that early parenteral nutrition caused the most harm in the most severely ill subgroup, whereas the intervention did not alter the outcome in the least severely ill patients.³ In addition, the administration of early parenteral nutrition aggravated rather than reduced muscle weakness in the sickest patients requiring prolonged intensive care.⁴ Third, a retrospective analysis showed that it was the dose of amino acids, not the amount of glucose, that explained the harm evoked by early parenteral nutrition, an observation that is completely in line with the results from a study of experimentally induced critical illness in rabbits.^{3,5}

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Since publication of their article, the authors report no further potential conflict of interest.

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Global Biomedical R&D Expenditures

TO THE EDITOR: In their Perspective article, Chakma et al. (Jan. 2 issue)¹ report estimates for global trends in expenditures on health research and development (R&D). Their analysis is questionable. First, expenditure data should be deflated in the national currency and then compared with the use of an appropriate exchange rate for one base year. The authors' approach overestimates growth in countries with relative currency appreciation. Second, the standard approach is to deflate expenditure data with the use of the implicit gross domestic product (GDP) price index, not the National Institutes of Health R&D price index, which flatters countries with high inflation. Third, it is better to compare R&D expenditures with the use of GDP purchasing power parities (PPPs) than with current exchange rates, which underestimate the contribution of countries in which exchange rates overstate the cost of domestic activities and thus of R&D.

When we recalculate the data using 2012 PPP exchange rates and 2012 GDP prices, China (up \$8.7 billion between 2007 and 2012) shows the largest increase in R&D expenditures, in-

stead of Japan (up \$2.8 billion). India (up \$1.6 billion) and South Korea (up \$4.3 billion) show larger increases than originally estimated; Australia's increase is smaller (up \$0.4 billion). The decline in the United States is not so marked (down \$4.0 billion).

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THE AUTHORS REPLY: We disagree with the un referenced assertion that the approaches suggested by Young et al. are “standard” or “better.” Most important, their suggestion to use the implicit GDP price index is problematic because it reflects economy-wide inflation, not biomedical R&D inflation, which diverges significantly from GDP.^{1,2} In particular, Young et al. are incorrect to conclude that there has been a “not so marked” U.S. decline on the basis of economy-wide inflation, when U.S. biomedical R&D inflation is known.^{3,4} Similarly, their suggestion to use GDP PPP is flawed, because costs of domestic biomedical R&D activities and corresponding PPP are unknown. Decade-long analyses of R&D-specific prices show that “at the industry level, use of GDP PPP as a proxy for R&D PPP is inappropriate.”⁵ Finally, we do agree that currency appreciation may overstate domestic growth, but on this point, our approach and their approach do not produce meaningfully dissimilar results. Adjusting historical nominal R&D expenditures at an exchange rate from a single time point shows similar annual growth rates, except for those in Japan and India. Our analysis supporting the relative and absolute decline of U.S. spending remains valid.

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Emphysematous Aortitis after Endovascular Graft

TO THE EDITOR: Huang and Wu (Jan. 9 issue)¹ report a case of death after endovascular aortic repair of a thoracic aortic aneurysm. I was surprised that the authors did not consider the diagnosis of aorto esophageal fistula, a rare but well-known and well-described complication of this surgery.²⁻⁵ Persistent mechanical pressure from the enlarged aneurysm sac causes an erosive communication with the adjacent esophagus, leading to sac infection and hematemesi s. The described findings of endoleak (persistent pressurization of the aneurysm sac), fever, air in the aneurysm adjacent to the esophagus, and death due to massive hematemesi s strongly suggest a diagnosis of aorto esophageal fistula rather than poor oral hygiene, as was presumed.

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THE AUTHORS REPLY: Johnston points out that our diagnosis should have been aorto esophageal fistula. We agree that aorto esophageal fistula may have been the cause of massive hematemesi s.