The result of both trials (*1*, *2*) was identical in that neither study demonstrated a statistically significant difference between treated and untreated patients (*2*) or baseline versus treatment (*1*) with respect to the clinical and magnetic resonance imaging (MRI) parameters.

It is correct that the NIH trial was not placebo-controlled or blinded; however, an analysis of the adequacy of blinding was not performed for the Kappos *et al.* study (*2*), and 8/8 patients in the NIH trial had substantial skin reactions at the injection site, i.e., induration, pain, and/or reddening, rendering effective blinding unlikely.

Conlon and Steinman refer to the three patients that worsened in our trial. They doubt the diagnosis of MS for patient MS601, yet we are unaware of data that would question the diagnosis of MS in this patient. Furthermore, this patient did not suffer from an inflammatory demyelinating neuropathy, but from a clinically silent hereditary neuropathy.

Patient MS503 showed a disappearance of MBP (83-99)–specific T cells after APL administration, and we therefore stated (*1*) that the MS exacerbation in this patient cannot be linked to APL therapy, even though the lesions of this patient were very different from all her previous lesions. Furthermore, the disappearance of MBP (83-99)–specific T cells does not prove that the drug had no relation to her atypical MS exacerbation.

Patient MS502 had an average baseline MRI activity of 13.5 contrast-enhancing lesions per month (median = 12). During APL administration, the average number was 55.5. During over 100 consecutive monthly MRI scans at the NIH, the second highest peak outside the APL treatment phase was 26 lesions, compared with the peak of 91 lesions during APL treatment. This is well above 3 standard deviations of the average. In addition, we have documented that the number of both APL- and MBP (83-99)–specific T cells increased more than a thousandfold, that most of these T cells had a proinflammatory phenotype, that most of them cross-reacted with both peptides, and that the increase in frequency was observed in the peripheral blood and the cerebrospinal fluid.

Conlon and Steinman mention that this patient had a total clearance of lesions, "making it difficult to blame the peptide for the patient's worsening." However, this "clearance of lesions" was observed after the second exacerbation of this patient and after 10 days of high-dose intravenous steroids followed by an oral taper, as shown in fig. 1c of our article (*1*). Both episodes of "clearance of lesions" are obviously attributable to steroid therapy and not APL treatment as they suggest.

With respect to the Kappos *et al.* trial (*2*), Conlon and Steinman fail to mention that one of the patients presented with three MS exacerbations in ≤4 months. This is equal to a yearly exacerbation rate of about 12 exacerbations, roughly 12 to 20 times the average exacerbation rate in relapsing-remitting MS. Therefore, it is not correct to state that exacerbations due to APL therapy were not observed in that trial (*2*). In addition, Kappos *et al.* did not study by immunological measures whether these exacerbations were related to APL therapy.

Conlon and Steinman mention that there was evidence for a desirable Th2 shift in the multicenter trial of the APL. This notion is based on ELISA measurements of interferon-gamma and IL-5 in primary cultures of peripheral blood cells in 7 of 144 patients [4.9%; only four are shown in (*2*)].

In summary, our data do not show clinical efficacy or lack thereof; however, they indicate that the treatment of MS patients with this particular APL is not safe at the dose that we administered. The fact that about 10% of the patients in the multicenter trial and the NIH trial showed signs or symptoms of generalized hypersensitivity—and this observation was made at all doses—underscores that this APL is not safe, probably not even at the lowest tested dose. The data and safety monitoring boards of both trials were concerned enough by these observations to terminate both clinical studies. We have discussed in detail the potential causes of the side effects upon APL treatment (*3*). Conlon and Steinman are correct that some of the immunological findings suggest that the potential efficacy of APL in autoimmune diseases should be pursued further. How this should be done and which APL should be used are not clear in the moment.

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Reassessing Research Assessment in the UK

JONATHAN ADAMS'S EDITORIAL "RESEARCH Assessment in the UK" (3 May, p. 805) paints an unduly selective and congratulatory picture of the Research Assessment Exercise (RAE). There is a strong belief among academic researchers that the apparent increase in UK research performance illustrated in his graph is mostly due to "grade inflation," as academics learn how to play the RAE game and tell the assessors what they want to hear. As a consequence, the recent RAE deemed more than half of the UK's academic departments to be of "international quality" in research, a figure that is manifestly ludicrous. This is why the "funding differentials are being flattened": If too many departments get the top grade, there is insufficient money to reward them all. An unfortunate side effect is that genuinely top-grade departments can no longer be distinguished from those of lower rank, so the truly top departments cannot be rewarded either. In short, the RAE has comprehensively destroyed the rationale for its own existence.

It is possible that the RAE has helped to improve the UK's research in some respects. It has certainly helped to increase the salaries of some researchers, by creating a "transfer fee" mentality in which academics who are likely to score well on the RAE are paid higher salaries to entice them to other institutions or to prevent them being so enticed. But Adams fails to mention the downside of this exercise, which is the amount of academic time and effort expended in preparing the required documentation. This was justifiable when the exercise produced tangible rewards, but it is a complete waste of time when it does not, and this is the real reason why the RAE has now pretty much run its course.

The RAE is not the only such exercise inflicted on UK academics. The worst example is the Teaching Quality Assessment (TQA), which would be better called the Document Quantity Assessment. This immense and tedious bureaucractic exercise consumes vast amounts of time and energy and achieves very little, aside from damaging academic morale, wasting time that could better be spent on actual teaching, and piling up mounds of unnecessary paperwork. The TQA is universally detested by the UK's academic community, whereas the RAE has been tolerated—until now. This tendency toward overassessment has done enormous damage to the whole of the UK's public sector, including police, teachers, nurses, doctors, and higher education. Workers in many of these areas are now leaving in droves.

I would like to think that the real reason why a system like the RAE is "a rarity internationally" is that other countries have observed the sheer stupidity of the UK's assessment procedures and vowed not to make the same mistake. Certainly, the RAE should be seen as a ghastly warning rather than as a model for other countries to follow. Unfortunately, I expect to see other countries heading down the same destructive path, seduced by the same simplistic arguments. Uncritical and selective reports like the one written by Adams will certainly encourage them to do so, and for this reason alone it is important for opposing views to be heard.

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Response

I AM SYMPATHETIC TO MUCH OF THE THRUST of Stewart's thinking, but just as he argues that there is a downside, so my Editorial argues that there is an undeniable upside to the RAE. There have been lots of articles written in the UK about what a burden the RAE has been for individuals; there have been fewer discussing what effect it has had on the system.

I think Stewart is confused about what I said in the Editorial, perhaps because the limited space meant that I necessarily left out some of the background and qualifying statements (hence his comment that it was uncritical and selective). For example, the graph showed citation impact from ISI, not average RAE grade, and was there precisely because it was not susceptible to the manipulation Stewart suggests.

I am not sure why it is "manifestly ludicrous" that half of UK academic researchers work in units that are producing a significant proportion of world-class research. How many departments has Stewart visited that would assert that this is not the case? However, I agree that this is mathematically why the differentials are flattened and that this is why the RAE has essentially outlived its original purpose.

As far as academic time and effort are concerned, it is the view of many senior research managers that a significant degree of effort should be invested in academic research management and that the marginal additional cost of the RAE is often overestimated. A review carried out by a major accountancy firm after the 1996 RAE suggested that the correct marginal cost of the exercise was about 1 to 2% of the funds disbursed. I agree that, however small the cost, it becomes a waste of time when the reward system breaks down.

Stewart is absolutely correct in his comments about other assessment and evaluation exercises in UK academia, many of which cost far more than the RAE in relation to the rewards. As far as the RAE is concerned, the evidence from surveys is that it does not deter anyone from taking part in research and that most researchers—particularly relatively new recruits—feel that some form of accountability is both necessary and desirable.

I cannot agree that the RAE path is destructive. UK research has improved, the system is more effective and efficient, and—as a consequence—UK universities have got more cash from the Treasury than might otherwise have been the case.

I have been invited to make presentations on the RAE to senior committees of research directors and academics in Copenhagen and Bonn. Despite all attempts to persuade them that this is a costly exercise to adopt and may have many unexpected impacts on the behavior of their staffs, the universal reaction is "Maybe, but look what its done to boost your research in the UK." As I said in my Editorial, the evidence seems to support their view.

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Letters to the Editor

Letters (~300 words) discuss material published in *Science* in the previous 6 months or issues of general interest. They can be submitted by e-mail (science_letters@aaas.org), the Web (www.letter2science.org), or regular mail (1200 New York Ave., NW, Washington, DC 20005, USA). Letters are not acknowledged upon receipt, nor are authors generally consulted before publication. Whether published in full or in part, letters are subject to editing for clarity and space.